Ethical Governance of Biological and Biomedical Research: Chinese-European Co-operation

TEXTBOOK

Life Sciences in Translation – A Sino-European Dialogue on Ethical Governance of the Life Sciences

Edited by Ole Döring
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Contents

Preface

Ole Döring

The 23 chapters in this collection are the outcome of three years of dialogue and research between scholars from Europe, China and other regions about the ethical governance of biological and biomedical research in Sino-European collaborations. This textbook provides insights into multifaced and fruitful discussions on this emerging, broad and difficult area of study.

The BIONET project, (Ethical Governance of Biological and Biomedical Research: Chinese-European Co-operation), was funded between 2006 and 2009 under the European Commission's 6th Framework program, as a Coordination Action, and received additional support from the United Kingdom's Medical Research Council and the Wellcome Trust. The focus was on advanced biological and biomedical research, in particular upon reproductive and regenerative medicine, clinical trials and the genomics of disease susceptibility. This area is a key national, commercial and scientific priority in both China and Europe. Such research raises many challenges and new opportunities for ethical governance of scientific and medical practice, many of which have particular relevance to ensuring best practice in EU-China scientific collaborations.

BIONET is a Consortium of 21 EU-based and Chinese partners examining the challenges facing the ethical governance of research in the life sciences and biomedicine in China and the EU (www.bionet-china.org). With the intention to build a sustainable network within and between China and Europe, BIONET has focused on three ***key areas***: (1) reproductive and regenerative medicine, (2) clinical trials and (3) biobanks and the genomics of disease susceptibility and treatability.

We made ***collaborative efforts*** to (1) map the rationales for and practices of ethical governance of advanced biological and biomedical research in and between China and Europe; (2) provide a platform for the development of comparative research on ethical governance in China and the EU; (3) advance social scientific understanding of key bioethical issues, challenges and approaches generated in contemporary biomedical research through dialogue between researchers and practitioners in China and Europe; (4) undertake training of researchers and practitioners in key issues; and (5) inform policy and practice in the ethics of biomedical research in China and the EU with particular emphasis on issues relevant for scientific collaboration.

This textbook offers some of the findings that were generated during this collaborative project. It is meant as a reference for students, researchers, practitioners and administrators, in the scientific, public, economic and political arenas. All authors and BIONET partners hope that our project will inform and inspire readers towards a refreshed understanding of the approaches to China-European collaboration in ethics and governance. This collection of chapters and materials will contribute to the BIONET's objectives of dissemination and science capacity building; and it is intended to motivate researchers to continue empirical and theoretical work in and between both regions.

This textbook draws from the BIONET's series of workshops and conferences. It is organised in three parts in order to express the pattern of material concerns addressed over the course of our interactions:

First, the topical chapters explore a number of core aspects in the areas of biobanks, genomics, and translational research, followed by investigations into the international dynamics of the field as relevant for Europe-Chinese ethical governance, and finally, by related cultural reflections.

Second, arguably the most remarkable product of the BIONET, the reports of the findings of the BIONET exchange students represent first steps into the future of cross-cultural collaborative research between our regions. BIONET was able to subsidize 7 Chinese and 4 European students with funding and personal support from the BIONET's network, to conduct fieldwork in various places and benefit from cultural encounters (http://www.bionet-china.org/student_exchange.htm). Some of these works are exemplary for the broad interdisciplinary design of embedded governance studies and illustrate both the need and feasibility of these research activities as they lay grounds for an enhanced scientific understanding of what makes ethical governance and best practice in the globalised life sciences.

Third, the final part includes a collection of key documents and resources that provide more context-relevant factual information and should encourage continued research.

First of all, this editor would like to thank all authors who contributed to this collection. Of course, I should like to thank the EC, the UK's MRC and the Wellcome Trust for providing us with financial support for different aspects of the work of the BIONET. To all colleagues who supported this project from the outside, including the participants of our workshops and conferences, who informed and engaged debate, the BIONET owes our heartfelt gratitude. 'Finally, thanks to all who believed in the underlying vision of this venture and offered their generous moral support which was much appreciated. We cannot predict the spinoff from these short three years, but some impacts on awareness, building of networks and initiatives for research and infrastructure development can already be seen.

PART 1:

MAIN TOPICS

Introduction

Ole Döring

The topic of "*biobanks*" was the focus of the fourth and last of the BIONET's workshops (URL: http://www.bionet-china.org/workshops4.htm). However, this is the most dynamic and the youngest of the emerging fields of ethical governance of the life sciences between Europe and China under the BIONET's scrutiny. Infrastructures for biomedical sciences, governance frameworks, ethical issues and awareness of the relevant social and cultural concerns are now taking shape, and there is no internationally established model to implement and follow. Therefore, discussion of "biobanks" offers fascinating opportunities to study these processes while they are being developed. Just a few months after the BIONET's final workshop in Shenzhen, in October 2009, the eminent Chinese Journal *Yixue yu zhexue* (Medicine and Philosophy, Vol. 30. no. 10, 2009) published a special issue dedicated to related topics, including several papers that had been presented at this event.

This is a unique situation, when compared with other debates in biomedical ethics. For example, the discussions on Ethical, Legal and Social Issues (ELSI) related to the Human Genome Project that have been going on since 1988 could only respond to the new scientific and institutional facts ex post, but could not anticipate the unfolding potential of the life sciences with their impact on societies. Questions around the governance of biobanking thus reflect a transitional state on a more general level; they come at a time when the related global economies are in flux, when China continues its course of transformation and the capacities of Sino-European collaboration are still contemplated on the agenda of planners and policy makers

(see URL:
http://www.co-reach.org/output/index_call2008results.cfm?CFID=322677&CFTOKEN=69692066&jsessionid=48303efb717e40536c3a and
http://www.co-reach.org/input/document/documents/734.pdf),

This situation calls for creative exploration and the structuring of largely uncharted territories.

In this sense of exploration, this chapter begins with a paper about the observed pressure to harmonize regulatory standards for biobanking. In their essay, "Should biobank regulations be harmonized?", Reinert Karlsen, Jan Helge Solbakk and Roger Strand discuss the impact of the thrust for harmonization that is driven by industrial biology and present in the current attempts to harmonize research biobank regulations, but not equipped with abilities to respond to cultural diversity of different regions. As the authors argue, the problems reside not only in the design of these attempts, but in their very objectives, arising in a general political culture that needs more contemplation in contemporary medical research ethics.

In the corresponding view from a successfully operating "biobank" in the Chinese city of Kunming, Chu Jiayou introduces an example for addressing "Informed consent"

and the Establishment of an Immortalized Cell Lin Bank of China's Different Ethnic Groups, in an internationally ambitious research environment.

The third article in this section, contributed by China expert and a pioneer in the field, Margaret Sleeboom-Faulkner, highlights "Biobanking in transnational perspective". Using examples from India, Indonesia, Japan and China, she shows how the transnational dynamics of biobanks need to be understood within the particular circumstances of issues that occur in specific locations.

"*Genomics*" is the topic of the following set of contributions. In the context of 21st century genomics research, "biobanks" are not just collections of biological samples or genetic data, but also of related medical records, health data, lifestyle information (gleaned from questionnaires) and sometimes also genealogical information (family history) for whole populations. Genomics thus has the potential to become a powerful resource in society beyond the immediate scope of research. The commercial implications of the term "bank" have become abundant with the reappraisal of many types of human tissue as a potential powerful source of knowledge, health and wealth rather than disposable "waste" owing to advances in the life sciences. However, genomics cannot be reduced to rationales of economics. It also raises issues that concern a much larger spectre of aspects of humankind. For ethical governance of genomic research, "trust" is a central theme, covering various specific areas of ethical concern, such as transparency, accountability, quality standards, communicative capabilities, oversight mechanisms and the role of medical sciences in society.

Wolfgang Hennig elaborates the connection between genomics and biobanking. In his article on "General implications of genomic research for society and governance in Sino-EU cooperations" he argues that only databanks that are coordinated internationally are going to be used in future research. So it is the core task to describe the field for further study. Hennig submits a cluster of key questions that could guide a related collaborative research program, including control and access to databases and biobanks, data protection, data quality and legitimate access.

Wang Xiaofeng and Jin Li provide an overview of a large-scale prospective study. They introduce an ambitious example from China, the "Cohort Profile: Taizhou Longitudinal Study – a prospective study of non-communicable diseases". Wang and Li explain a study design that is aimed at determining the interconnectedness of environmental, genetic and interacting factors of common non-communicable diseases. Their research intends to illustrate the roles of especially those factors concomitant with the economic transformation in China.

Finally, among the papers on different aspects of genetics and genomics, Zhang Xiaoyong elaborates on the current development of implementing benefit-sharing, as a concept originating in international law, in the governance of Chinese research. His article, "Benefit-Sharing in Human Genetic Research: International Experiences and Chinese Legal Choices" uses a case involving stake holders from China and other countries in international cooperative projects in order to argue for a comprehensive set of recommendations for the advancement of China's regulations.

In the discussion about *Translational Research*, the methodical focus on informed consent opens the narrow "from bench – to bedside" view to a socially embedded

approach, were more than just a clinic-laboratory-bedside relation is at stake. The BIONET's work made it clear that relationships and interactions within institutional and public spaces should also be assessed, that span the complex social home-clinic-laboratory-bedside relations, involving family members and friends, fertility experts, fertility counsellors, embryologists, stem cell researchers, and more. Here lies a huge and dormant field for collaborative interdisciplinary studies.

In the first of three articles that address topics surrounding the theme of Translational Research, Tu Ling, He Jing and Lu Guangxiu introduce a model for the "Practice and Evaluation of Ethical Governance in Assisted Reproductive Technologies (ART)". They describe how, in their own institution, in the southern-central Chinese city of Changsha, a governance concept is being implemented that covers the entire process, from "sourcing" and research to application in medical practice. They identify the awareness and resolve among professionals involved in ART at any stage, to observe and co-produce best practice, as the key to ethical governance. With an emphasis on the relations between doctors, researchers and other staff with their patients, in the context of informed consent, Tu, He and Lu propose mechanisms to monitor the implementation of medical ethical standards.

Then, Erica Haimes takes up a rarely discussed perspective in the ethics of hESC research, from a European view, namely that of the embryo provider, in her article, "Acquiring eggs and embryos for hESC research: Socio-Ethical Considerations". This work indicates that a more rounded understanding of the cultural and scientific, standing of hESC research comes when including tissue providers and when going beyond conventional preoccupations with the narrow moral status of embryos. Their wider social, contextually dependent views can provide biology and ethics with an understanding that appreciates variability of meanings about embryos and eggs. Later in this volume, some of the students' reports address this topic as they encounter it within Chinese institutions (Rosemann, Mitzkat, Allyse).

Then, Pei Xuetao offers a stem cell scientist's view on "Human Stem Cell Research and Ethical Regulations in China". He summarises the current scientific outlook on the therapeutic potential and ethical and scientific challenges in regenerative medicine, from bench to bedside, and in the light of China's related regulatory approach. Pei points out that ethics should match the development of science and the needs of history, thereby contributing to a constructive collaboration for the benefit of medical research. He makes it clear that it is difficult to assess the state of stem cell research in China at this point in time because of the dynamic state and rapid developments that characterise this field.

Research takes place in international and often globalised arrangements. This makes it necessary to pay attention to the diversity of regulatory standards within and between participating regions, and, even more importantly, to the cultures within which the related practices are being interpreted and implemented. This area includes issues for national and international law, systems of ethics, practical hermeneutics, social sciences and anthropology as well as scientific and business communities in their self-regulating capacities,

In the section on *International Dynamics*, Ayo Wahlberg and Thomas Streitfellner discuss "Stem cell tourism, desperation and the governing of new therapies". This

topic is related to ethical issues raised in the context of translational research, but, since national regulatory solutions cannot stop citizens from travelling to other countries to get access to treatments that are not available or allowed at home, it is also a challenge for collaborative international governance. The authors observe that global stem cell tourism is fuelled by a combination of patient desperation, hopes, regulatory uncertainty, low cost travel and the emergence of biotech industries eager to translate laboratory research into therapy and revenue. Concern arises about the vulnerability and safety of desperate patients as well as fundamental ethical values.

In a view from the pharma industry, on "Research in Humans in China: The Role of Industry in Governance and Protection of Research Participants", Detlef Niese proposes that Biobanks and Genetics offer new opportunities for pharmaceutical research. He emphasises that a solid trust basis between science and society is essential for efficient application of new research technologies. This trust depends at large on respect to the research subjects autonomy. He argues that, in different cultures and by different indivuduals, the specific risks associated with genetic information may be assessed differently. It would be vital to find sincere ways to respect those differences.

In a report from China's neighbouring country, India, R. Kishore reckognizes the potential of clinical trials to contribute to the country's national health programmes by helping discover vaccines, drugs and devices at affordable cost for mass use. In his article, "Clinical Trials: The Indian Perspectives", Kishore warns that in India – a developing country with a large market for foreign investors – the individual and the community have to be protected against undue experimentation and its consequences. He worries about a breach of distributive justice, since products that disadvantaged populations bear the burden of testing are likely to be marketed in affluent countries and be unavailable to populations of poor countries that serve as testing sites. Policy makers ought to realize that clinical research is an essential part of the country's health delivery system as it has the promise of addressing many difficult issues through the indigenisation, innovation, cost-effectiveness and optimization of resources. However, there are many international correlations and complexities that need to be taken into account.

Conceptual reflections are at the core of any dialogue about the ethical governance of the life sciences. Although the BIONET did not focus on the related philosophical and cross-cultural discussions in particular, (see the special issue of *Contemporary Chinese Thought*, Number 2 / Winter 2007-8, that is dedicated to some of the related bioethical questions) these perspectives have been present during the course of our interactions. In this section, two papers indicate the importance of such cultural reflections, between China and Europe.

First, Chinese philosopher Zhu Wei, in her article, "Does Chinese Culture Constitute Challenges to Informed Consent?", considers some doubts about the adaptability of the ethical concept of "informed consent" in China, owing to its historical origins in Europe and North America. Zhu argues that the concept, especially in its established legal form and in terms of medical practice, can be culturally challenging, especially when not only individual patients are taken into account, but also their social context. However, this point is made with reference to Europe as well. In essence, Zhu concludes, there exists no real difference between the West and China in the matter of

informed consent. There is agreement that in informed consent the highest principle is the assurance of the best interest of the patient/subject. The task is to organise ethical governance accordingly.

Second, in his essay on “Concerns and principles. Bioethics and the challenge of cross-cultural biopolitics”, Christoph Rehmann-Sutter, a philosopher from Luebeck, discusses an approach to bioethics that is grounded in principles rather than one that is grounded in concerns. As he proposes, a concerns-based bioethics could have advantages especially in a transnational public sphere. It would help to deal with the meaning of principles in practice; in a more context-sensitive manner; thereby advancing bioethics’ capabilities for dealing with the ethical governance of cross-cultural practice. Namely, the focus on concerns would put emphasis on the importance of communicative practice as an intrinsic part of the function of bioethics.

BIOBANKS

Should Biobank Regulations be Harmonized?

Jan Reinert Karlsen, Jan Helge Solbakk and Roger Strand

Introduction

This paper is based on J.R. Karlsen, J.H. Solbakk and R. Strand's, "In the ruins of Babel: Should biobank regulations be harmonized?", the last chapter in Solbakk JH, Holm S, Hofmann (Eds.), *The ethics of Research Biobanking*, a book published by Springer Verlag in August 2009. The aim is to critically assess whether – and eventually to what extent – harmonization can still be perceived as a justifiable aim in research biobanking. More specifically, what we aim at is an analogical reading of a famous narrative about harmonization, i.e. the narrative of the Tower of Babel, and through this reading draw attention to some of the unacknowledged pitfalls involved in the attempt at building a uniform regulatory language for research biobanking.

The thrive for harmonisation

The need for harmonizing existing regulatory frameworks and practices seems to be a widely shared perception among different stakeholders within the field of research biobanking (BBMRI 2007; PHOEBE 2008; ESF 2008; OECD 2008). Even among ELSA researchers in the field, "harmonization" has become a highly esteemed petword (Maschke 2005; Knoppers 2007; Fleming 2007; Chalmers 2008).

The primary aims of harmonization are to boost: (1) the technoscientific power of research biobanking, and (2) the industrial and monetary benefits of research biobanking. Additionally, spokes-men and -women of harmonization point to the increase in public health and welfare that research biobanking is assumed to entail.

The Tower of Babel

The Tower of Babel is not just an allegory about the loss of a unifying language. It is also a narrative about the negative and positive implications of such a loss. Finally, it is a narrative about the potential of *hubris* embedded in the striving for a world in which nobody falls apart, i.e. a world in which everybody is linked to each other through "one language and a common speech".

When the descendants of Noah moved eastward and settled in Shinar they were in the privileged possession of a global community speaking the same language. For this reason, says the Biblical author, they were living unified lives void of any form of confusion. A common language also functioned as a safeguard against the dispersion of lives; everyone became an inhabitant of a global city. What this part of the narrative unveils to the reader is the unifying power of common speech: it binds people together; it builds and preserves a community. When we compare this situation of harmony and unity with the language situation of research biobanking, it may seem reasonable to say that the different stakeholders here live in dispersed communities in need of a language that could bridge the gaps between them and do away unnecessary confusion. Consequently, the quest and striving for a common regulatory language also seems to be a morally and legally justifiable endeavor.

It is in view of this widely shared perception that the second part of the narrative about the Tower of Babel may contain some fruitful clues for further deliberation. That brings us first to an earlier chapter in Genesis, chapter 9, where the author gives an account of God's Covenant with Noah and his descendants:

> "Then God blessed Noah and his sons, saying to them, 'Be fruitful and increase in number and fill the earth'" (Genesis 9, 1).

This, according to the Biblical author, was their prime mission and responsibility. However, instead of pursuing these noble goals, they turned their attention elsewhere: to the building of a tower to empower and glorify themselves. At first glance this may seem to represent a completely irrelevant part of the narrative as the end result communicated is Jahve's punishment in terms of linguistic confusion. A second reading, however, may raise the critical question whether the striving for harmonization in research biobanking has taken on a role that risks turning the attention away from the primary responsibilities of research biobanking for society, including what we later in the chapter shall call the production of socially and ethically robust knowledge and technology.

The thrust for harmonization: industrial biology

Above, we introduced harmonization of biobank regulation as a language issue: the introduction of a shared set of concepts and vocabulary to ensure communication and understanding, and to avoid confusion.

In our view, there are two noteworthy features of the regulatory context of research biobanking. Both are related to the value that biobanks now take on. Somewhat simplified, we may say that they relate to the *creation* and *distribution* of value. What makes biobanks so valuable in the genomic era? In part, the answer is that they allow so-called "brute force" methodologies in which large numbers of genes or genetic activities can be correlated with large numbers of phenotypic features through multivariate analysis.

Biobanks create value in the following way: they may provide rigorous, representative medical knowledge of the population. Furthermore, their comprehensiveness also means that unique biological features will be found: The needle in the haystack, be it a variant form of a gene, enzyme or cell tissue, no longer represents an almost impossible task as it can be found by automated routine techniques.

Two conditions must be met, however, for this value to be created. First, the research needs access to extensive, well-characterized and high quality collections of human biological material and health information: Size matters (Khoury 2004). Secondly, the research is capital-intensive in the sense that the necessary technical rigor and excellence is (also) a matter of investment. But it is also *attractive* to investors because of the expectations of new powerful medical technologies.

From the research perspective, both biobanks and their utilization, as well as the regulatory solutions to facilitate their construction and utilization, is a matter of building adequate infrastructures for research activities. This is how the uniformity of language is related to the tower of Babel: In order to build the tallest tower, the workers must speak the same language, know the same methods of construction and

use the same materials. It is not a question first and foremost of understanding or confusion; it is a question of coordination and efficiency of industry.

Weaker ethics for stronger technoscience

The question *whether* biobank regulations should be harmonized, is clearly dependent on how the question '*What* is to be harmonized?' is answered. Conversely, we cannot infer from any answer to the latter question a negative answer to the former, because it is equally clear that there are many ways of regulating biobanks, some of which could be ethically and politically sound to harmonize, while others would not.

A minimum criterion for a harmonized regulatory framework, however, should be *social and ethical robustness*. Social robustness was introduced as a concept for discussing the unforeseen consequences of science and technology in their long-term contexts of *application* and *implication.* By *ethical robustness* we mean that ethical guidelines and institutions are legitimate in their own right and that this legitimacy will hold when assessed from a variety of value perceptions and social contexts, including those of affected parties outside the power centers.

Until now, the regulations adopted for research biobanking have to a considerable extent been cast in a language originally developed to address ethical challenges in clinical trials, medical research and transplantation medicine (WMA 2008). The language we have in mind is particularly the language of informed consent. Adopting informed consent in this new context has enabled policy makers and NGOs to frame the ethical challenges of research biobanking within existing ethical principles and institutions – with some modifications – *as if* the nature of these challenges is the same for research biobanking as for clinical research involving human beings (OECD 2008; NCI, NIH and HHS 2007).

Our concern in these matters is that there is an *asymmetry* between the social and ethical robustness of informed consent, and the increased techno-scientific *power* that research biobanking attains when traversing the spectrum from local biobanks (type 1), through regional biobanks (type 2), to the integration of local and regional biobanks in global research bioinfrastructures (type 3) (Table 1). If this is the case, then integrating biobanks into such infrastructures will stand at risk of boosting the techno-scientific power beyond the ethical foundation, institutional framework and control mechanisms supported by adopted regulations. A socially and ethically fragile regulation, if harmonized, will dramatically raise the stakes for persons and society, potentially short-circuiting the democratic and moral legitimacy of research biobanking.

Type of biobank	**Localization**	**Examples**	**Organizational model**
Type 1	Local	Hospital, Ph.D. project	Laboratory
Type 2	Regional, national	HUNT, Biobank for Health	Industrial sized laboratory
Type 3	International, global	BBMRI, GenomeEUtwin	Hubs, nodes

Table 1: Types of biobanks

The Biobank of Babel: should biobank regulations be harmonized?
From the above considerations, there follow two general points, regarding the regulatory harmonization of ethics with the intended function to facilitate scientific progress. First, harmonization of ethical principles and practices comes at a potential *cost*: it implies a reduction of the multitude of values and concerns represented in legal and ethical discourse. Hence, it is conceivable that harmonization results in institutions and practices that are less rather than more socially and ethically robust. Secondly, as has been argued in the preceding sections, there are some aspects of the scientific development in this field, i.e. the construction of global infrastructure carrying personal information and possibly producing vast biomedical predictive power of the individual, which by themselves indicate a risk of decreased social and ethical robustness. Let us add that all this happens within a global capitalist *Realpolitik* of the so-called knowledge-based economy in which the objectives of scientific progress and public health and welfare are inscribed in expansive and competitive innovation policies. Is it then conceivable that attempts at harmonization could have *social and ethical robustness* rather than facilitation and efficiency as their objectives?

The answer, when considering regulatory and institutional harmonization in other sectors, appears to be affirmative. An interesting example in this respect is the international nuclear inspectorate function of the IAEA, the International Atomic Energy Agency (see http://www.iaea.org). IAEA has a threefold mandate: to promote science and technology, to promote safety and security, and to promote safeguards and verification.

European political and intellectual history gives ample opportunity to corroborate the utility in differentiation of mandates and balance of powers. In the case of IAEA, it would intuitively appear dangerous if their mandate was collapsed into the one of promoting science and technology. Indeed, it is reassuring that the inspectorate function is one that identifies with, and is identified with, a globally recognized power to *slow down science* when called for in a given installation or country. The inspectorate function is not solely to facilitate efficiency; within the nuclear sector, efficiency and progress is not the only value.

In the biomedical sector, ethics was constituted as the power which could balance the intrinsic value of the scientific endeavour, laying the rights of the patient-subject into the other scalepan. This is clearly seen in the Declaration of Helsinki. In the preceding section we argued that this scalepan becomes lighter as biomedical science is lifted out of the individual laboratory and into the global infrastructures. Ethics thus risks being transformed into a means of de-differentiation. It is this phenomenon that was called "*the unpolitics of ethics*" by a European expert group (Felt and Wynne 2007).

In our view, it becomes urgent to pose the question: what is then required? From our analysis of the *function* of harmonization, we conclude that harmonization of biobank regulations also needs to address the function of promoting social and ethical robustness. Such robustness is a matter of the long-term societal consequences of science and technology, and it should not be assessed from within one value system only, such as the currently hegemonic ideologies of innovation-based capitalism and

biological reductionism, assuming that citizens will be happier in a wealthier society, and healthier when provided more services using biomedical technology. In other words, the value perception of biobanks as a great scientific, societal as well as biopolitical asset needs to be viewed in the light of other, existing value perceptions, such as the perception of biobanks as institutions of a *dangerous* kind or the perception of biobanks as instutions of a *mysterious,* yet undetermined and poorly understood, nature. While the first – and dominating – kind of perception leads one to focus on the need for resolving disagreements about the real *value* of biobanks, resolving disagreements about the *medical*, the *scientific* as well as the *commercial* and *societal* value of biobanks focuses one's attention on ways of coping with the different possible forms of danger that may arise from research biobanking, such as infraction upon privacy, forms of discrimination and secret policing. Finally, the perception of biobanks as a mysterious kind of institution frames the moral landscape in a third possible direction, i.e. into a discourse about the *institutional nature* of biobanks (What is this thing called 'biobanks'?), the *ontological* nature of a society with such institutions as well as the bioethical and legal nature of biobanks. Consequently, the question of social and ethical robustness needs to be approached by asking "what-if"-questions (Ravetz 1997) along a number of value dimensions and scales of implication of science and technology in society: What if the political situation drastically changes in the countries with access to global biobank infrastructures? What if state racism reappears in Europe? What if the current affluence in Western/Northern countries disappears? In the words of Nowotny et al., the contexts of application and implication must be continuously addressed (see Nowotny et al. 2001).

Following the European expert group (Felt and Wynne 2007), it is not apparent that this function, which really requires a supra-national, if not harmonized, approach in order to gain any force, should be delegated to the academic expertise or political institutions and practices labelled "ethics" and "ethical". It may be that "ethics" as a professionalized phenomenon is too entrenched in a certain social order to be able to deal with the questions of *goodness* of which social and ethical robustness is ultimately at stake. Let that remain an open question; in any case it appears sound to ensure methodological interdisciplinarity and transversality when dealing with such a difficult issue as social and ethical robustness. Another useful comparison in this respect, closer to biomedicine, is the political and academic debates on nanotechnology. A key concept in these debates is that of *governance* of science and the ideal of more open, transparent and inclusive decision-making and social dialogue at an early stage in research (Toumey 2006; Kearnes and Wynne 2007; Rogers-Hayden and Pidgeon 2007).

In the nanotechnology sector, 2008 saw the first comprehensive governmental attempt at harmonization for the sake of social and ethical robustness: The Code of conduct for responsible nanosciences and nanotechnologies research, published in February 2008 as a recommendation from the European Commission to its member states (EC 2008). Among its principles, it states that nano-researchers do not only have duties in terms of achieving scientific excellence, and innovation, but also sustainability, ethics, precaution, and – more innovatively – towards *inclusiveness* and *meaning*:

> "N&N research activities should be comprehensible to the public. They should respect fundamental rights and be conducted in the interest of the well-being

> of individuals and society in their design, implementation, dissemination and use" (EC 2008, principle 4.1).

The recommendations are an instance of "soft law", giving the member states the choice of how to implement them. Of course, the method and impact of implementation are far from obvious; rather, the recommendations may be seen as an opportunity for the creative design of novel instruments of governance. Again, we see how the value of efficiency and internally measured progress is intended to be balanced by other values.

Conclusion: back to Babel

We have tried to show what we hold to be important problems in current attempts to harmonize research biobank regulations. Indeed, the problems appear to reside not only in the design of these attempts, but in their very objectives, arising in a general political culture that needs more contemplation in contemporary medical research ethics.

We have contrasted these developments with examples from two other sectors: the nuclear inspectorate function of IAEA and the recently published European Code of conduct for nanoscience and –technology. We believe that ethicists should articulate, delineate and clarify underlying controversies and conflicts between the values at stake in the issue, rather than always trying to give them an operationalizable resolution, which typically assumes more or less invisible but substantive political assumptions. Let us therefore return to the tale of the tower of Babel.

No tree grows into Heaven. Culture, civilization, science and technology can be seen as attempts at getting further than we may achieve through mere co-existence with Nature. In this sense, humans do build towers to reach further. In what resided Jahve's discontent? We cannot know. We can note, however, the apparent surprise when He faces the fact that it is *this* they do – they build the one tower, they do not spread out into the country, all stakes are put into the one *monolith*, literally: "Behold, the people is one, and they all have one language, *and this they begin to do*" (Genesis 11, 6).

The words of Jahve do not carry legitimate weight in contemporary bioethics and biopolitics. At least not *these* words. We did not introduce the tale of Babel in order to draw upon its possible legitimacy. Rather than legitimacy, we have been interested in the reflection it inspires, believing that the value of reflection, hesitation and broad dialogue is what needs to be incorporated in the discourse on harmonization of biobank regulation. We hold that this is vital also for ethics. Stephen Toulmin once explained how medicine once saved the life of ethics. (Toulmin 1986). It now seems due that the patient emancipates himself from his doctor; be it for his health or his natural death, lending space for other institutions and practices for the socially and ethically robust governance of biomedicine.

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“Informed Consent” and the Establishment of an Immortalized Cell Line Bank of China’s Different Ethnic Groups

Chu Jiayou

There are 56 ethnic groups in China, each inhabiting different areas. Some of them are genetically isolated populations. In the biological sources from ethnic groups and genetic phenotypes, we find that each ethnic group has its own unique characteristics. For example, there are significant differences in enzyme systems, HLA antigens and incidences of some genetic diseases.

At present, as more and more youths marry across different ethnic groups, the genomes of some ethnic groups are in danger of extinction. Therefore, the preservation of different ethnic group’s genomic material and data becomes an urgent project.

Based on the principle of “informed consent”, and after consulting with national scholars, blood samples of healthy individuals, with no common relatives and belonging to different populations were collected at the ethnic groups’ living areas, and 3 generations are investigated. This arrangement can guarantee the representativeness of samples.

For people from minority groups, we must pay special attention to the practice of “informed consent”, using local national minorities’ language to explain the significance of the research, explaining the risk that volunteers undertake and the benefit volunteers may obtain. In particular, some persons within ethnic groups care about the security of their family and religious information. Explaining to them how to protect their privacy is most difficult but also of utmost importance since we have to make considerable effort to establish trustful relationships. Obtaining local minorities’ doctors, village teachers and cadre's support is helpful. Sometimes we need to communicate with local religious leaders. This is important in order to reassure them that donating is not against their religious principles. Finally, before leaving the sampling site, researchers should leave the information of a contact person. Usually, the local doctor is the best choice.

“Informed consent” is a new practice in such activity. In the past it was done by order of the government. This was much “easier”, but obviously donors did not get the respect they deserve, and therefore we had to change the practice accordingly.

After more than 14 years of hard work, the immortalized cell lines bank has been established, with material and data from 70 populations from 47 Chinese ethnic groups. It includes 3,982 immortalized cell lines and 7,210 DNA samples. This makes it the largest immortalized cell lines bank in China at present. It can meet the scientific requirements for long-term studies. The immortalized cell lines and DNA samples have been provided to research institutions and universities all over China for related studies. Meanwhile, DNA samples from the bank were used in some international cooperative studies, such as between China and Japan, China and the United States, and China and Europe Cann and de Toma, 2002; Chu, 2009).

According to the agreement signed by the Chinese Human Genome Organization and the Human Polymorphism Study Center (CEPH), and with the approval of the department in charge of human genetic resources, we provided the CEPH with 149 immortalized cell lines, which were tested to meet international standards and have been highly approved of by European colleagues. The DNA extracted from these cell lines was supplied to international institutions for collaboration (Noah et al., 2002; Lev et al., 2003).

No.	Ethnic groups	No. of cell lines	No. of DNA	Places of cell lines Reserved	Sampling places
1	Achang	93	100	Kunming	Luxi County, Dehong Municipality, Yunnan Province
2	Bai(Eryuan)	32	100	Kunming	Eryuan County City, Yunnan Province
3	Bai(Dali)	61	100	Kunming, Beijing	Dali City, Yunnan Province
4	Bulang	54	100	Kunming, Beijing	Luxi County, Dehong, Dai and Jingpo Autonomous Municipality, Yunnan Province
5	Buyei	64	120	Haerbin, Beijing, Kunming	Qiannan Buyei Autonomous Municipality, Guizhou Province
6	Korean	58	120	Haerbin, Kunming	Yanbian County, Korean Autonomous Municipality, Jilin Province
7	Daur	56	120	Haerbin, Kunming	Hongyan Darr Autonomous County, Inner-Mongolian Province
8	Dai	63	100	Kunming, Beijing, Haerbin	Jinghong City, Xishuangbanna Autonomous Region & Luxi county, Dehong, Dai and Jingpo Autonomous Region, Yunnan Province
9	Dai-Huayao	5	50	Kunming	Xinping County, Yunnan Province
10	Deang	55	100	Kunming，Beijing	Luxi County, Dehong, Dai and Jingpo Autonomous Region, Yunnan Province
11	Dongxiang	65	100	Kunming, Beijing	Dongxiang Autonomous County, Gansu Province
12	Dong	50	100	Beijing, Kunming	Sanjiang County, Guangxi Province
13	Dulong	76	100	Kunming	Dulongjiang Region, Gongshang County, Nujiang Municipality, Yunnan

					Province
14	Oroqin	38	120	Haerbin, Kunming	Alihe Oroqin Autonomous County, Inner-Mongolian Province
15	Ewenki	43	120	Haerbin, Kunming	Nehe County, Heilongjiang province
16	Hani	63	100	Beijing	Mojiang County, Yunnan Province
17	Hani-aini	75	100	Kunming	Jinhong City, Yunnan Province
18	Kazakh	64	120	Haerbin, Kunming	Yinin Kazakh Autonomous County, Xinjiang Autonomous Province
19	Han(Fujian)	58	120	Haerbin	Mingqin County, Fujian Province
20	Han(Gansu)	62	100	Kunming, Beijing	Wuwei, Gansu Province
21	Han(Guangdong)	43	100	Kunming	Shaoguan City, Guangdong Province
22	Han(Guangdong)	57	100	Beijing	Guangning County, Guangdong Province
23	Han(Henan)	60	100	Beijing	Fangcheng County, Henan Province
24	Han(Hunan)	59	100	Beijing	Shuangfeng County, Hunan Province
25	Han(Shangdong)	61	100	Kunming	Zhoupin County, Shangdong Province
26	Han(Shanxi)	58	100	Beijing	Lingyou County, Shanxi Province
27	Han(Sichuan)	56	120	Haerbin, Kunming	Leyu County, Sichuan Province
28	Han(Zhejiang)	59	100	Beijing	Jinyun County, Zhejiang Province
29	Hezhen	18	120	Haerbin, Kunming	Tongjiang County, Heilongjiang Province
30	Hui(Ningxia)	63	120	Haerbin, Kunming	Tongxing city, Ningxia Hui Autonomous Region
31	Hui(Ningxia)	73	100	Kunming	Wuzhong city, Ningxia Hui Autonomous Region
32	Hui(Yunnan)	46	100	Kunming	Najiaying Town, Tonghai County, Yunnan Province
33	Jinuo	73	100	Kunming、Beijing, Haerbin	Jinuoxiang, Jinghong City, Xishuangbanna Autonomous Municipality, Yunnan Province
34	Jing	94	100	Kunming	Dongxing City, Guangxi Province
35	Jingpo	47	100	Kunming,	Luxi County, Dehong, Dai

				Beijing	and Jingpo Autonomous Municipality, Yunnan Province
36	Kirgiz	57	100	Beijing, Haerbin, Kunming	Wuqia, Xinjiang Autonomous Province
37	Lahu	90	100	Kunming, Beijing	Monghai County, Xishuangbanna Autonomous Region, Yunnan Province
38	Li	57	100	Kunming	Baisha County, Hainan Province
39	Lisu	107	100	Kunming	Nujiang Municipality, Yunnan Province
40	Manchu	65	120	Haerbin, Beijing, Kunming	Youyan Manchu Nationality Autonomous County, Liaoning Province
41	Maonan	22	100	Kunming	Huanjiang County, Guangxi Zhuang Autonomous Province
42	Mongolian(Damoqi)	48	100	Kunming	Damoqi City, Inner-Mongolia Province
43	Mongolian(Dongsheng)	54	100	Kunming	Dongsheng City, Inner-Mongolia Province
44	Mongolian(Hailaer)	61	120	Haerbin	Hailaer City, Inner-Mongolia Province
45	Miao	43	100	Beijing, Kunming	Songtao County, Guizhou Province
46	Mulam	63	100	Kunming	Luocheng County, Guangxi Province
47	Naxi	36	100	Kunming	Lijiang City, Yunnan Province
48	Naxi-Moso	45	100	Kunming	Yongning Xiang, Ninglang County, Yunnan Province
49	Nu	100	100	Kunming	Fugong County, Nujiang Municipality, Yunnan Province
50	Pumi	82	100	Kunming	Lanping County, Nujiang Municipality, Yunnan Province
51	Qiang	48	100	Beijing, Kunming	Mao County, Sichuan Province
52	Sala	71	100	Kunming	Xunhua County, Qinghai Province
53	She	46	100	Kunming	Fuan City, Fujian Province
54	Tajike	63	100	Kunming, Beijing	Tashikurgan, Xinjiang Autonomous Province
55	Tujia	56	100	Beijing, Kunming	Laifeng County, Hubei Province
56	Tu	39	100	Kunming	Huzhu County, Qinghai

					Province
57	Wa	57	100	Kunming	Cangyuan County, Yunnan Province
58	Wa	69	100	Kunming	Ximen County, Yunnan Province
59	Uygur	60	100	Beijing, Kunming、Haerbin	Yili, Xinjiang Autonomous Province
60	Xibe	43	120	Haerbin, Kunming	Chabuchaer Xibe Autonomous County, Xinjiang Autonomous Province
61	Yao (Guangxi)	58	100	Beijing	An County, Guangxi Province
62	Yao (Yunnan)	60	100	Kunming	Mengna County, Xishuangbanna Autonomous Region, Yunnan Province
63	Yi(Sichuan)	49	100	Beijing、Kunming	Butuo City, Sichuan Province
64	Yi(Yunnan)	47	100	Kunming	Paomaping Xiang, Ninglang County, Yunnan Province
65	Yugur	55	100	Beijing、Kunming	Gannan County, Gansu Province
66	Tibetan(Qinhai)	46	100	Kunming	Guinan County, Qinhai Province
67	Tibetan(Lhasa)	57	100	Kunming	Lhasa City, Tibet Autonomous Region
68	Tibetan(Yunnan)	23	100	Kunming	Chungtien County, Yunnan Province
69	Tibetan(Yunnan)	48	100	Kunming	Pengdang region,Gongshang County, Nujiang Municipality, Yunnan Province
70	Zhuang	55	100	Kunming, Beijing	Baise County, Guangxi Zhuang Autonomous Province
Total		3982	7210		

Table 1: Cell lines established of Chinese ethnic groups and sampling number and places of collection

On the basis of the Different Chinese Ethnic Groups' Immortalized Cell Line Bank described above, research projects on genomic diversity of Chinese populations are being conducted, including genotyping analysis of autosomal microsatellites, polymorphism studies on the Y chromosome, studies on mtDNA and HLA genes and so on, which provided an initial explanation of the origin, relationship, genomic structural differences and the genetic significance of different Chinese ethnic groups. [1] Research on the genetic diversity of related genes and susceptible genes for different diseases are being done too, and some significant achievements have been reached. For example, after a genotyping study, using primers of microsatellite loci selected from human autosomal chromosomes from 28 Chinese ethnic groups, phylogenies based on microsatellites were constructed by using the neighbor-joining

method. The genetic distance of different ethnic groups was measured. Based on analysis, a remarkable hypothesis, namely that main Asian gene pools originated from Africa, was proposed and a preliminary genetic distribution of Chinese ethnic groups was obtained. This is the first time genetics has proven that there is a relationship between Chinese populations and Africans (Chu et al., 1998).

Further studies based on the cell and DNA bank of different ethnic groups, including genome diversity and the relationship between disease gene loci and polymorphism, are being conducted. We call for international co-operation to do further researches.

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Biobanking in Transnational Perspective

Margaret Sleeboom-Faulkner

Abstract
Biobanking almost always involves international collaboration and the traffic of knowledge, data and materials between countries and regions. Nevertheless, problems related to tissue sampling and the maintenance of biobanks in Asia and Europe are usually explained in static terms of cultural, economic, historical and political dichotomies between the West and China, neo-liberalism and socialism, modern and traditional. A broader perspective shows that, when defined in such static opposites, the transnational dynamics of biobanks are hard to understand. But none of these contrasts by themselves are sufficient to understand the particular circumstances of biobanking issues that occur in specific locations. Examples from India, Indonesia, Japan and China show that only by situating the specific *local* situation of biobanks in their *global* contexts can we appreciate the transactional spaces and transnational traffic involved in biobanking.

Biobanking in transnational perspective

In analogy with the enclosure of agricultural land, entitlement and property of the body is now spoken of as the 'new enclosure' (Dickinson 2007).[1] Especially in transnational efforts to make biobanking a lucrative activity, such enclosures entail complex bioethical issues related to genetic sampling and the use of biobanks in different localities. In this article I argue that these issues, if thought of in terms of dichotomies between East and West, advanced and backward societies, and modern and traditional societies, cannot be understood adequately. I also argue that concepts of informed consent and personal or communal rights are often inadequately suited to the local environments in which they are supposed to be practiced. I will illustrate this with examples.

Dichotomies based on divisions between healthy and backward people

It has been argued that cultures with collective decision-making in India should be able to make use of community consent and family consent when making decisions about genetic sampling or genetic screening when setting up a register for the DNA of tribal communities. According to research in tribal areas in Northern India, village leaders or family heads have made decisions about genetic sampling regarding tribal communities suffering from sickle cell disease. This meant that when genetic information was yielded for sickle cell disease, it came to the village leaders. In various cases information leaked and was used especially against female carriers (Patra & Sleeboom-Faulkner 2009).[2] They feared that their husband would divorce them, or that they had lost their chances to find a partner in marriage. In some

[1] Donna Dickenson (2007) Property in the Body. Feminst Perspectives. Cambridge: Law, Medicine and Ethics.
[2] Prasanna Kumar Patra & Margaret Sleeboom-Faulkner (2009) The Indian genomic biobank initiative and emerging bioethical issues: a community based perspective, in *Human Genetic Biobanks in Asia: Politics of trust and scientific advancement*, London & New York: Routledge.

villages, members of the community were even given colour cards: Red for being symptomatic, Yellow for carrier, and White for disease free. To these communities, the register meant not only problems for individuals, but also a loss of face and reputation among other villages as an 'incestuous' community (Ibid.).

Dichotomies based on ideas about economic progress

Rich and poor countries, it is argued, should be able to improve their own financial fate. Therefore, according to the argument, poor people should have the chance to take part in genetic sampling exercises to improve their situation in exchange for a reduction of medical bills or in exchange for money. In those cases a simple blanket informed consent would be sufficient. It should be clear, however, that such exchanges rarely provide a solution to the structural poverty in which individuals find themselves consenting to exchange tissues. One example is the Indian-Japanese joint venture ZM, which licenses Japanese 'advanced' technologies to Indian hospitals, but claims to be a charity helping poor and needy people (Sleeboom-Faulkner & Patra 2009).[3] At the same time, this company collects tissues from all parts of the body from patients for a small fee with which it tries to set up biobanks in exchange for considerable investment from governments and large companies. Even if the biobank would provide biological tissues or the data on these tissues to researchers for free, it would still demand a financial share from the results of the research the biobank enables by sharing data. Though the biobank engages in 'commercial benefit sharing' vis-à-vis other enterprises, the original donors are not in a position to negotiate substantial benefit. This common form of commercial biobanking, in this case organised by the Indian-Japanese joint venture, advertises itself as a charity and as a tool for helping the poor survive. In fact it is a commercially sound enterprise, creating functional links between the poverty of some people in India and the research needs of scientists in Japan.

Dichotomies based on ideas about historical development

Preconceived ideas about the difference between modern and traditional societies, developing countries and advanced countries, and scientifically advanced and backward countries allow researchers to take a paternalistic stance when taking genetic samples. For instance, a Dutch biochemist, Prof. X, went to Indonesia, a former colony of the Netherlands, because he thought that he could help Indonesia in setting up an ethnic diversity biobank (Sleeboom-Faulkner 2007).[4] An Indonesian institute had invited Prof. X to come and set up a laboratory in the jungle, where he believed a biobank could offer Indonesia information about the history of the country, and a database for conducting research on the human genome and medical research. Protection of the people's privacy or the consequences of having a bank for the local communities did not play a role in his thinking. He thought that exchanging medical help for genetic samples was a good way of helping, what he regarded as, 'backward'

[3] Margaret Sleeboom-Faulkner & Prasanna Kumar Patra (2009), Experimental stem cell therapy in Japan and India: Bionetworking, biohierarchies and boundary objects. Unpublished paper presented at the *SMAP-symposium: Political Cultures of the Life Sciences in Asia*, International Institute for Asian Studies (IIAS), Leiden, 9-11 April 2009.

[4] Margaret Sleeboom-Faulkner (2007) Collecting families: An institutional approach to human genetic biobanking in Indonesia, *The Asian Social Science Journal* 36(1), 2007. Pp. 626-656.

ethnic groups in Indonesia (Sleeboom-Faulkner 2007). Similarly, I have spoken with various well-meaning doctors in other parts of Asia, who built up relations of trust when providing inoculation to ethnic communities. Later they would come back to ask for their genetic samples in return.

Dichotomies based on simplistic contrasts between nations as political systems

Foreign and national interests: In various developing countries, such as China, India, Indonesia and Tonga, there have been cases of foreign researchers practising unethical forms of genetic sampling, without following due informed consent procedures, and exporting biosamples abroad. These cases have been of great importance, partly because they showed the potential commercial and scientific value of the biological samples (Sleeboom 2005).[5] These cases also highlighted the clash between interests of foreign researchers and companies and the host countries. But the transnational traffic brought out discussions about national political interests, which was a condition for the creation of the regulation of the export of biomaterials in, for instance, India and the PRC. And, because the same practices of taking people's samples without informed consent happen within these countries as well, the regulation also stimulated discussion of biobanking at home. This shows that the problems of genetic sampling were not limited to problems between foreigners and home country. The problems with foreign countries actually highlighted the problems at home.

Dichotomies of neoliberal and socialist market economies

Taizhou, in Jiangsu Province, harbours what has been called the world's largest human genetic biobank in Taizhou's Medical Hi-Tech Industrial Park. China Medical City (CMC), a quasi-governmental organization established in September 2006, hopes that the genome data bank will help the city leap ahead to the cutting edge of 21st-century medical developments. According to CMC's deputy director, the medical park needed an estimated US$10bn in its first five years, 20-25% of which obtained through central, provincial and local government funding (Toland 2007).[6] The sources of the rest of the required funding are estimated to be partners that hope to process the data. The deputy-director claims CMC collects samples from people on a voluntary basis, and it has obtained permission from housing committees in different areas within Taizhou to visit residents to ask for their participation. The efforts of the biobank would be very fruitful if it succeeds to collect genetic data from one-fifth of its five million citizens, in agreement with its five-year plan.

An important issue in biobanking is the marketization of knowledge resulting from research. This potential exists in all political systems, whether neoliberal or socialist market economy. A well-known issue in biobanking is whether it is ethical that participants gain little from their 'gift', while researchers are allowed via patenting law to obtain financial profit from their research findings. A more relevant issue in the case of countries without adequate healthcare provision is the issue of who will benefit from the knowledge and medicine the biobanks are supposed to yield. Most biobanks operate on a public health model in which little or no personal health

[5] The Harvard Case of Xu Xiping: Exploitation of the People, Scientific Advance or Genetic Theft? *New Genetics and Society*, Vol. 20, first edition, 2005. Pp: 57-87.
[6] Poppy Toland 'China plans 'largest gene bank''. Available at http://news.bbc.co.uk/1/hi/sci/tech/7046586.stm

feedback is offered, donations of human tissue are conceptualised as gifts in service of the public good. This notion of public good rests on the idea of a social contract between donor and banker: the donor gives in the expectation that ultimately others in need of healthcare will receive. To rely on assumed altruism and notions of the public gift, while focusing on the future commercialisation of research results, seems like an imbalanced relationship, made possible only in the context of global medicine, global knowledge and transnational interests.

Discussion

The cases discussed in this article show that, when defined in static opposites of culture, economics, politics and development, the transnational dynamics of biobanks are hard to understand. Only by situating the biobanks in their global contexts can we appreciate the transactional spaces and transnational traffic involved in biobanking activities.

A transnational perspective on biobanking shows that informed consent, instead of empowering, can be disempowering. A difficulty appears when biobankers claim to work for the benefit of mankind, contributing to global medicine, national development and science while doing lucrative business. Donors often do not know about the consequences of storing information about their body and do not always realise the importance of discussing sensitive issues about privacy, trust and the question of who will benefit from the work done by biobanks in both the present and the future. Especially, if donors do not have the ability to nurture, sustain and develop themselves, the notion of the personal right of informed consent is misleading. Concepts of personal and communal rights and consent are inadequate when potential donors are not in a position to worry about the long-term consequences of the consent. If biobanking is to benefit local communities and societies, we need to think how samples can be donated as a gift and how such gifts can be turned into an ongoing obligation to the benefit of the community. This has far-reaching implications for, first, the question of whether donation for immediate payment should be practised; and, second, for who should define the purpose of biobanks and the research they enable; and, third, for the way in which international property rights (IPR) are organised when built on commercial biobanking.

GENOMICS

General Implications of Genomic Research for Society and Governance in Sino-EU Co-Operation

Wolfgang Hennig

In earlier meetings of BIONET, several aspects of relevance in biomedical research have never been touched. I shall try to give a short overview as I think that they are important for the final goal of BIONET.

This presentation will address three different aspects:
(1) The possibility of carrying out biomedical research in animal model organisms
(2) Problems related to databases
(3) Future developments in biological research

Genome research and "animal models"
Up to now our discussions have been limited by the silent assumption that biomedical research has necessarily to be done at the level of human individuals. However, the last decades in biological research have shown that considerable parts of biomedical research can be initiated and promoted by research on model organisms. Hence, any biomedical research project should consider the possibility of using model organisms.

The indications that the use of a model organism is indeed justified reach more than 15 years back. To our surprise, often the basic developmental pathways are very old in evolution. Their origin can sometimes be traced back to the lowest animals. Walter Gehring in Basel has given an intriguing example. In contradiction to our earlier assumption that insect and mammalian eyes have independent evolutionary origins, his studies of the genetics of the fly eye revealed that almost identical genes regulate the basic development of human and *Drosophila* eyes. Further research demonstrated that the same genetic background was already established in lower animals such as planaria and even as low as Coelenterata (jellyfish *Tripedalia*) (Gehring 2004).

Even more unexpected was the observation that the same gene can induce the mammalian or the *Drosophila* "complex eye", dependent on its environment during development. After this was recognized it was less of a surprise that the consequences of defects of the respective gene show similar phenotypic effects. In *Drosophila* mutation of the genes *eyeless* (*ey*) causes small or absence of eyes. The same effect was found for the defective gene *small eye* (*se*) in mice. Such mice have no eyes, no forebrain and no nose. The corresponding gene of humans, ANIRIDIA, produced similar effects. Homozygous mutant foetuses have no eyes, no nose and brain damage.

Today we have further examples for such ancient evolutionary developmental pathways and there can be little doubt that their exploration will provide invaluable information with regard to human diseases. We can hence conclude, that it is essential to evaluate any particular genetic situation with regard to the possibility to carry out fundamental genome studies on model organisms instead of starting with human experimentation.

Research in model organisms belongs in principle to the field of genomic research. If we consider the range of applications of genome studies in a more general way, the following applications can emphasize the wide spectrum of applications important for biomedical aspects:

- Identification of an individual
- Constitution of particular genes of an individual with regard to genetic defects
- Identification of genes of particular developmental pathways
- Addition or substitution of (defective) human genes
- Research on human evolution and migration

Databases

The size of genomes make it essential to create databases before further investigations on such data can be carried out. However, today not only in genome research are databases of major importance but also in all fields of biological research they form the basis for further work. Biological research without databases is no longer possible. Databases include all kinds of information including images. They may also be accompanied by sample collections (sometimes called biobanks – a term which is used synonymously with "databases").

Databases with or without sample collections grow with enormous speed. In order to make adequate use of such databases it is essential that they are centralized and coordinated, otherwise valuable information might be lost or will be duplicated at high cost. Databases, as a consequence of such centralized organization, become more and more complex and difficult to handle. As an example I shall show some details of the "Gateway to Neurosciences on the Web" (NDG Database: http://ndg.sfn.org) (Fig. 1).

This data collection contains:
(a) An experimental database
(b) A knowledge database
(c) Software tools for neurosciences
(d) Bioinformatic resources
(e) Providers of research materials
(f) A neuroscience database

This emphasizes that not only data are stored but that the complex techniques, which become increasingly more sophisticated, need their own databases. The same holds true for software tools and other aspects.

If we select one of these different databases for closer inspection (Fig. 2a, b), we shall see that they split up into a complex tree of widely different aspects of research (http://ndg.sfn.org/eavObList.aspx?cl=81&at=278&vid=28872&menu_item=dblist1). Data not included in such public databases receives little attention today and will lose any significance in future. This means that a decision to hold back data from these public resources will lead to loss of significant financial and intellectual investment. International co-operation is therefore only useful if agreements regulating the deposition of data obtained in international data collection can be made.

I now wish to give a few impressions of the ways data collections can be used to facilitate research diverging into the different aspects of a developmental system. I

have, on purpose, given an outline of the evolutionary background of eye development in the beginning of my presentation. I like to demonstrate in a comprehensive way how complex eye research has already become. The following pictures display the complexity of aspects of human eye research by selecting subsections of the database (http://neibank.nei.nih.gov/index.shtml and http://neibank.nei.nih.gov/cgi-bin/libList.cgi?tissue=retina) (Figs. 3, 4).

While in this research field images play an essential role in data collections, research on schizophrenia demands different types of data collections (http://ndg.sfn.org/eavData.aspx?db=10&cl=81&o=29111)(Fig. 5).

Both examples represent different kinds of problems in brain research. In a lecture *"Integrating neuroscience knowledge: Brain Research in the digital age"* (http://neuroinformatics2008.org/congress-movies/Mark%20Ellisman.flv/view) the neurobiologist Mark Ellisman has emphasized a more general aspect of biological research. He said: *"This is an important time in the history of Science: We are enjoying the benefits of convergent revolutions in biology and technology. However: Biomedical research activities are now more complicated, involving larger interdisciplinary groups, sophisticated instruments, and coordinated cooperative work by teams based in multiple locations (and in many countries)."* Implicated in this statement is that the results of research have to be shared and cannot be buried in single laboratories or institutes. This is a fact, which is still not generally accepted but will determine the funding of projects in the future.

In this context it is very important to consider how reliable data in databases are. Are data obtained by applying comparable parameters? Have they carefully been checked before deposition in databases? But these are not the only questions to be raised. I have shown some details of relatively complex databases. This clearly documents that it is also important to consider how databases are organized. How complete is the information deposited? How can it be verified?

This is not the only concern regarding the present situation of data collections. A real concern is the size of databanks: Data on Brain Image data, for example, have increased to 4 Million imaging files between 2002 and 2008 (http://neuroinformatics2008.org/congress-movies/Mark%20Ellisman.flv/view). Mark Ellisman in his lecture emphasizes in this context: "*The rate at which we generate new data is rapidly increasing....", ..."but the rate that we are losing data is also increasing. Efforts to organize and preserve community data have lagged far behind development of methods to gather and preserve new knowledge!"*

To clarify the potential of data collections I wish to continue presenting data from brain research. The techniques of fluorescent imaging have recently been dramatically expanded. As a consequence we can stain different cell types in the brain individually and detect them by fluorescence imaging methods (Livet et al., Nature 450, 56 (2007)). Computing techniques permit one to create 3D reconstructions of the arrangement in the brain. This permits one to recognize individual connections between neurons in a 3D image (Fig. 6). I think that it is not necessary to say more about the potential of such a methodology for the analysis of brain functions and defects.

Future development of biological research

This leads me to a final aspect of my presentation: Neurobiology will in the future facilitate extended studies of human behaviour. This research is still in its infancy. Recently, a German TV report showed studies on the potential of our brain to take up information and apply it, even without us realizing that this information was given. Our eyes have a limited capacity to distinguish signals given in short intervals. This permits us to see movies as fluent processes rather than recognizing the single pictures individually. If pictures of a different content, which are shown in half of the time span the eye can individually register are inserted into a movie, we cannot realize the presence of such information. However, in experiments where such pictures with sexually stimulating content were inserted into an otherwise neutral movie, the person watching this movie became sexually stimulated. The conclusion is that our brain takes up and evaluates information, which is strongly filtered and partially eliminated from our visual recognition.

This example emphasizes that brain research may in the future provide a powerful basis for manipulating people. As a consequence, neurobiology will in the future raise even more ethical concerns than genome research does today. Even though this is a relevant problem to be considered in the context of ethics in biomedical research, we have not even touched on this problem in our prior discussions in BIONET.

Finally, I would like to consider the problem of control and access to databases and biobanks. This includes the following aspects:

- I have already pointed out that only databanks that are international in scope are of use in science, while local databases may be insignificant in the future.
- International databases raise the problem of:
    - Data quality control.
    - Data access legitimation.
    - Justification of the use of data.
    - Protection of databases.
    - Protection of individuals providing samples.

Several of these aspects have not been discussed much in our meetings although they present important aspects of biomedical research.

On the question of data protection the "*New York Times*" has, on March 29th, 2009, reported a situation emphasizing the danger of data intrusion in an article entitled "*Vast Spy System Loots Computers in 103 Countries*". "*A vast electronic spying operation*" was discovered by Canadian researchers. This operation infiltrated and stole documents "*from hundreds of governmental and private offices around the world*" including those of the Dalai Lama. The investigation was, in fact, initiated at the Dalai Lama's office, as this is where the intrusion was first recognized.

The important conclusion is that, for example, any primary information which permits identification of individuals from databanks must permanently remain on offline computers to prevent intrusion. Similar conclusions were already made for primary databases engaged in money banking.

Such a request is very important as the availability of private data in databases creates many problems. Some examples are:

- In the medical context: Does the individual wish to know about genetic defects in his or her own genome? Often we do not even know what a particular genetic profile implies because environmental effects are usually of great relevance (especially in schizophrenia).
- In commercial contexts: Misuse of health data, for example, by employers or health insurance companies.
- In other contexts: Misuse of information by criminals or in politics.

Although I am aware that I have touched on a very broad field of subject matter, which cannot be considered in an approach such as BIONET, I think that such topics must be considered in more detail and that future developments in biomedical research are taken adequately into account for SINO-EU co-operation projects.

Legends

Fig. 1.
Overview of the NDG database Gateway
http://ndg.sfn.org

Fig. 2.
Subsection of the "Database of experimental data" from Fig. 1.
http://ndg.sfn.org/eavObList.aspx?cl=81&at=278&vid=28872&menu_item=dblist1

Fig. 3.
NEIBank giving access to different components of the human eye.
http://neibank.nei.nih.gov/index.shtml

Fig. 4.
Section of "Retina" data from Fig. 3.
http://neibank.nei.nih.gov/cgi-bin/libList.cgi?tissue=retina

Fig. 5.
Schizophrenia database from "Database of experimental data" from Fig. 1.
http://ndg.sfn.org/eavData.aspx?db=10&cl=81&o=29111

Fig. 6.
Fluorescence labelled neurons from a section of xxx indicated in (a).
(a) Overview of a section of the cerebellum. (b) Magnified picture from the region indicated in (a). (e)-(g) Connection of single neurons to neighbouring neurons which can individually be identified by their different colours.
From Livat et al. Nature 450, 56 (2007)

Cohort Profile: Taizhou Longitudinal Study—a Prospective Study of Non-Communicable Diseases

Wang Xiaofeng and Jin Li

Summary
Here we describe the profile of a 20-year prospective study – Taizhou Longitudinal Study (TZL study) aimed at determining the environmental and genetic factors of common non-communicable diseases (e.g. myocardial infarction, stroke, hypertension, diabetes, stroke, common cancers). The sample size of the cohort will be 100,000 adults aged 30-80 from the general residents of Hailin, Gaogang, and Taixing districts (sample frame 1.6 million) of Taizhou (a city with a medium-size population and moderate economic level in China). A three-stage stratified sampling method will be applied. Baseline investigations include interviewer-administered questionnaire, anthropometric measurements, and buccal mucosal cell and blood specimen collections. DNA will be extracted for genetic studies and serum samples will be used for biochemical examinations. A follow-up survey will be conducted every three years to obtain information on disease occurrence and information on selected lifestyle exposures. All study participants will be followed-up indefinitely using a chronic disease register system for morbidity and cause-specific mortality. Information on non-fatal events will be obtained for certain major categories of disease through established registry systems. The electronic data of the cohort participants will be linked to the data in the Centers for Disease Control and Prevention (CDC) of Taizhou, the general hospital of Taizhou and the corresponding Community Health Service Center (CHSC) to obtain current and historical data on health information. The TZL study will provide a unique opportunity to elucidate the roles of many important environmental factors, especially those concomitant with the economic transformation in China, for common non-communicable diseases, solely or via interaction with genetic factors.

Introduction
Dramatic changes have taken place in China in the past 30 years since the government of China initiated the reform process in 1978. China has introduced sweeping reforms in the structure of its economy, family planning programs, and financial accountability within enterprises and service sector organizations. A rapid rise in productivity has resulted in continuing increases in income and food supply. However, the growth was accompanied by urbanization, aging, westernization of diet and lifestyle, stress, and widespread air and water pollution. At the same time, China is undergoing a rapid epidemiological transition — from infectious diseases such as diarrhea and pneumonia to chronic ones such as heart disease, stroke, diabetes, cancers. Chronic, non-communicable diseases now account for an estimated 80% of total deaths and 70% of disability-adjusted life-years (DALYs) lost in China (Strong et al., 2005). For cancers alone, the absolute numbers of deaths from all cancers increased from 1.2 million in 1991 to 1.5 million in 2000, and 1.8 million in 2005. For cardiovascular disease alone, people aged 35–64 years lost 6.7 million years of productive life during the year 2000 at a cost to the country of around US$ 30 billion (Leeder et al., 2004).

Some risk factors are known to have contributed to the rise in non-communicable chronic diseases in China. In 2000, 60.2% (147 million) of men and 6.9% (16 million) of women aged 35–74 years in China were current smokers (Gu et al., 2004). Findings from the 2002 National Nutrition and Health Survey (NNHS) indicate that about 18% of Chinese adults are hypertensive, which equates to 153 million affected individuals (Wu et al., 2008). Data from the 2002 NNHS showed that there are 184 million overweight people and a further 31 million obese people in China. The number of overweight and obese is still increasing rapidly, especially among children (Wu, 2006). Westernization of lifestyle may also contribute to this scenario. Today, supported by generous pensions, most of the salaried persons can enjoy their leisure time. However, delicacy enjoyment and sedentary entertainment such as playing Mahjong and watching TV are usual activities on which people spend during their leisure time in China, which may lead to an increased risk of chronic diseases. Nevertheless, many other factors emerged concomitant with the economic growth of China in the past 30 years (e.g., TV watching, using mobile phones and microwave ovens), the effects of which on development of chronic diseases need to be appraised. In addition, the effects of genetic factors, and the modifying effects of environmental factors on genetics, need to be appraised with regard to the risk of chronic disease.

Case-control studies are universally used in epidemiologic studies seeking to identify factors that may contribute to a disease. Such studies can be easily and inexpensively carried out by small research teams or individual researchers. However, their retrospective, non-randomized nature limits the conclusions that can be drawn from them. Prospective cohort studies are considered to be the gold standard of epidemiologic methodology since they can facilitate the study of multiple outcomes and since they can minimize many of the biases that can hamper interpretation of case-control studies (Samet and Munoz, 1998). In the last decades, large prospective cohort studies addressing the etiology of common non-communicable diseases were well underway in Western developed countries. However, it is scarce in China.

Taizhou is located at the junction of north and south China, downstream of the Yangzi River, which is one of the two largest rivers in China. In terms of population size and economic development, Taizhou is a medium sized city in China. Taizhou consists of two districts (Hailin and Gaogang district) and four county-level cities (Taixing, Xinghua, Jiangyan, and Jingjiang). The resident populations for Hailin, Gaogang, Taixing, Xinghua, Jiangyan, and Jingjiang were 0.41, 0.18, 1.22, 1.48, 0.86, and 0.66 (measured in millions), respectively, according to the fifth national population census of China in 2000 (Office of Taizhou, 2008). The economy of Taizhou is at the medium level among the cities of China (Ou et al., 2004). Historically, Taizhou's population is composed of a mixture of people from north and south China (Wen et al., 2004). Nevertheless, after the establishment of the People's Republic of China in 1949, the gene flow has been very limited. Additionally, Taizhou is well-known for a high prevalence of digestive cancer in China. According to a survey on causes of death (1988-2002), the cancer mortality rate in Taixing was 288.67/100,000 person-years, outclassing the average of the whole country (108.26/100,000). Among these, esophageal cancer (77.52/100,000), stomach cancer (56.02/100,000) and liver cancer (67.86/100,000) were the most common malignancies (Zhou and Wang, 2005).

Study design

The Taizhou Longitudinal Study (TZL study) is an open-ended prospective study initiated by Fudan University and the government of Taizhou in 2007. The main objectives of the TZL study are: (1) to describe the mortality and morbidity characteristics of common chronic diseases such as cardiovascular diseases, diabetes, and cancers; (2) to determine environmental risk factors (diet, lifestyle, occupation) and life course causes of common chronic diseases, which are emerging with the economic development of China; (3) to determine genetic risk factors underlying common chronic diseases; and (4) to determine the contribution by gene-environment interactions to common chronic diseases.

The baseline investigation of the TZL study will include a two-phase survey and a three-stage stratified sampling method.

Two-phase baseline survey

(1) Phase I: ~100,000 adults aged 30–80 will be interviewed through questionnaires and samples of buccal mucosal cells will be collected.
(2) Phase II: Fasting blood samples will be collected for biochemical measurements (e.g., lipid, glucose, hepatic function, renal function, etc.), in half of the communities from Phase I.

Three-stage stratified sampling

(1) Stage I: 1/3 subdistricts (urban communities) or towns (several rural communities) were sampled from Hailing and Gaogang, representing the geographic and economic characteristics in their regions.
(2) Stage II: 50% of the communities were randomly selected from each subdistrict or town.
(3) Stage III: all individuals aged 30-80 from each household will be chosen.

After the baseline investigation, continuous monitoring of morbidity and mortality will be conducted through a chronic disease register system. Follow-ups will be conducted every three years for event endpoint. A data bank, specimen bank, and a detecting and analytical platform will be constructed for long-term molecular and genetic epidemiological studies. The study will use a ‘nested’ case–control approach for studies on serological or genetic biomarkers, when sufficient numbers of subjects have developed or died from particular diseases of interest. By seeking differences in biomarkers in the stored DNA and plasma, a wide range of genetic and environmental correlates and causes can be studied. Such an approach allows many different factors to be studied in relation to many different diseases at a relatively low cost (Figure 1).

Questionnaires and physical measurements

A roster of all persons aged 30–80 years was obtained from the offices of the Public Security Bureau, the Bureau of Statistics, and the Community Committee. Three to seven days before the baseline survey, the study staff distributed the advertisement material to every household within the target community. Then a trained interviewer conducted a face-to-face interview. All interviewers were natives who knew the dialect of Taizhou to ensure smooth communication with the participants. An in-person interview was conducted using a semi-structured questionnaire to collect the

baseline data. The interviewer-administered questionnaire covered socioeconomic status, demographic characteristics, residential history, personal habits (e.g., cigarette smoking, alcohol consumption, tea and coffee drinking), dietary habits (semi-quantitative food frequency questionnaire), family history of selected diseases, cognitive function, physical activity (over the past 5 years and during the adolescent period), medical history, menstrual and reproductive history and hormone therapy use (for women only). Lifetime occupational history was also obtained in the survey, including all jobs held for at least a year. For each job, the following information was obtained: name of workplace, job title, major products produced or handled, and years that each job started and ended. For dietary habits, the questionnaire was designed to capture information on consumption of major food items such as soy foods, allium-type vegetables, and cruciferous and dark-green, leafy vegetables (Table 1). The in-person interview takes on average about 50 minutes.

After the interview was completed, the subject's weight, height, waist and hip circumferences, and systolic and diastolic blood pressures were measured. Blood pressure was measured twice by a standardized mercury sphygmomanometer. Systolic blood pressure was recorded to the nearest 2 mm Hg at the appearance of the first Korotkoff sound, and diastolic blood pressure was recorded to the nearest 2 mm Hg at the disappearance of the fifth Korotkoff sound. The first reading of each interviewer was discarded, and the second readings of the two physicians were recorded and averaged. Body weight and height were measured with subjects wearing only light indoor clothing and without shoes. The waist circumference was measured midway between the caudal point of the costal arch as palpated laterally and the iliac crest. The hip circumference was measured at the symphysis-trochanter femoris level. Two measurements were taken, with a tolerance for differences of less than 1 cm for height, 0.5 cm for circumferences, and 1 kg for weight. A third measurement was taken if the difference between the first two measurements was larger than the defined tolerances.

Sample collection and storage conditions

After the questionnaire interview and physical measurements, a buccal mucosal cell sample was collected by rinsing the mouth. A blood specimen was drawn after overnight fasting and subjected to centrifugation within three hours and analyzed within eight hours for biochemical markers. A total of 10 ml non-fasting blood was collected into an EDTA containing vacutainer, a small part of which will be used for onsite rapid dipstick testing of random blood glucose and hepatitis B antigen (HBsAg) before the vacutainer is placed in cool boxes at ~4˚C. At the end of each day, the blood samples were centrifuged at the local study laboratory and then aliquoted into four bar-coded cryovials (three plasma samples and one buffy coat) for long-term storage in nitrogen tanks.

Follow-up, ascertainment of outcome, and linkage

All study participants will be followed-up indefinitely by using a chronic disease register system for morbidity and cause-specific mortality already established at the Community Health Service Center (CHSC) and the Centers for Disease Control and Prevention (CDC) in Taizhou. The quality and completeness of both mortality and morbidity follow-up data in each study area will be checked regularly during the study period. This will involve monitoring the number of people who die or are lost to follow-up each year, assessing overall mortality patterns in the study cohort, levels of

diagnostic bases for individual diseases, and the proportion of deaths (in middle age and, separately, in old age) with unknown cause. In addition, a follow-up survey will be conducted every three years to obtain information on disease occurrence and information on selected lifestyle factors. The electronic data of the cohort participants will be linked with the first and fourth general hospital of Taizhou to obtain current and historical data on health information. Nearly all adult deaths in these study areas will undergo some form of investigation, with their underlying causes being certified by a doctor. In rare situations (currently 5%) when death occurs at home without recent medical attention, a diagnosis will be conducted by qualified staff based at the regional coordinating centre to help determine the most likely cause from symptoms or signs described by family members. Information on non-fatal events will be obtained for certain major categories of disease (such as cancer, stroke, and myocardial infarction) through established registry systems, and by periodically visiting doctors at subdistrict or village health clinics. For any suspected cases of non-fatal stroke, coronary heart disease or cancer, further confirmation about their diagnoses will be sought by reviewing hospital or other medical records.

Ethics, informed consent, and privacy protection

The TZL study was approved by the Human Ethics Committee of Fudan University. A series of programs aiming at specific research objectives will be carried out in the cohort. These will need further ethics approval whenever and wherever needed. For informed consent, several steps were designed and performed as follows: (1) employ multiple forms of mass media city-wide (TV, radio, newspapers, internet, etc.); (2) reach the community three days before entering. Efforts were made to explain the purpose and process of the study to the subjects individually and at the community level; (3) display posters on all entrances of each building; (4) set up a manned booth for questions at the community center; (5) collect signed informed consent forms from each participant; (6) call back for more questions and establish a hot line. For privacy protection, several steps were designed and conducted: (1) a bar-coded ID was given to each subject; (2) the first page of the questionnaire containing ID information was removed; (3) the ID information was entered separately from other information; (4) all ID information was kept in a separate database.

Quality assurance and quality control

To ensure the implementation and the quality of the TZL study, we have established a special leadership group, technical advice group, and quality control group. The method of sampling, questionnaire design, training, physical examination, lab examinations, and data management have been centralized and standardized. Training of field staff involved in data collection and office staff handling data entry, checking, and cleaning has become an established part of our work. The internal controls on the quality of measurement are based on collecting measures of selected factors. All interviewer candidates were required to complete standardized training and were certified to conduct independent surveys. All interviews were tape recorded, and 5 percent of the tapes were evaluated for interviewing quality. About 3–5% of subjects were re-contacted by phone to evaluate the interviewers' work. All questionnaires and forms were coded twice and were double entered by different clerks. Inconsistent records were manually checked and corrected. Computer programs were also developed to check the logic and reasonable range of responses throughout the questionnaire to identify contradictory responses. In addition to the component-specific quality-control procedures noted above, other procedures were implemented

to standardize and monitor the quality of data collection and processing. These included training and certification for all interview and examination components, comprehensive manuals of operation, site visits, and blind duplicate blood measurements (5% sample). The quality and completeness of both mortality and morbidity follow-up data in each survey site will be checked regularly during the study period by the study coordinating centers.

Statistical power calculations

Although the baseline survey of 100,000 subjects in the study areas is expected to take 2 years to complete, the mortality follow-up for particular administrative units (such as villages or subdistricts) within each study area will start within 6 months of the start of the baseline survey in that geographically defined area to allow for the establishment of computerized long-term follow-up systems. The proportion of deaths with unknown cause or proportion of subjects lost to follow-up should both be 5% (at least up to age 80). It is anticipated that during the first 10 years of follow-up there will be 6,000 deaths from cancer, 6,000 deathes from stroke, and 2,000 from coronary heart disease (plus, perhaps, even larger numbers of non-fatal events). The substantial size of the study will yield sizeable cases of common cancers (e.g. esophageal carcinoma, gastric cancer, and liver cancer), stroke, and coronary heart disease and will generate sample statistical power in estimating the relationship between common exposures where the disease outcome dependent on exposure is also common (table 1). However, the present sample size may still be insufficient for studying diseases of low incidence, such as specific types of cancer (e.g. prostate cancer).

Discussion

Here we described the rationales, design and recruitment of the prospective TZL study, which aimed at exploring the environmental and genetic factors of common non-communicable diseases such as myocardial infarction, stroke, hypertension, and cancers. The morbidity and mortality of these common diseases increased rapidly along with the rapid economic growth of China. We hypothesized that the rapid growth of these common chronic diseases were largely the result of environmental factors, especially lifestyles and behaviors that can be changed, which were modified by genetic factors, modulating the prevalence of these diseases. Lifestyles and behaviors have indeed changed during the past 30 years, as evidenced by a number of the demographic parameters in the initial pilot phase baseline survey conducted from August, 2007 to March, 2008, which recruited about 17 thousand subjects from the Hailin district of Taizhou (Table 2). For example, before 1979, air conditioning, computers, microwave ovens and mobile phones were dreams for Chinese residents, but now about 71%, 22%, 72% and 21% of the middle-aged and elderly use these devices. Air pollution and noise brought new challenges to urban residents along with economic development in China. About 48% and 26% of residents in Taizhou live in houses that are less than 300 meters or 300-1000 meters from main roads and factories, respectively (Table 2). The impact of these environmental exposures, solely or in combination with genetic factors, on the prevalence of non-communicable chronic diseases urgently calls for evaluation. With years of follow-up ahead, the TZL study will provide a valuable opportunity to test many important etiologic hypotheses for chronic diseases that cannot be adequately investigated in studies conducted in western populations.

Large-scale prospective studies are still scarce in China at present, although several epidemiological surveys have been conducted in China in the last several years. In 1996, a large cohort study, the Shanghai Women's Health Study (SWHS), was initiated to recruit 75,000 women and to collect blood and urine samples from 20,000 cohort members (Zheng et al., 2005). Nevertheless, the aim of SWHS was to address some important etiologic hypotheses for cancer and other chronic diseases for women only. The China Health and Nutrition Survey (CHNS) (Chen et al., 2005) is an ongoing international collaborative project designed to examine the effects of the health, nutrition, and family planning policies and programs implemented by national and local governments and to observe how the social and economic transformation of Chinese society is affecting the health and nutritional status of its population. But the survey is a multistage, random cluster survey, which covers nine provinces that vary substantially in geography, economic development, public resources, and health indicators. The Guangzhou Biobank Cohort Study (GBCS) (Jiang et al., 2006) is an international collaborative study with aims to examine genetic, lifestyle, occupational and environmental factors, and life course causes of common chronic diseases, which are emerging with economic development. But the sample frame of the GBCS is the Guangzhou Health and Happiness Association for the Respectable Elders (GHHARE) aged 50 years or older. Their subjects are unlikely to be completely representative of the older population of Guangzhou. For the TZL study, however, a multi-stage stratified random cluster sample method guarantees the representativeness of the original population.

The TZL study has several strengths. Firstly, a drawback to cohort studies is the lack of follow-up that can harm internal validity and statistical power. However, when conducting our baseline investigation, we linked our database to the CDC, the CHSC, and the general hospital of Taizhou, which will increase the possibility of acquiring most newly diagnosed case subjects. Secondly, this prospective cohort study was designed to investigate a wide range of chronic diseases simultaneously. Thirdly, a unique strength of the TZL study is that it will appraise the relationship between non-communicable diseases and several important exposures that emerge with the economic development of China. In summary, the TZL study will provide a unique opportunity to elucidate the roles of many important environmental factors, especially those concomitant with the economic transformation of China, for common non-communicable diseases, solely or via interaction with genetic factors.

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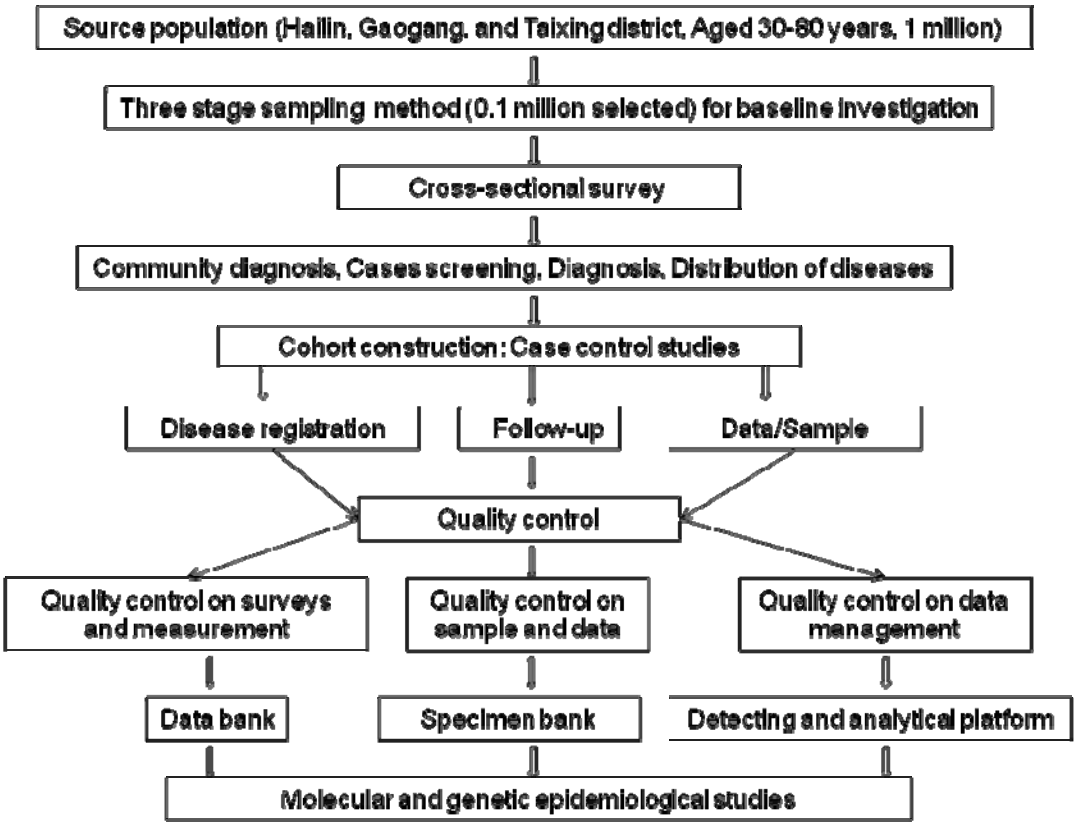

Figure 1: Study design of the Taizhou Longitudinal Study

RR	Exposure rate %	α=0.05, 1-β=0.80 Sample Size (A:B)
1.1	0.05	2336 (1168:1168)
	0.10	1122 (561:561)
1.2	0.05	766 (383:383)
	0.10	370 (135:135)
1.3	0.05	418 (209:209)
	0.10	202 (101:101)
1.4	0.05	278 (139:139)
	0.10	134 (67:67)

Table 1: Power of detecting multiple disease-associated SNPs of identical risk ratios and allele frequencies

Exposure	N of subjects (N=17314)	%
Use of air conditioning	12412	71.28
Use of microwave	12454	71.52
Use of computer	3832	22.01
Use of mobile phone	3056	17.7
Current house from the main road		
<300 meters	8403	48.25
300-1000 meters	4528	26.00
Current house from the factory		
<300 meters	4003	22.99
300-1000 meters	1853	10.64
Moving into new house during lifetime		
Once	8007	45.98
≥twice	1245	7.15

Table 2: Distribution of selected demographic parameters among subjects recruited in the pilot phase of Taizhou Longitudinal Study

Benefit-Sharing in Human Genetic Research: International Experiences and Chinese Legal Choices

Zhang Xiaoyong

The emergence and justification for benefit sharing in human genetic research

Benefit-sharing is a concept originating in international law. It stems from the concept that certain of the earth's resources are the common heritage of mankind and that the benefits of exploiting these resources should be universally shared. In 1992, the Convention on Biological Diversity established the principle of equitable and fair sharing of the benefits that arise from the utilization of genetic resources. Since then, benefit-sharing has become a legally binding provision in international law.

In the medical research relevant to human genetic resources, benefit-sharing takes different forms under different research models. Originally, benefit-sharing arrangements were established in the reciprocal context between researcher and participant. This kind of benefit-sharing arrangement is based on the consideration of fair compensation. Since participants accept risks and inconveniences, researchers have an obligation to compensate participants. In this context, ethical principles, such as compensatory justice and altruism, constitute the justification for benefit sharing in traditional biomedical research.

However, different from traditional biomedical research, human genetic research shows some novel characteristics. For example, human genetic research, as undertaken in the form of biobanks or genetic databases, boosts the number of participants considerably, and also blurs the very concept of the participant, as genetic information is by its nature shared. Increasingly, there is a consensus in human genetic research that to limit the sharing of the benefits to those who are directly involved cannot be justified. Thus, benefit-sharing arrangements in the context of traditional biomedical research cannot be applied in human genetic research.

In fact, stimulated by scientific and commercial power, human genetic research has raised some critical social and ethical concerns. One representative viewpoint argues, that human genetic research has the potential to produce both, more benefits and greater harm. More importantly, some practices and behaviours in human genetic research are contrary to ethical principles and concepts of justice and fairness. In order to respond to these concerns and alleviate people's anxiety, benefit sharing is put forward as an important means to resolve the problem of distribution of research achievements resulting from human genetic research and realization of justice and fairness. Obviously, in the context of human genetic research, ethical principles also provide substantial justification for benefit-sharing. These ethical principles should be distributive justice and solidarity.

International legislation and guidelines to regulate benefit-sharing issues in human genetic research

Currently, at the international level, the international community has reached a consensus about the protection of human rights, co-ordination of human gene and genome research and about conservation and sustainable use of biodiversity, and has

enacted some principal international legal instruments and non-legally binding guidelines that regulate benefit-sharing in human genetic research. These legal instruments and guidelines are categorized into three types.

(1) International human rights law and related ethical guidelines

- The UN's International Covenant on Economic, Social and Cultural Rights (1966) first enunciated the concept of mutual benefits and that of freedom of research. It also maintained the right to benefit from scientific progress.

- The UN's International Covenant on Civil and Political Rights enshrined the concept of the need for consent to medical research. Generally speaking, the international conventions on human rights provide general guidance for benefit-sharing in human genetic research.

- UNESCO's Universal Declaration on Human Genome and Human Rights (1996) regards the human genome as human heritage in the symbolic sense. Although benefit-sharing is not mentioned explicitly in this Declaration, Article 18 and 19 of the Declaration emphasize that international collaboration should benefit developing countries and the free exchange of scientific knowledge.

- Article 10 of the WHO's International Ethical Guidelines for Biomedical Research Involving Human Subjects (2002) provides that, before undertaking research in a population or community with limited resources, the sponsor and investigator must make every effort to ensure that any intervention or product developed, or knowledge generated, will be made reasonably available for the benefit of that population or community.

(2) International ethical guidelines related to genetic research
The Human Genome Organization's Statement on Benefit-sharing defines the concept of benefit.

A benefit is a good that contributes to the well-being of an individual and/or a given community (e.g. by region, tribe, disease-group). Benefits go beyond the avoidance of harm (non-maleficence) in so far as they promote the welfare of an individual and/or of a community. Thus a benefit is not identical with profit in the monetary or economic sense. Determining a benefit depends on needs, values, priority and expectations.

The Statement on Benefit Sharing recommends that:

- all humanity share in, and have access to the benefit of genetic research;
- benefits not be limited to those individuals who participate in such research;
- there be prior discussion with groups or communities on the issue of benefit sharing;
- even in the absence of profits, immediate health benefit as determined by community needs could be provided;
- as a minimum, all research participants should receive information about general research outcomes and an indication of appreciation;
- profit-making entities dedicate a percentage (e.g. 1%-3%) of their annual net profit to health infrastructure and/or humanitarian efforts.

UNESCO's International Declaration on Human Genetic Data (2003) provides that, benefits resulting from human genetic data, human proteomic data or biological samples collected for medical and scientific research should be shared with the society as a whole and the international community.

In this Declaration, benefit is defined broadly to include many important non-monetary benefits, such as special assistance to the person and group that have taken part in the research; access to medical care; provision of new diagnostics, facilities for new treatment and drugs stemming from the research.

(3) International biodiversity conservation law and guidelines
The third objective of the Convention on Biological Diversity (CBD) is the fair and equitable sharing of the benefits arising out of utilization of genetic resources.

Article 15.7 provides that, each Contracting Party shall take legislative, administrative or policy measures, as appropriate, with the aim of sharing in a fair and equitable way the results of research and development and the benefits arising from the commercial and other utilization of genetic resources with the Contracting Party providing such resources. Such sharing shall be conducted upon mutually agreed terms.

Although it is not directly applicable to human genetic resources, the CBD can inform the development of a rational benefit-sharing regime concerning human genetic resources.

The Bonn Guidelines (2002) are intended to assist states in developing an overall access and benefit sharing strategy. The most practical and useful provision in the Bonn Guideline is about the categories of monetary and non-monetary benefits.

To summarize, the principles and specific mechanism provided in the CBD and Bonn Guidelines are sufficiently comprehensive, flexible and extendable to human genetic resources, in order to provide a reliable framework for the ethical governance of benefit-sharing in human genetic research.

One case involving the utilization of Chinese human genetic resources
On July 19, 1996, Science Magazine published one report entitled "Harvard and China, Probing disease genes". It referred to a program by scientists at Harvard University in collaboration with some institutions in China to conduct research on common diseases related to genes, such as asthma, hypertension, diabetes, obesity, etc. According to the report, researchers had collected samples from patients in the mountainous regions of several counties in Anhui Province, China. But the types and exact number of samples have never been completely revealed.

It should be noted that this program has some serious problems and drawbacks. It is reported that only three of the Harvard projects have been approved in accordance with the Interim Measures for the Administration of Human Genetic Resources, which was published and implemented on June 10, 1998. Another important problem related to this program is whether donors can benefit from the program involving the utilization of their genes. In fact, researchers had not reached contractual agreements on benefit-sharing with donors at all. Regrettably, researchers did not even fulfil their

ethical promise about provision of free medical treatment. The Washington Post published an investigation series in December of 2000 reporting that samples for these projects were taken in the name of "health check-ups" and "treatment". Villagers of Anhui Province who gave their blood said: "we were told that there would be free medical care. So of couse everybody came out." However, the expected treatment never came.

Obviously, this situation is unfair and inequitable for donors and participants. Donors and participants do not receive necessary remuneration for their donation. This kind of practice violates ethical principles and international legal requirements.

Responses and choices of the Chinese legislation on regulation of human genetic resources

In order to prevent illegal access and misappropriation by commercial corporations especially from developed countries, China enacted Interim Measures for the Administration of Human Genetic Resources in 1998. Interim Measures established a legal system for the collection, storage, export, and research and development of human genetic resources from China. To some extent, the Interim Measures safeguard the interests of donor and collector.

However, the Interim Measures have not provided for some sub-systems that are relevant in the application of the law, such as informed consent and benefit-sharing.

In the absence of provisions on benefit-sharing, the requirement of domestic donor and research organizations for benefit-sharing cannot be fulfilled to a large extent. Furthermore, the biotechnological and medical research and development capability of domestic organizations cannot be improved greatly through the principle of benefit-sharing.

Currently, Chinese legislative agencies have begun to modify the Interim Measures accordingly. In my opinion, legislators should explicitly recognize and create provisions with regard to the practice of benefit sharing.

Compared with ethical obligation, since legal obligation is enforceable, to recognize the benefit-sharing requirement in Chinese legislation can ensure the realization of sharing the benefit resulting from the use of human genetic resources.

I recommend that provisions on benefit sharing include three aspects, i.e.

- the principles of benefit-sharing,
- the legal means or tools of benefit-sharing and
- statutory categories of benefit.

The provisions about statutory categories of benefit constitute the core of a benefit-sharing system. Chinese legislation should set up six minimum contract clauses in the statutory sense. These are:

(1) Joint ownership of relevant intellectual property;
(2) Sharing and joint usage rights of other research and development results;
(3) Dedication of a fixed percentage of profit to a trust fund;
(4) Full participation of Chinese researchers in collaborative research and development activities.

(5) Provision of training for Chinese researchers during the research and development.
(6) Proper access to health and medical care for Chinese donors of human genetic resources that are utilized in the collaborative research.

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TRANSLATIONAL RESEARCH

Practice and Evaluation of Ethical Governance in Assisted Reproductive Technologies (ART)[1]

TU Ling, He Jing and Lu Guangxiu

Abstract
The rapid development of assisted reproductive technologies (ART) raises complex ethical and social problems. This article explores how to perform ethical governance in ART and evaluates the social consequences. In order to urge doctors and patients to abide by medical ethics and moral norms and to ensure the successful development of ART, we argue that ethics committees must be robust and that their guidelines must be followed. Specifically, it is necessary to improve awareness of the fundamentals of ART and related ethical principles among doctors and patients. This includes the need to intensify mechanisms to fully monitor the implementation and enforcement of medical ethical principles and doctrines, such as informed consent.

The rapid development of ART has made positive contributions to alleviate the suffering of those who have reproductive dysfunction, to realize the desire of having a healthy child and to boost the healthy development of human beings. However, the implementation of these technologies has changed the natural pregnancy process and separated it from sex and marriage, which has initiated a series of ethical conflicts. Thereby there is a pronounced need to determine how best to carry out the effective ethical management of assisted reproduction techniques and to carry through ethical assessments that address its social consequences.

The implementation of the ethical management of ART fundamentally depends upon a well designed and fully functioning medical ethics committee

The rapid development of assisted reproductive technologies (ART) raises complex ethical and social problems. When people make use of advanced technology to relieve the suffering of infertility and sterility and enjoy family happiness, this poses such questions as: Can we disturb and control the pregnancy process? Does it or does it not violate natural rules? What can and should we do in the process of bearing children? Those questions undoubtedly exist throughout the whole process of ART implementation and we continually attempt to find the answers. Therefore, a committee for medical and reproductive ethics has been set up, with the purpose to provide ART services in accordance with the highest moral standards. It is our goal conscientiously to implement the ruling of the ethics committee in the practice of ART, and to implement best practice through continued education and the multi-disciplinary background of the committee members.

Such medical ethics committees in China have a history of more than twenty years. These committees draws on the guidance and ethical principles set out by the Ministry of Public Health, which state that: “we should establish a medical ethics committee in the organization of ART with implementation and accept its supervision and

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guidance, which standardize the organizational establishment of the medical ethics committee and its monitoring function" (Ministry of Public Health of China, 2003). But, in fact, some reproductive centers established the ethics committee only to satisfy inspections conducted by the superintending department. In such cases, the committee is only an affiliated institution of the hospital. It consists of main members, such as the director of the hospital and the head of the reproductive center, and other members, including the heads of clinical offices and relevant departments. Sometimes, the Chairman of the ethics committee is an official from the local government. This composition made the committee largely useless and caused great misconceptions about its nature and function, leading some people to think that the ethics committee "can not carry out routine work," or "monitor the performance of a normal exercise and the 'review' process is under the governor's leadership".

The Ethics Committee for Reproductive Medicine, however, is not a simply an image maker for the hospital reproductive center or a "rubber stamp", but a pragmatic operating organization composed of part-time staff including "medical professionals, non-medical professionals and laymen" of different ages and genders. The focus of the committee is to safeguard the dignity and fundamental interests of patients and subjects, to handle the conflicts and the interests between doctors (hospital), researchers and patients with "fairness", and conduct correct and objective ethical inspection of new technologies related to reproductive medical research and clinical treatment. Additionally, the committee should put forward suggestions for modification, monitoring and improvement of clinical work, and ensure that the institutions and staff strictly abide by the principles of medical ethics such as respecting and safeguarding the interests of the patients and informed consent.

Although members of the Ethics Committee for Reproductive Medicine are part-time staff, they should have an independent office and a permanent secretary to be responsible for routine work, and with a formal working constitution, system and plan. The ethics committee should have proper training and an information and education mechanism in order to qualify to take on the responsibilities of ethical consultancy, information and supervision, inspection and evaluation. Additionally, members' ability to implement ethical principles and to handle ethical uncertainty? can be gradually improved. "Although an ethical committee is not an organization of power, it is an organization with authority. It judges, guides and solves difficult ethical problems by certain ethical principles" (Guo, 2006: 5-10). Its effective work can prevent actions that violate ethical principles and do harm to human beings.

The Reproductive and Genetic Hospital CITIC-XIANGYA in Changsha, which is approved by the Ministry of Public Health, is a medical organization with a licensed human sperm bank and qualified to conduct an entire ART implementation. The hospital has engaged in the research and clinical application of ART since 1981, and its ethics committee is formed according to appropriate guidelines. The ethics committee consists of nine members, three of them have no direct relationship of benefit with the hospital, six of them are women and three of whom have academic ethical backgrounds (among them, two members have a bioethical background), one member has a law and sociology background, and one member is the patient representative. The director and vice director are ethicists and lawyers/legal experts from other organizations who have no direct relationship of benefit with the hospital. The committee ensures the objectivity and equity of ethical inspection and decision-

making and avoids possible conflicts of interest. Also, the hospital has set up a separate office and provides a secretary for the committee to deal with daily work under the authority of the director. Members with bioethical backgrounds take charge of daily consultancy of ethical problems, supervise the implementation of the ethical principles, check and modify the informed consent forms/procedures and related regulation in the hospital and among the staff. Furthermore, they monitor whether the hospital and the staff here respects the patients and safeguards their rights and interests, the informed consents are effective or not, and report to the committee. The ethics committee as a practical organization ensures the implementation of ART-related ethical principles in the hospital.

Thus, an important foundation and organizational guarantee for ethical management in ART practice is the requirement to set up a well orgnaised and pragmatic ethical committee in reproductive medicine as an effective working institution.

Expanding the education of ethical principles is an effective approach to enhance the moral awareness in ART among doctors and patients

As assisted reproductive technology is a new biomedical technology, we must strengthen its basic rationales and also develop education in related ethical principles. One of the basic tasks, as well as the main format of ART medical ethics control for the committee according to the ethical principles of ART and human sperm banks issued by the Ministry of Public Health, is to "develop the public dissemination and education of ethics on reproduction technology" (Ministry of Public Health of China, 2003). Ethical morality is a non-legal social criterion, and the ethical and moral measures necessary to manage ART ethicaqlly are different from measures of law, administration and regulation. "Public opinions, customs and model influence are used to form people's concept for goodness and badness, sensibility and belief". (Luo, 1999) Continual education and information are required to ensue that the ethics of ART go deep into the hearts of the medical staff, as only in this way will we achieve profound value management of all processes and procedures. Strengthening the understanding and education of ART and bioethical principles will not only meet actual needs, but also create a scientific moral guideline system that can be accepted by the ART doctors and patients.

The Reproductive and Genetic Hospital CITIC-XIANGYA insists on the information and education of the basic theory of ART and related ethical principles among doctors and patients. The hospital mainly takes the following measures:

- A combination of training and examination for medical staff. We regularly invite experts to the hospital to give lectures on ART-related ethical understanding. Periodically, we invite experts from other organizations to give lectures on special topics about ethical problems. The staff is then tested on what they have learnt. Such a test result will be the basic requirement for the staff so that they can begin to work in the hospital and an important element for new staff in order to pass the probation period.
- We train cadres on medical ethics in order to ensure that the team is better able to understand the ethical principles and analyze ethical problems. The hospital will also arrange for the staff to attend various kinds of national or international seminars and workshops on ethics.
- We give lectures on ethical principle and ART-related knowledge to the patients in order to build up consciousness of rights for patients and topics in the

communication between doctors and patients. These lectures are chaired by a member of the ethics committee. The hospital prepares lectures for first-visit patients once a week, three times a week for the patients beginning their treatment, and twice a week for the inpatient. Over 120 lectures have been hosted since 2005 and over 10,000 patients have attended the lectures.

Both, medical staffs and patients should receive this kind of training. The education and information related to ART medical ethics and regulations are good for the practitioner's professional ethics and inform the ways in which they deal with individuals and society according to medical and moral norms and ethical concepts advocated by the people. Additionally, the patient's understanding can be trained so that they can develop their own knowledge and skills to protect their own rights, and realize the importance of the choices they make about ART and understand the consequences of the decisions they make. This helps both the doctors and the patients carry out their respective obligations during the process of ART to reach a common understanding. It improves the relationship between doctors and patients and reduces the disputes between them in order not only to satisfy the needs for ethical governance in ART , but also to build a harmonious environment for medical treatment.

Continued strengthening of the supervision of medical ethics is an important mechanism to build up good moral conduct ability

“The basic problem of ethics is the relationship between morality and benefits, in which morality is used to adjust the relationships between people”. (Luo Guojie, 1999) Transforming ethical principles into individual consciousness cannot be realized by political and administrative command or by powerful and mandatory measures, but only via people's innermost consciousness and beliefs, values and social consensus. Innermost belief is the way to effective self-discipline, and the conscience is the regulator of social behavior and the judge of good and bad in social activity. But as the supervision of social consensus may be disciplined by others, so ethics is a combination of innermost belief and social consensus.

We should approach this issue from two sides, in order to consolidate the supervision mechanism of medical ethics. The first of these is the internal mechanism of moral supervision. ART practitioners’ understanding of the principles of medical ethics, virtue sensitivity, and the training and the strengthening of their moral ideal and belief can motivate their sense of justice, honor or disgrace, together with their moral conscience. Thus, they can maintain correct behaviors and reject improper ones. Thereby they can strengthen the acceptance of good professional ethics among medical staff and realize the best practice of ethical principles and good ethics in ART.

The other one aspect is the exterior mechanism of moral supervision. Firstly, for supervision by the people and society, for example, we have set up a public box for letters with suggestions and recommendation; we regularly hand out ethical questionnaires in order to find out the patients’ opinions, ideas and requests regarding the respect and safeguarding of their rights. Secondly, for the supervision by the ethics committee, for example, every member of the committee should check case files regularly, in order to verify that informed consent forms are signed and legal certificates are provided.

Moreover, regular clinical rounds and communication with patients can demonstrate the quality of the implementation of ethical principles during the ART process in medical institutions and among medical staff.

A third aspect is administrative law and regulation management. For example, the 'Ethical Principles for ART and Human Sperm Banks' issued by the Ministry of Public Health set criteria for ethical principles in ART and human Sperm Banks in the form of trade rules and guidelines. The Ministry of Public Health organized a group of experts to conduct strict evaluations. It announced that organizations implementing ART and sperm banks should be appropriately qualified and that the technology, equipment and ethical principles must meet ethical, technological and legal requirements. Organizations or practitioners cannot implement ART if they do not meet these requirements, and furthermore, they will be banned and fined if there is any violation. "Thus, the formulation and issuing of the principles symbolizes the constitution of a standard ethical guideline system to guide and control ART based on the characteristics of its range, quality content and structure" (Li and Lu: 40-41). The guidelines, as a form of ethics, define a certain set of behaviors or actions in the field of ART so that people's orientatation towards appropriate or inappropriate actions become more firmly established. Morality relies on such exterior mechanisms of adjustment, as well as the recognition and support of administrative law and regulation, to fully realize its role in society.

The Reproductive & Genetic hospital CITIC-XIANGYA pays special attention to the combination of exterior and inner mechanisms of ethical supervision during the whole process of ART implementation. Operating strictly according to ART ethical regulations and guidelines, any development and application of new research projects and clinical treatments must pass strict inspections by the ethics committee in reproductive medicine, which is responsible for supervision of implementation and follow-up in order to ensure the legal rights and interests of researchers and patients. The hospital sets up suggestion boxes, undertakes regular or irregular clinical rounds and inspections of case files, so as to understand the patients' opinions on the hospital and medical staff and to identify weak spots in the ethical work in medical treatment. Moreover, the ethical work in the hospital is scrutinized through elaborately designed ethical surveys.

The following are some questions from the ethical questionnaire in our hospital:
(1) After medical examination, how do doctors and nurses treat your medical condition?
Explain in detail Briefly explain No explanation
(2) What do you know about the whole process, basic procedure and expenses, etc. of the treatment?
Know completely Know partially Know nothing
(3) After succeeding in taking ART, you may/ may not (delete one) have miscarriage, ectopic pregnancy or bear children with physical or mental defects?
(4) After signing informed consent, you can\ cannot (delete one) terminate the treatment at any time?
(5) What did you do before you signed the informed consent form?
Read it carefully Skim over randomly Didn't read it

The first four questions from the survey show whether the medical staff respect patients, abide by the principle of informed consent in their work, inform patients about ART-related matters completely and honestly, whether they tell patients their rights, and which parts should be strengthened for the medical staff. However, the fifth question reflects patients' attitudes towards safeguarding their rights and the attention to individual legal rights and interests.

We should listen to patients' (the public's) opinions and suggestions frequently and extensively and use the exterior mechanism of ethical supervision to expose weaknesses in ethical management at each stage of ART in order to create a suitable environment for healthy and harmonious development of reproductive medicine. Thus, both inner and exterior mechanisms supplement each other in the governance of ART. The various kinds of supervision measures should be brought into play in order to realize the value of ethical morality in ART management, to urge medical staff and patients to abide by good medical ethics regulations, and foster the healthy development of human ART.

Full informed consent is the embodiment of ART ethical management in practice

"Informed consent is the most basic ethical concept and principle involved in the doctor-patient relationship". (Xu, Liu and Qu, 1986). It is also an important principle in medical law. Informed consent refers to the whole process, from a doctor's giving information to a patient to a patient's free consent in clinical medicine domain.

'Informed consent' is a right for patients and a legal obligation for doctors. It is stipulated in the 'Law of the People's Republic of China on Medical Practitioners' that doctors should tell patients or their family members the facts when they discuss the patient's condition, and that experimental clinical treatment should be approved by the hospital and consented to by the patient himself or his family members. Through current laws and regulations such as the 'Law of the People's Republic of China on Maternal and Infant Health Care', the 'Regulations on the Administration of Medical Institutions', 'Implementing Rules of Regulations on the Administration of Medical Institutions' and so on, defining the proceedings of informed consent, patients enjoy the right of informed consent during medical treatment, including rights of understanding, informing, making choices, refusal and consent, etc. ART can not only effectively solve the family and social problems caused by the couple's sterility but also provide effective solutions for having a healthy child and ensuring reproduction. Nevertheless, due to its intervention in the natural procreation process, this reproductive technology had significant impact on order, law and ethics in human society.

Additionally, the long-term influence of the technology on the offspring is still under observation. The consequences of ART involve benefits to individual, family, offspring and even kindred and society, so "it is necessary for consent to be willingly given during ART treatment" (Nuremberg Code, 2000: 515-516). The participants should be rational subjects with ability to make judgments of their own accord. Thus, informed consent is one of the seven great ethical principles for ART and human sperm banks issued by the Ministry of Public Health with significant importance in the ART field.

During long-term ART practice, our hospital fully carries out the entire process of informed consent, with following procedures and methods according to different stages of patients' treatment:

- Information telling is repeatedly carried through all stages and procedures. Patients are informed at least five times during their treatment. The first time is a wide-ranging lecture when patients make their fist clinical visit; the second time is when the doctor gives individual treatment to the patient; the third time is the directive lecture before patients are making a treatment plan decision; the fourth is the talk between the doctor and the patient before signing on informed consents; the fifth is the information giving before the oocyte retrieval and transplantation operation (insemination for AID couples)
- Information should be told in simple and straightforward mode, and avoiding technical words, according to specific objects.
- Information should be fully and accurately told according to the facts, including possible results and limitations to related examination and operation, deficiency of the technology, influence on the future child and possible benefits and risks.
- Informed consent forms have to be detailed and precise in relation to the individual case.

After detailed medical and ethical consultation and before making therapeutic regimen decision, both the doctor and the patient should sign the informed consent so that both of the two parties can effectively define the benefits, risks, obligations and responsibilities related to ART treatment. Because informed consent has a function of contract and definition of responsibility and obligation, morality and rights, both doctors and patients can be responsible for various kinds of decisions they made.

Patients need to fully understand the whole process of ART and the limitations of the technology through accurate and true information giving in order to attain the correct understanding and to make rational and willing decisions on whether to participate in a certain ART treatment. All doctors know that informed consent is not simply consent to a certain medical treatment or intervention suggestion. Patients have to be informed before approving a behavior and consent willingly to it. For example, doctors may suggest that patients to accept ART and the patients weigh the risk and benefit of the technology before they agree to do so. Thus, in fact, there is a contract between the doctor and the patient, doctors are approved and authorized to operate within the consent range. The consequence of ART treatment is not only related to the patient, but also to the benefit of the patient's family, relatives and even society, and most importantly to the welfare of the offspring. Therefore, it is very important for patients to understand the information they have been told.

Although informed consent has the function of a contract, it is not a business contract or a simple agreement as in commercial transactions. If one signs a business contract, one has to assume corresponding obligations with no pulling back. However, patients can change their thinking about their ART treatment plan at any time according to their physical status and changes of family relations even if they have signed the informed consent form. The basic idea of informed consent is to respect the self-determination and autonomous right of human beings; "it is a kind of freedom of will and absolute value of pursuit in ethics" (Pi and Wei, 2003: 124-126). It accords with ethical principles for people to make suitable and timely choices on the ART treatment scheme based on their own value choice. Thus, there should be an

obligation in morality and justice for consent with the right procedures that accord with patients' real will before ART treatment commences. As the embodiment of the practice of ethical principles in ART, informed consent is used to ensure the maximum protection of the ART subject and to safeguard everyone's benefit, including the medical staff, ART subject, offspring and family members, to take precautions against unpredictable medical disputes and potential harm to the beneficiaries.

"Ethics is the science of good morality and about moral values and the method, process and realizing approach of good morality constitution" (Wang, 2003). The practice of ethics needs to rely on certain conditions and environments and should become a guideline (regulation, line, policy and law) with exterior mechanism adjustment of moral operating as a corresponding system. Implementing ethical management in the ART treatment has an important significance for the present and the future.

It is a commonplace in modern times that technology is a double-edged sword. We have to be careful and to think about whether the innovative results of ART cause any undesirable consequences to humankind even though it also brings benefits. But as the Nobel Prize winner Richard Feynman said: "Science is the key to heaven and hell" (Zhou, 2004: 26-29, 121). In this sense, we should know how to make use of the key to open the door to heaven. As long as we insist on using medical ethics principles to manage ART and we make sure that it operates according to good morality and for the benefit of the people, it can exert active and revolutionary significance.

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Socio-Ethical Considerations in the Provision of Eggs and Embryos for hESC Research: Lessons From the UK[1]

Erica Haimes

Introduction

This paper is written from a UK perspective and it is acknowledged that practices in hESC research vary widely across the world, not least within Europe. Nonetheless the issues raised here are of relevance to any country seeking to develop its profile in stem cell science – which clearly applies to the UK and to China. The paper explores some of the wider social and ethical issues around embryo experimentation, in and for stem cell science. It is based on material from two empirical research projects: first, an ongoing Wellcome Trust funded study on the views of IVF patients asked to provide embryos that are unused in, or unsuitable for, treatment and that are commonly designated as 'spare' (Haimes and Taylor in press) for embryonic stem cell research and, second, an ongoing project funded by the UK's Medical Research Council to conduct the world's first study of women participating in an 'egg sharing' scheme for hESC research in exchange for reduced fees for fertility treatment. Both studies give prominence to the perspectives of the potential providers of the eggs and embryos since their voices are rarely heard in these debates. It is important to include their views and values if we are to gain a fully-rounded understanding of the social and ethical implications of research on embryos. This is particularly important in light of recent debates about the applications and implications of the use of embryonic stem cells for research and the development of therapies. Providers' views add fresh insights to these debates.

The overall aim of these studies is to provide practical feedback to the scientists, the clinical practitioners, and the policymakers concerned with genetic and reproductive medicine. They will provide much needed empirical data on the ethical and social acceptability of embryo experimentation to potential donors. They will also contribute new knowledge to bioethical debates on embryo research. As we shall see, consideration of the providers' perspectives enlightens our understanding of conceptual debates as well as helps us to address practical questions, such as how to devise the best forms of governance in this field.

In many ways the UK has taken a series of bold steps when compared with many other countries, in being particularly permissive towards enabling developments in hESC research. It is therefore useful to examine at least some aspects of UK practices to see what can be learnt from these. Do empirical investigations and analyses of these practices suggest this is a route for others to follow or do they provide cautionary tales and warnings that others might wish to be more wary?

Acquiring human embryos: the legal and ethical context

'As tissue sources, embryos present the same sort of opportunities for controversy as do donor cadavers and fetuses: they reside at the margins of human life, and their

[1] This paper has been updated from that presented at the BIONET Workshop in Shanghai, October 2007.

relationship to the human community and human status is ambiguous and contestable.' (Waldby and Squier, 2003:29)

Law and practice in the UK

Embryo experimentation raises many questions, including the ethics of conducting research on potential human beings, the definitions of the start of human life, and the possible destruction of that life. However, it has been established as an acceptable practice in the UK by the Human Fertilisation and Embryology (HFE) Act 1990. Following this, in 2001, the UK became the first country in the world to allow hES cell research. Many other jurisdictions have not followed this move because hES cell research raises all the ethical concerns around embryology just mentioned (Heinemann and Honnefelder, 2002; Romeo-Casabona, 2002).

Ongoing ethical debates

Legislation has not silenced debates in the UK and several issues are still frequently raised. These include, most commonly, the moral status of the human embryo and also whether adult stem cells could be used instead.

On the first point, the justifications given for embryo research include:

- 'the argument from suffering' (because of its potential to lead to treatments for disease); this argument has gained strength through the promises of hESC research to make significant contributions to curing conditions such as Parkinson's disease, Alzheimer's and diabetes;
- 'the argument from twinning' (i.e. that early embryos are not human individuals because of the potential of blastocyst cells to develop into two human beings);
- 'the argument from capacities' (i.e. that embryos lack the ability to think, act and communicate so cannot therefore be accorded full status as human beings);
- 'the argument from potentiality' (i.e. that the embryo is not a human being even though it has the potential to become one, under specific circumstances).

Such positions proved persuasive in the UK. Even so, most regulatory bodies, in the UK and elsewhere, agree that respect for early human embryos is appropriate and that research requires careful regulation.

The question of whether adult stem cells could be used 'instead' of stem cell lines from embryos, is interesting given advances in adult stem cell therapies. In the recent parliamentary debates in the UK over the Human Fertilisation and Embryology Bill (Hansard, 2007-8), this question was frequently raised, as being of interest in its own right and also as a way of objecting to the use of hybrid embryos. Nonetheless, a major difficulty in stem cell research is the lack of understanding of how stem cells differentiate into particular cell types, demonstrating the need for further basic research on embryos. This suggests that embryonic research needs to progress alongside the development of therapies from adult stem cell lines – neither is a substitute for the other. Similarly, it has been argued, in the same parliamentary debates, that the development of induced pluripotential stem (iPS) cells could eventually remove the need for hESC research but again the response was that research needed to advance on a number of different fronts simultaneously and that hESC research was still needed.

Given that, in the UK at least, the need for hESC research remains, it is interesting to note that this means that it is subject to increasing scrutiny from bioethics and social research. These approaches raise further considerations such as what happens when the treatment setting of the IVF clinic is reconfigured as a treatment-research setting? In requesting embryos from IVF treatment for hESC research, the social space of the clinic is transformed from one of treatment to one of treatment-research (Haimes et al, 2008). An analysis of our UK data alongside that of a parallel study in Switzerland showed that in the UK this happens as part of the IVF process, whereas for the Swiss it occurred retrospectively. Whilst the extent and impact of the transformation differed (for the UK interviewees IVF remained the dominant 'definition of the situation') it nevertheless presented all interviewees in both studies with the task of re-examining their views of their embryos, and of embryos in general. It also required them to accept expansions and new definitions of their own role, from 'IVF patients' to that of being 'embryo donors'. None was able to articulate these transformations with ease and all struggled (to varying extents) with the conceptual, moral and social distinctions that such deliberations required.

Equally, the language of practices around IVF clinics' interface with hESC research has raised questions. For example, in what sense are IVF embryos 'spare'? This raises not just questions of linguistics but also questions of power and authority: who determines the 'spare-ness' of embryos and the terms in which they can be so designated (Haimes and Taylor, in press)?

In addition, questions have been raised not just about the practices at this interface but also the consequences of such practices, such as the question of the immortality of stem cells. Do embryo providers realise the potential for their cell lines to be 'immortalised' and if so, does this concern them? To what extent do embryo donors (as well as scientists, clinicians, and regulators) understand the possible long-term consequences of donations to hESC research?

Providing human embryos: the socio-ethical experience

The question then has to be: how much can these questions be addressed by talking to potential and actual donors?

Until recently, only rarely have discussions about the ethics of hES cell research involved consideration of the embryo providers' perspective. Exceptions included the Nuffield Council (2001), Harris (2002) and Parry (2003), who suggest that it is important to know whether embryo donors understand the purpose and nature of the research they are contributing to and whether there is indirect pressure on IVF patients to donate, given their possible gratitude to their clinicians. Generally, therefore, there has been a lack of data on the views and values of the couples who are asked to donate embryos for ES cell research. It is this gap, which our ongoing study aims to fill. It is important to know whether those asked to donate embryos for research assign a similar relevance to the arguments of scientists and ethicists or whether they appeal to other arguments, in explaining why they do, or do not, donate their embryos. The following material provides a snapshot insight into the findings of this study: more detail can be found in Haimes and Taylor (2009).

Embryo providers' views and experiences:

Five major themes emerged from our study:

(1) how interviewees spoke about the embryo;

(2) why and how they made the decision to donate or to refuse;

(3) their evaluations of the consent process;

(4) their understandings of the research projects they were being asked to donate to,

and finally, as a cross-cutting theme,

(5) the context in which interviewees were asked to donate their embryos.

How interviewees speak about the embryo needs to be seen in relation to these other themes since they provide the social context in which interviewees were asked to donate and in which they made sense of their experiences. Choosing to donate, or not, is a decision positioned in relation to other decisions and choices in interviewees' lives, including, most crucially, the decision to seek IVF treatment in the first place. Even this brief glance at the other themes provides insight into the interconnectedness of these experiences and considerations. The last theme is particularly important since couples are only in the position of being asked to donate because they are going through IVF; successful fertility treatment and having 'our baby' is their primary concern and forms the backdrop to the experience of being asked to donate embryos. They are, from their point of view, 'IVF patients' rather than 'potential embryo donors'.

The following emerged as key reference points for interviewees' discussions of the embryo (see Haimes et al, 2008 and Haimes and Taylor, 2009 for further detail).
(i) Deliberations over whether the embryo is a baby/child, and whether the embryo is a living entity;
(ii) distinguishing between eggs, embryos and fetuses;
(iii) the 'calculus of conception': the mental arithmetic that couples constantly have to perform when considering the possible combinations of outcomes of treatment (Haimes and Taylor, 2009);
(iv) the experience of seeing, or declining to see, the embryos to be transferred, on a screen, prior to transfer;
(v) comparing the embryos transferred into a woman with those donated for research.

The following features emerged from interviewees' talk:
a) 'Baby talk' predominates
'Baby talk' emerged as the dominant framing for how interviewees discussed the embryo. This is not surprising given the IVF context but neither is it insignificant therefore in understanding how the embryo is located in the overlapping lexicons of reproduction and research. This is not to say, however, that the embryo was simply seen as the equivalence of a baby; rather, that 'baby talk' frames the context of deliberations, being the initial and most prominent reference point from which further distinctions developed.

Two clusters of views emerged: the possibility that the embryo *is* a baby or could be regarded as such, either actually or in its immediate potential, and the view that the embryo is clearly *not* a baby, though this in turn often leads to a debate over whether the embryo is nevertheless living. These two positions do not represent hard and fast groupings to which interviewees could be easily allocated, however; rather they were clusters of considerations which they voiced as they struggled to reach a settled view.

b) Wanting choices with 'spare' embryos
Questions have to be raised concerning the status and designation of these embryos as 'spare' since this term implies that they are superfluous to treatment, which might not strictly be the case. A woman undergoing IVF treatment might produce more viable embryos than can be used in one cycle of treatment, since currently in the UK accepted practice is for only two embryos to be transferred at any one time (and practice is moving towards single embryo transfer). Couples might wish to freeze good quality embryos for future treatment cycles but this can only be done at high cost and also at high risk that the thawed embryos will degrade during the thawing process. Clinics vary in their freezing policies, setting different limits on the numbers of embryos they will freeze for couples and the costs charged for this service.

If couples have not produced enough embryos to qualify for the freezing policy of their clinic or cannot afford to have them frozen, they might donate them to research as the 'next best thing', so they are not 'going to waste'. However the designation of such embryos as 'spare' is a simplification of the process whereby they become available for research and a label that couples themselves can find contentious. Overall, couples want to have a choice about the destination of their embryos but acknowledge this is not always possible. Evidence also suggests that the outcomes of such choices are not always as clear as couples, and indeed clinics, might presume them to be, prior to freezing (Haimes and Taylor, in press). This is an area that requires more investigation.

c) Interviewees' understanding of hESC research?
Interviewees felt that they had understood the explanations they had been given for the research, at the time they were given it, but felt unable to repeat those explanations with confidence at a later date (i.e. in our interview). This is not surprising perhaps though this does raise questions about the nature of 'informed consent'. That is, what does the term 'informed' refer to – understandings at the time of the consent process, or understandings that are deemed adequate by those being informed, or understandings that can be retrieved at a later date with the equivalent degree of authority as when first given? All our interviewees felt happy about the clinic's consent procedures and were mostly very complimentary about the clinic and clinic staff. It might be the case therefore that this is an example of 'informed trust' (Busby, 2004) at play. A question for future research would be to assess whether informed consent or informed trust provides the more effective ethical protection.

d) The social*, as well as moral, status of embryos*
The study reveals a multiplicity of definitions, identities and meanings attached to embryos by interviewees, legislators and ethicists. From the interviewees' point of view we can see, at the very least, differences between:

- 'embryos', the highly valued resources that provide hope of a pregnancy and which are therefore a primary goal for patients in the IVF treatment process; once a batch of embryos has been achieved they have then to be categorised according to quality;
- 'an embryo' which could be any embryo that results from the IVF process; most interviewees felt that those embryos that are not of very good quality can be used for research;

- ‘our embryo’, though is the one (or two) high quality, transferred embryo that is imbued with particular social and moral values by the couple, because ‘our embryo’ might become ‘our baby’; and
- ‘the embryo’**,** the abstract entity with special moral status, much debated by bioethicists and theologians, that is acknowledged by patients as having significance but which features little in their everyday world of IVF, babies or decision making over the provision of embryos for research. (Haimes and Taylor, 2009)

Therefore for IVF patients, the treatment process introduces additional layers of variability and changing definitions of embryos, as seen above. (See also Haimes et al, 2008)

It is clear that while interviewees do not refer to established ethical principles concerning the moral status of the embryo (although echoes of these can be heard in some of what they say) they do nonetheless use moral framings in trying to work their way through the variable social statuses they (and legislators and ethicists) ascribe to embryos. One strong (moral and social) framing is the wish not to see this precious entity ‘go to waste’. However, it is equally clear that interviewees are as concerned, if not more so, with the multiple, and changing, social value and status of embryos, as they are with the abstract moral entity that so preoccupies others.

Acquiring human eggs for SCNT / hESC research

The MRC funded study focuses on the practice of ‘egg sharing’ for somatic cell nuclear transfer (SCNT) research, in which IVF patients are offered reduced fees in exchange for eggs. The study is investigating the views, values and experiences of those coming forward to donate eggs, in order to evaluate whether the potential scientific and therapeutic gains from SCNT are achieved at social and ethical costs, or benefits, to egg sharers. This is the first empirical study of this subject; it will therefore provide vital evidence to inform the deliberations and practices of policymakers, stem cell scientists, fertility clinicians, and the wider community, in the UK and worldwide.

Background

As we have seen, hESC research promises to improve understandings of the genetic basis of disease; provide an investigative resource for developing new drug therapies; establish cell lines to give patients with diseases resulting from the degeneration of certain cell types (e.g. Alzheimer’s, Parkinson’s, heart and liver disease) the chance to replace these cells. A difficulty of the latter is that transplanting genetically unrelated hESC lines into a patient will provoke an immune response. Nuclear reprogramming, through SCNT, and the subsequent derivation of stem cell lines, enables the development of patient and disease specific hESC lines to avoid this problem.

Progress in developing SCNT techniques and applications has been hindered by the shortage of fresh human eggs. Eggs could come from healthy women or women undergoing IVF treatment. The donation of eggs from healthy volunteers is ethically questioned because of the physical risks of ovarian hyperstimulation syndrome, and of egg retrieval, to the donor. One aspect of the Korean scandal was the abuse of the egg providers through the inappropriate recruitment of healthy female staff as ‘donors’. The HFEA public consultation on egg donation acknowledged these concerns and therefore distinguished between ‘non-patient donation’ and ‘egg sharing’. However

women undergoing IVF treatment encounter these risks anyway, so providing eggs entails no additional physical danger for them.

Regulation and practice in the UK

Therefore the UK-based Newcastle Fertility Centre (NFC) is running an 'egg sharing' scheme. This scheme, approved by the Human Fertilisation and Embryology Authority in July 2006 (and now funded by the MRC), involves advertising for women to donate some of their eggs for SCNT research in return for reduced (up to 50%) IVF fees. This replicates the HFEA-approved scheme for acquiring eggs for the treatment of others. Egg sharing has attracted much social and ethical debate and extensive media coverage, though some women had already written to the NFC to volunteer for it, long before the scheme was approved and funded, suggesting that not all women share the concerns expressed by others. Clearly the ethical and social concerns raised by the scheme require a robust evaluation and one, which includes the voices of women volunteers.

Key questions for SCNT research

Although closely linked to the issues already considered in this paper. SCNT is an additionally interesting practice because of the number of distinct questions that it raises for debates in bioethics. First, there is the question of whether SCNT raises the same morally challenging issues about research on embryos, and indeed on the moral status of the human embryo, given that it could be argued that the entity created is not in fact an embryo since it is not the result of the fertilisation of the egg by sperm. Second, there is the question of whether SCNT (otherwise known as 'therapeutic cloning') will lead us down the slippery slope to reproductive cloning, despite bans, such as in the UK, against reproductive cloning. Questions are also raised from within the community of stem cell researchers as to whether the science is yet ready to take full advantage of SCNT techniques. It has been argued that the technique should first be perfected using animal eggs, so that precious human eggs can be saved until they can be of most use. Putting aside questions of whether human eggs can be 'saved' in this way, it has also been argued, in response, that animal eggs will only show how the SCNT techniques can be perfected on those animals and that the translation of knowledge across the animal/human divide would be of limited value. Another question raised in the UK during consultations on the use of SCNT techniques (HFEA 2006) was about the still large gap between the promise of such research and any therapeutic applications. Such a question has some legitimacy of course but it is far from specific to SCNT research. Further questions concerned: (i) the 'relative value' of donating for research compared to donating for treatment and the less immediately obvious gains from the former; (ii) the fear that donors might not fully understand the research, especially that immortal hESC lines might be derived; (iii) the fear that egg donation for research would compound the shortage of egg donation for treatment; (iv) the need to ensure that donors are able to give proper informed consent.

Finally, it was queried whether SCNT research, using eggs from IVF practice represented a conflict of interest for clinicians wishing to do both the clinical work and also contribute to research. (HFEA, 2006) This possible conflict has been addressed at the NFC, by introducing structures to ensure a clear separation between those providing IVF treatment and those asking for consent for eggs and those conducting the SCNT research. However, a necessary social proximity between these roles, and a physical proximity of clinic and laboratory, and a generalized sense of

gratitude to an IVF team, might still be factors in women deciding to donate eggs. However, the UK government amended the HFE Act in 2002 to permit SCNT research, because of its therapeutic potential.

Key questions for *egg sharing* for SCNT research

Egg sharing raises additional questions, some of which arise in egg sharing for the treatment of other couples.

A major issue is whether a reduction in fees constitutes an inducement to donate, and whether this, in turn, results in the exploitation of vulnerable, desperate and poor patients. It is suggested that this might therefore compromise the patient's autonomy and capacity to give fully informed consent.

It is argued that in the UK, the provision of more widely available National Health Service-funded IVF (Ashcroft, 2003) would mean that egg 'sharing', in exchange for reduced fees would not exist and that truly altruistic donation would be possible (Pennings, 2006; Pennings and Devroey, 2006). This in turn raises questions about the lexicon of tissue provision (for both eggs and embryos) for hESC research (and for other contexts too). What is meant or implied by the term 'donor' and 'donation' and to what extent are these meanings challenged by practices such as egg 'sharing'? Should the language of the market be introduced instead and terms such as egg exchange, or selling or trading be deployed? What do the egg and embryo providers themselves see as their role and the best ways to describe those roles? It is for these reasons that I prefer to use the term 'provision', which, although not entirely neutral (what words would be?), nonetheless conveys a less morally laden interpretation of the practice. Its moral significance, or otherwise, can then emerge from the research, in terms of how those providers themselves view it (Haimes, 2008).

Social science and related research suggests that the following should also be considered: (i) what are the effects of these practices on wider research relationships? Does egg sharing set a precedent for payment-as-inducement in other research studies? Also are there (ii) wider effects on organ donation? Does the egg sharing scheme affect debates about payment and other aspects of living organ and tissue donation (Friedman, 2006)? And is it the case that (iii) the market in eggs (through egg sharing or any other schemes) encourages the growing commodification of the human (particularly female) body (Waldby and Mitchell, 2006)?

These concerns have not gone without response.
Others have argued that:
(i) Egg sharing is more ethical than embryo donation for research because it reduces the chances of excess embryos being created;
(ii) the moral status of the enucleated egg cell transplanted with a somatic cell nucleus is less controversial than that of the embryo;
(iii) there is little evidence that egg sharing compromises the success of fertility treatment;
(iv) payment or 'compensation' is legitimate acknowledgment of donors' contributions as healthy research volunteers;
(v) ethically robust schemes that facilitate donation whilst protecting donors can be devised, within effective governance structures. (Hansen, 2002; Thum, 2003; Bernier and Gregoire, 2004; Heng, 2005)

The European Society of Human Reproduction and Embryology (ESHRE) Task Force on Ethics and Law reviewed the ethical concerns about egg sharing and concluded that non-patient donation (with reimbursement), and patient based egg sharing, are acceptable within certain protective structures. Compensation should be modest in egg sharing since the discomfort and inconvenience are the woman's choice for her treatment and substantial sums would be tantamount to payment for eggs. They also called for more research into alternative sources of oocytes (Pennings, 2007).

In the UK, egg sharing for research (along with non-patient donations) was approved, with safeguards, by the HFEA in February 2007. Nonetheless, many concerns remain.

An important perspective missing from the above material is that of the potential egg sharers themselves. Until recently it was rare for discussions about the ethics of hESC research to consider the views of those asked to provide the very scarce resource central to this work, let alone to ask them to contribute to the debates. However, it is clear from the embryo donation study that this is an important perspective that needs to be included if we are to understand fully the social and ethical impact of such research. Of particular interest in egg sharing is how requests to provide eggs fit with a clinical treatment that is largely paid for by the patient-donors themselves; this puts the above concerns in a very distinctive context that needs to be explored, especially from the perspectives of the patient-donors themselves. Currently there are no data on the views, values and experiences of women asked to donate eggs for SCNT research. The MRC study is filling that gap.

Broader questions

It is clear that a consideration of hESC research from the perspectives of those providing the embryos and eggs raises questions that go beyond the more narrow, but highly important, concerns of consent and doctor-patient relationships. Other aspects of hESC research and practice take on a new light when seen from the viewpoint of the tissue providers. This is particularly true when seen within a range of different social, cultural, economic, as well as ethical, contexts.

A brief exploration of these wider issues indicates the following areas are worthy of further exploration, particularly cross-culturally.

First, what role do, and should, providers' views and experiences play in shaping policy interventions, and influencing procedures around clinical and scientific practice and debates, on the national stage within any country and indeed on the international stage?

Second, can conventional European bioethics debates accommodate the views and experiences of tissue providers, particularly when those views and experiences challenge the normal boundaries of such debates, taking the moral status of the embryo into wider, hitherto unexplored, considerations of the social status of the embryo? Can the bioethics of non-European countries accommodate such experiences or are they also so challenged (see Mitzkat et al, 2009 for an early indication of such issues in embryo provision in China; see also Gottweiss, 2009)?

Third, to what extent do adult stem cells, human-animal hybrid embryos or the use of iPS cells reduce concerns over embryo donation or egg sharing for hESC research? The answer to this depends on the priority of concerns within any particular country, since these alternatives might introduce new problems whilst resolving others. It would appear that many of the issues raised by the providers in our research arise from the specific regulatory and practice contexts in which they are being asked to give their tissue. Further comparative research would indicate the extent to which these concerns are culturally specific and which cross national and cultural boundaries.

Fourth, questions are raised about understandings of translational research. This is usually preoccupied with the translation of knowledge from 'the bench to the bedside'. However, a tissue provider's perspective broadens out and opens up other relevant spaces for inclusion in this process. Consideration of the ethics of practice needs to include the transitions involved in moving from the tissue providers' home circumstances (e.g. wanting a baby) to the clinics for IVF treatment, which then becomes transformed (partially) into a research setting which takes that tissue back into the laboratory, on the promise of eventual treatments at the bedside for (completely different) conditions. To what extent do these other spaces and transitions 'matter', ethically and practically, particularly for those countries wishing to follow the UK in allowing such practices?

Fifth, is it the case, in the UK and elsewhere, that success in stem cell science is pursued at the cost of other developments and interventions which might be just as, or even more (in the short term at least) effective, for conditions such as Parkinson's (where community based care and interventions might make more immediate difference to the patients' conditions and circumstances)? The promissory nature of the curative capabilities of stem cell research is persuasive for potential providers: a question to pursue further, particularly in countries with different familial and community structures to the UK, is whether alternative strategies for supporting those with such illnesses are more, or equally, persuasive. Would this make a difference to providers' willingness to provide tissue?

Sixth, attention to governance structures needs to be able to take into account the global nature of both the research and the commercial developments arising out of the research. However much any particular country takes a particular stance on the regulation of the science, the effect of this will be limited in light of developments and funding elsewhere. It may well be that definitions of 'abuse' or 'good standards' are highly variable, in relation to tissue providers as well as other aspects of hESC research. 'Research tourism' (like reproductive tourism) (Haimes and Taylor, 2009b) might well proliferate as governance structures vary within particular countries. How others should benefit from research that their own countries find ethically reprehensible is not a new question. Nonetheless, it is not necessarily the case that consistency is inherently 'good'. Equally what might *appear* to be the same processes in a range of different countries might in fact be highly variable in practice. It may well be that ethics-in-practice is the most effective form of governance in a topic such as this; that is, an ethics that develops within cultural and contextual variations. But is such an ethics possible?

Concluding comments

Given how much is added to our understandings of the UK context for hESC research by taking tissue providers' views and experiences into consideration, it is highly likely that other countries will learn as much by taking account of tissue providers' views in their own social, ethical, economic and regulatory circumstances. This work challenges universalistic assumptions in biology and in ethics, about embryos and eggs. Given cultural variations on meanings of kinship, embodiment, and community, let alone on law and ethics, the insights gained in different countries might be highly variable, but also, inevitably, highly valuable.

The question at the start of the paper asked whether the UK was setting a route map or providing a cautionary tale for other countries. It is not the case that there can be a simple extension of experience from one country to another, given the social and cultural variations that frame hESC science in general, and embryo and egg provision in particular. However, what the studies described here do indicate is that a more rounded understanding of the cultural, as well as scientific, standing of hESC research comes (i) from being inclusive towards tissue providers and (ii) from going beyond conventional European and Western preoccupations with the narrow moral status of embryos and encompassing instead their wider social, contextually dependent identities.

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Human Stem Cell Research and Ethical Regulations in China

Pei Xuetao

The research and application of stem cells, cellular reprogramming and cloning techniques are involved in almost all fields of life science and biological medicine research. Meanwhile it is hoped to exert a revolutionary influence in some research fields such as regenerative medicine, including tissue replacement therapy, regeneration and reparation, tissue engineering, tissue and organ transplantation, gene therapy, functional genome and proteome research, systems biology, developmental biology models, exploitation of new drugs, pharmacodynamic action and toxicity assays, etc. This exciting field includes stem cell therapy, ES cell development research, somatic cellular nuclear transfer (SCNT) and therapeutic cloning, cellular reprogramming and iPS cells, stem cell banking programs, tissue engineering, tissue/organ substitutes, artificial organs, and transgenic xenografts.

Diseases and injuries as potential targets of regenerative medicine could potentially benefit from stem cell-based therapies. Many of them, such as Parkinson's disease, cardiovascular disease, diabetes, Alzheimer's disease, cancers, severe burns, spinal-cord injuries, and birth defects have few or no treatment options today, so millions of patients and doctors around world are currently looking for (innovative) cures.

Besides its great theoretical meaning and hopes for medical application value, the research and application of stem cells and cloning techniques also raise considerable attention among governments, scientists and the public to some sensitive problems. These include the sources of embryonic stem cells (ESCs), human/animal nuclear transfer, human cloning, the right to life, organ reconstruction, security of biotechnology, etc. These problems have close relations to human life ethics and the security and stability of society. In addition, with different cultural and religious backgrounds in different countries, some other questions also lead to prolonged disputes and enormously different opinions.

Some questions that arise are: if and when all the above-mentioned techniques become suitable for medical science, how does one appropriately use these techniques? What is the definition of human life? How does one avoid damaging human dignity, etc.?

The disputes and social repercussions caused by the intervention and control of birth and aging, sickness and death have always been discussed. However, they became more obvious and more profound with the advancement of new life science technologies. How to coordinate and solve the ethical disputes that arise from human embryonic stem cell research is a very realistic and urgent problem for many people.

Uncontroversally, stem cells are the source of all kinds of human cells. They have the potential for self-renewal, proliferation and multi-differentiation, and the characteristics of implanting and reconstruction, etc. The main achievements of stem cell research in recent years include the cloning of human ESCs, the development of somatic nuclear transfer techniques, cellular reprogramming and iPS cells, and

plasticity research on adult stem cells. Stem cell research has already become the commanding point of biomedical research that each country has tried to be the first to harness.

In recent years, a number of key disputes have arisen between stem cell research and the field of life ethics, including:

1. ESCs research has caused the fiercest and most sensitive ethics battles. One is how to think about the human embryo, namely the dispute as to whether and in what sense an embryo is a living life. This has become a highly contested question. Another question is about its source; no matter which kind of source that ESCs were derived from, an embryo is certain to be destroyed during the process of obtaining them. This is tantamount to destroying life, in the eyes of opponents.
2. Another concern is about cloning techniques. Many ethicists and members of the clergy argue quite strongly that human clones will be created, sooner or later, if therapeutic cloning research is implemented by using human ESCs. So they object fiercely to any kind of cloning research. But the majority of people treat therapeutic cloning research more rationally. They are confident that, if the cloning technique can be utilized appropriately, there will be positive outcomes on several areas, such as the respect of maintaining biological variety/diversity, the application of medical experiments to humans, protecting endangered species and improving people's quality of life.
3. Derivation and application of oocytes also raises ethical questions. Some ethicists believe that any kind of experimental study involving the use of human oocytes would infringe on basic human dignity, so the study is immoral and should be forbidden.

The principled stance of the Chinese government with regard to some severe diseases and sensitive problems is: to support and pay more attention to the research and development of biotechnology, particularly life ethics and biology security problems, and to acknowledge and observe the internationally acknowledged basic principle of life ethics. Therefore China supported actions to form the international convention forbidding human reproductive cloning. In December of 2003, the State Ministry of Science and Technology and the Ministry of Health jointly promulgated “Ethical Guidance on Human Embryonic Stem Cell Research” guidelines. They stipulate clearly that any research on human reproductive cloning shall be prohibited in our country. At the same time, the guidelines also limited the methods to obtain human embryos and set up behavioral norms for human ESCs research.

The theory of ethics needs to meet the development of science and the needs of history. Bioethics will develop and change constantly with the deepening of stem cell research, the elucidation of mechanisms of stem cell application, and it will help to define the ethical limits for stem cell research. We are convinced that bioethics can develop and promote the sound development of stem cell research in the future.

The Chinese government has been paying great attention to the studies on stem cells and tissue engineering, and has given their full support. The State High Technology Research and Development Program (the “863” Program), the National Basic Research Program (the “973” Program), and the Natural Science Foundation of China

have contributed large amounts of funding to this field. During the period of the "10th Five-year Plan", great progress has been made in this field. Some research teams and techniques in stem cell research and regenerative medicine have developed considerably, such as animal cloning, embryonic stem cells and somatic nuclear transfer techniques, plasticity of adult stem cells, stem cell banking programs, stem cell therapy, tissue engineering, biomaterials and substitutes for tissues and organs. More than ten licenses for clinical trials have have been awarded by the SFDA.

During the period of the "11th Five-year Plan" (2006-2010), the "863" Program will emphatically carry out studies on stem cells, tissue engineering, tissue and organ substitutes, and animal models for regenerative medicine research, as well as developing some technical standards and ethical guiding principles, etc.

The primary areas of emphasis of research and development in stem cell research and regenerative medicine in China include:

1. Therapeutic cloning and cellular reprogramming, the Key Project of the State's High-tech Project (863 Program), the "Stem Cell and Tissue Engineering" program is still carried out under the "11th Five-year Plan" (2006-2010). In 2011, it may be possible to provide an overview of places and scientists who play a leading role in this field and the fields mentioned below in China.
2. Embryonic stem cell banking program, is a Key Project of the State's 863 Program, too. "Stem Cell and Tissue Engineering" is also carried out under the "11th Five-year Plan".
3. Stem cell therapy for diseases including cardiovascular disease, liver disease, Parkinson's disease, diabetes, Alzheimer's disease, cancers, etc. are targeted under the 863 Program as well.
4. Developing and applying tissue engineering to skin, bones, cartilage, tendons, nerves, cornea, muscle lumens, etc. are also supported under the 863 Program.
5. Developing and applying substitutes for tissues and organs, such as artificial liver devices, artificial joints, etc. is also mentioned in the 863 Program.
6. Another target area under this program is the development of primate animal models for stem cell and regenerative medicine research.

The research and application of stem cells, cellular reprogramming and cloning techniques are involved in almost all fields of life science and biological medicine research. Some problems in this hot field, such as the sources of embryonic stem cells (ESCs), human/animal nuclear transfer, human cloning, the right to life, organ reconstruction, security of biotechnology, etc., are closely related to human life ethics and the security and stability of society. In addition, with different cultural and religious backgrounds in different countries, some other questions also lead to prolonged disputes and enormously different opinions. So, I think collaboration with international and European partners plays a very important role for furthering achievements in this field.

INTERNATIONAL DYNAMICS

Stem Cell Tourism, Desperation and the Governing of New Therapies

Ayo Wahlberg and Thomas Streitfellner

One of the areas that BIONET has focused on is regenerative medicine. As BIONET Research Fellow and BIONET Research Student respectively, we have both been interested in ethical aspects related to the growing number of stem cell therapies currently on offer to patients around the world. For Ayo Wahlberg, this interest has arisen out of research on the concept of quality in reproductive and regenerative medicine and for Thomas Streitfellner regenerative medicine has been central to his PhD research on aspects of ethical governance in Chinese and UK stem cell research. In this chapter[1], we examine the context in which stem cell tourism is fast developing by comparing a European and a Chinese case.

Introduction

It is possible to roughly divide social and ethical studies of the frontier technologies of the life sciences into two groupings. The one emphasises the importance of hope, expectation and/or promise when biological or genetic citizens form biosocial communities in their quests to find cures and/or meaning (Gibbon and Novas 2007; Petryna 2003; Rabinow 1996; Rapp 1999; Rose 2006). In these studies, new biological knowledge is seen to provide individuals and communities not just with new forms of therapeutic intervention but also new ways of understanding, relating to and acting upon one's self and others in terms of genes, cellular make up or neurochemistry. Biology here is possibility.

The other cluster of analyses is firmly grounded in a context of fear, caution and/or trepidation. In these commentaries, new technologies of genetic manipulation, neurochemical enhancement or cellular regeneration are seen as putting in jeopardy the very authenticity and dignity of humanity (Duster 2003; Fukuyama 2002; Habermas 2003; President's Council on Bioethics 2003). The new biological sciences are seen to be precariously balancing on a slippery slope and so they must be carefully monitored and regulated. Biology here is hazard.

Somewhere in between this hope and caution we find stem cell therapy, a form of bio-technological therapy, which is both old and new. Old because the reconstitutive capacities of haematopoietic stem cells have been sought after and clinically applied through bone marrow transplants in the treatment of blood disorders since the 1960s (Brown, et al. 2006), yet new because recent advances in cellular biology have allowed for the isolation and *in vitro* cultivation of more pluripotent stem cell colonies which has in turn considerably expanded the scope of treatment possibilities. In particular, harnessing the regenerative capacities of stem cells has become a 'promising' avenue of pre-clinical research into hitherto untreatable conditions such

[1] This paper appears in French translation in Leibing, A. & Tournay, V. (eds.) (2009) *Technologies de l'espoir. Les débats publics autour de l'innovation médicale - un objet anthropologique à définir*, Québec: Presses Universitaires de Laval, collection Société, cultures et santé.

as traumatic spinal cord or brain injury and degenerative diseases such as Multiple Sclerosis or Parkinson's disease. It is hoped that damaged and/or degenerated tissue can be regenerated or replaced using the innate capacities of stem cells to differentiate and proliferate. Importantly, the word 'hope' in this case is both speculative and tangible – stem cell therapy is both a 'long way off' and very much on offer (Gage and Verma 2003; Pearson 2003).

In this article, which results from our BIONET research, we will explore the global shape that a new and expanding field of 'stem cell tourism' is taking. Medical tourism is a form of global movement of peoples for healthcare-related purposes that has been discussed by many (see Connell 2006; de Arellano 2007). It moves in all directions, between South and North, West and East, and it remains controversial in each of these locations. Economic migrants from the South have been described as flocking to Europe to 'rip-off' state-sponsored healthcare systems, while affluent Westerners have been tracked as they travel overseas in search of organ transplants, reproductive medicine or cosmetic surgery, often to poorer developing countries where medical costs are lower, ethical oversight is perceived as more lax and a large proportion of people do not have access to even the most basic healthcare (Scheper-Hughes 2004). A number of companies in, for example, Thailand, Singapore, India and Cuba have begun advertising health travel packages to attract affluent customers from Europe, Australia and America and it has recently been estimated that "medical tourism has become a US$60 billion a year business and is growing by 20% a year" (MacReady 2007).

If healthcare in the past has first and foremost been a national issue, in more recent years, substantial changes in and around access to healthcare information and treatments, together with a growing diversity of national regulatory forces relating to both demand (access, delivery, and pricing) and supply (research, approval, and application) of therapies have contributed to a transformation of the global healthcare landscape. In the following, we will suggest that there are a number of factors, which have contributed to making stem cell therapy a regular feature of the 'treatment mix' that organises global medical tourism and the health travel industry. These include the controversies that have surrounded (especially embryonic) stem cell research internationally in recent years, the status of stem cell treatment as an 'experimental therapy' which is still "a long way off", its claims to be able to treat hitherto untreatable conditions, the formation of patient networks, falling travel costs as well as the establishment of high quality medical facilities combined with undeveloped or non-existent national regulations. All of these factors have fuelled a growing global stem cell tourism economy. How have so many individuals bought into the promises made in the stem cell economy?

Importantly, we will argue that rather than sticking to customary North/South or East/West dichotomies in an analysis of stem cell tourism, it is more helpful to look at the particularities associated with pre-clinical research into and clinical application of stem cells. These particularities play out in different ways in different geo-political, regulatory and cultural localities. We start by distinguishing between two different 'worlds' when it comes to stem cell therapy – a pre-clinical/clinical 'world' of scientific research according to rigorous mechanism-of-action investigations, quality controls and clinical trial protocols on the one hand, and a 'shadier' 'world' of experimental therapies being offered to patients at often very high costs. We then go

on to discuss two cases, one from the Netherlands and another from China. In particular we show how there are common tactics at stake in the mobilisation of patients, including: individual testimonials from patients as 'evidence of efficacy' which are disseminated using internet video-streaming technologies and web diaries; the invocation of frontier science as a promise in the face of incurable conditions; and the expressly commercialised form of stem cell therapy as a 'treatment package'. The empirical material stems from scientific documents, interviews with regulators and scientists, media reports as well as websites that advertise stem cell therapy. Data has also been collected during a series of workshops and conferences organised by BIONET in China (Beijing, Shanghai and Changsha) on the topics of reproductive and regenerative medicine which were attended by leading stem cell experts from Europe and China (BIONET 2007).

So far, yet so close

Although bone marrow transplants (which harness the regenerative capacities of haematopoietic stem cells) have become routine in the treatment of leukaemia and other blood disorders, research into stem cell therapy is for the most part still pre-clinical (feasibility, mechanism of action and toxicity research). There are over 2,100 ongoing trials with stem cells, but most of these trials focus on the development of devices (e.g. markers, cell populations, growth factors or support structures for tissue engineering) for therapy rather than therapy itself. In the European Union, stem cell therapy falls under the *Regulation on Advanced Therapies: Tissue Engineering, Cell Therapy and Gene Therapy* which came into force on 30 December 2007 (European Commission 2007). The regulation seeks to set up a system of scientific evaluation (safety, quality and efficacy of advanced therapies), the creation of a traceability system for monitoring starting materials (cell lines), products and patients and a central approach to marketing authorisation of products across the EU. Still, for the most part, it is stem cell research rather than routinised clinical application of stem cells that is taking place today.

Of the many different forms of stem cell research, it is human embryonic stem cell (hESC) research that has become most notorious and controversial internationally because of ethical and moral debates surrounding the use and/or creation of human embryos for research or therapeutic purposes (see Franklin 2006). Embryonic stem cells are seen as especially promising because of their pluripotent ability to become any kind of cell in the human body. However, there are currently only six trials worldwide using donor material aiming at better understanding of embryonic stem cell repair mechanisms in humans, in Israel (at the Hadassah Medical Organization) and in the United States (Stanford University, UCI and the National Cancer Institute Maryland). The California-based Geron Corporation has for some years announced that FDA-approved clinical trials are imminent using oligodendrocyte progenitor cells cultured from embryonic stem cells in the treatment of spinal cord injuries by injecting them "directly into the injured spinal cord site" (Edwards 2006). But these trials have been delayed by the FDA's cell and tissue therapy branch who have warned that "[t]he agency also may require longer trials of stem-cell therapies than it does for conventional drugs" (Waters 2008).

So, when it comes to clinical research on actual stem cell therapies today, it is by far what are known as adult or somatic stem cells that are being investigated and used. These include haematopoietic stem cells (sourced from bone marrow, umbilical cord

or placenta), mesenchymal stem cells (sourced from bone marrow), neural stem cells (sourced from brain tissue) and olfactory ensheathing cells (sourced from the nose). Although some adult stem cells are pluripotent (e.g. those found in umbilical cord blood), most are multipotent which is to say their regenerative capacities are restricted to the kinds of tissues they are sourced from. For the purposes of therapy, adult or somatic stem cells can be sourced autologously (from the same person into which they will be transplanted after *in vitro* cultivation), from donors (umbilical cord or peripheral blood) or from foetuses (aborted foetal tissues), which, in the latter two cases, raises the problem of possible immunological rejection by recipients.

What is important to point out is that the move from 'bench to bedside' (as basic stem cell research is translated into therapeutic application) is considered by most researchers to be in very early stages. As recently put by the Department of Health in the United Kingdom: "Much stem cell research is still in its infancy, and there is a long way to go before treatments are developed, but it has the potential to revolutionise medicine in this century in the way that antibiotics did in the last" (BBC News Online 2006a). The reasons for this are twofold. First of all, there is little understanding of stem cells' 'mechanisms of action' if and when they repair or regenerate damaged human tissues. Secondly, there are a number of difficulties related to ensuring that stem cell therapies are standardized and of 'clinical grade' quality, which are both requisites for clinical trials.

Stem cell scientist Jack Price from King's College London has recently argued that pluripotentiality may well be less significant than previously thought. Alternative modes of action might include, for example, induced plasticity mechanisms, anti-inflammatory mechanisms or immunomodulatory mechanisms. Nevertheless, he also argues that this uncertainty should not necessarily hinder clinical research:

> You may not at the outset have a defined clinical mechanism for the therapy, by the end of the study you will certainly know more but you still might not have a very refined mechanistic understanding. Why don't regulatory authorities demand this? Why don't they demand you understand the mechanism before you go to the clinic? Because it is too high a hurdle and too imprecise a hurdle, and we would end up denying safe, efficacious medicines to sufferers who need them. You might think you know how a medicine works, but you might be wrong and a thorough scientific proof might take twenty years. The process is more trustworthy – experience tells us that if a medicine is demonstrably safe and efficacious then we have a basis on which to proceed with care. (Price 2007)

What is more important than having a complete understanding of precise mechanisms of action, it is argued, is ensuring the purity (safety), type (source) and potency (efficacy) of stem-cell-based products in a consistent and standardized way. And as put in the UK Code of Practice for Tissue Banks, "in order to provide safe tissue of reliable quality, current good practice standards must be observed in the selection of donors, retrieval of tissues, testing, processing, storage and delivery of finished tissues" (Department of Health 2001). Establishing such systems of quality control is a very expensive endeavour as it requires avoiding contamination during movements of biological samples from clinic (sourcing) to laboratory (processing, cultivation, storage) and back to clinic (therapy). What is more, the templates for these quality

control systems and good manufacturing practices are almost entirely imported from the pharmaceutical industry. Indeed the analogy is often made by stem cell researchers themselves, such as CEO of Geron Thomas Okarma: "living cells will be tomorrow's pharmaceuticals" (Associated Press 2001). However, as pointed out by Halme and Kessler "unlike pharmaceutical products, many stem-cell-based products may originate in academic laboratories where researchers are unfamiliar with the applicable regulations" (2006). And hence, one can not always be sure whether patients are having 'research grade' or 'clinical grade' stem cells injected into them.

Company	Location	Conditions	Patients	Costs	Therapies
Xcell-Center	Cologne, Germany	diabetes, stroke, cardiovascular diseases, spinal cord injuries, MS, ALS, Parkinson's, Alzheimer's, arthrosis	+400	+9,000 US$	autologous, bone marrow stem cells
Hadassah University Hospital	Jerusalem, Israel	ALS, MS (clinical trial)	25	NA	autologous, bone marrow stem cells
StemCell Biotherapy	Guatemala, Mexico, U.S.A.	25, including spinal cord injury, cancer, Alzheimer's, MS, ALS, autism, AIDS (HIV) and ageing	+200	10,000 US$	allogenic, differentiated stem cell lines from cord blood and adult stem cells
Shenzhen BEIKE Biotech	Shenzhen, China (HQ), Thailand	Alzheimer's, arteriosclerosis, ataxia, autism, vascular diseases, ALS, muscular dystrophy, brain trauma, cerebral palsy, Guillain-Barre, MS and spinal cord injury	+3,000	25,000 US$	umbilical cord blood stem cell
PMC Rotterdam	Netherlands, Belgium	+50, including spinal cord injury, Alzheimer's, Parkinson's, MS, ALS and ageing	+200	18,000-26,000 US$	umbilical cord blood stem cell
ACT	Switzerland	same as PMC	NA	NA	umbilical cord blood stem cells from Pakistan
HSIPL, Tristem	Pakistan	Aplastic Anaemia, Thalassaemia, Sickle Cell Anaemia, Spinal Cord Injury, Degenerative Neurological Disorders such as Parkinsons,	NA	+10,000 US$	"Retrodifferentiated Stem Cell Therapy"

		Alzheimers, Motor Neuron Disease, Multiple Sclerosis, Muscular Dystrophy, Cerebellar Ataxia, Organ (Liver and Kidney) Dysfunction, Hepatitis C, Diabetes Type I and II and Congestive Heart Failure (CHF)			

Table 1: Stem cell therapy sites[2]

Despite these many uncertainties and the spectre of stem cell therapies being a long way off, it is very clear (as any cursory internet search will show you) that "many patients with untreatable debilitating diseases aren't willing to wait and are making their way to far-flung places, where clinics are administering unproven cell therapies to patients who can pay for them" (Baker 2005). The places are not as far-flung as Baker suggests, as clinics throughout the world from America to Europe, Asia and Latin America have profited from what has been described as the 'stem cell craze' (Danilova 2005), offering "tomorrow's medicine today". The list of diseases that these clinics claim can be treated is long, covering spinal cord injuries, brain trauma injuries, degenerative diseases and more. Prices are often hefty, ranging from US$ 10,000-30,000 for treatments consisting of a series of injections (see Table 1). Most of these treatments are based either on umbilical cord blood stem cells or autologous stem cell transplants, although some clinics have offered injections of embryonic stem cells (Enserink 2006).

In most cases, access to treatments is administered via word-of-mouth, patient forums, internet sites as well as doctors acting as brokers for private stem cell treatment companies. People like Dr. Wise Young, known in the stem cell field through his studies on spinal cord injury as well as his treatment of American actor Christopher Reeves who himself became an icon of regenerative medicine, have taken on public roles as "stem cell research activists" by administering patient network websites such as CareCure (http://sci.rutgers.edu/). Through such networks of mobilisation patients are encouraged to apply for treatment by e-mail or phone and companies will often refer to the Good Laboratory Procedures that their clinics follow. Yet, since these treatments are being offered outside of 'traditional' health delivery systems, patients and scientists are hardly able to assess the quality of treatments provided. We will now turn our attention to two cases where stem cell therapies have been offered to patients in the Netherlands and in China.

[2] Derived from Baker (2005), sources: http://www.xcell-center.com/, (Jerusalem Post 2007), http://stemcellbiotherapy.com/, http://www.hsipl.com/, http://stemcellschina.com

"Not intended for human use"

In 2005, the Preventief Medisch Centrum (PMC) in Rotterdam began treating Multiple Sclerosis patients with human cord blood stem cell injections for € 15,000 claiming that they "target cells in a manner specific to an individual's condition" (Sheldon 2006). In their first year, sixty percent of their patients came from the United Kingdom, referred through a 'franchise system'. According to PMC's manager Niels van Gent, stem cell therapy fit very well with his clinic's philosophy of harnessing the body's own healing capacities:

> Stem cells are basically a repair kit. Injections differ from person to person and the doctor finds the acupuncture 'trigger' spots for the injections… We have had some spectacular results, a man from South Africa is walking again after years in a wheelchair. (cited in GMTV 2007)

The multiple sclerosis patients who came for stem cell therapy were often suffering from severe symptoms including difficulty walking, pain, numbness and fatigue. Many of them had exhausted all treatment options and had all but lost hope, a predicament acknowledged by doctors at PMC: "Afterwards you can say it was wrong, it was this or it was that, but at this moment it's our purpose to give people a chance who have no chance at all" (Anneke Matthijssen in Lindsay 2006).

Four such patients were UK citizens from Inverness, Essex, Hythe and High Halden, each of whom suffered from the crippling effects of Multiple Sclerosis leaving them wheelchair-bound or dependent on others. These patients paid between €11,000 and €15,000 to the PMC for a course of three injections at different times in the period November 2005 to May 2006, with one having to borrow money to be able to meet the high costs. Included in their treatment packages was a 'detoxification', medical check-up by a local physician as well as standard blood and urine tests. Their testimonials, which were widely reported in British media (see BBC News Online 2005; Lindsay 2006), range from euphoric to more tempered, yet with a consistent highlighting of hope:

> Within 10 minutes after the treatment I went to the bathroom on my wheelchair, I went to stand up and I thought I was jumping off my chair. It felt absolutely fantastic, brilliant. I thought at first 'this is in my mind', but I spoke to the nurse who told me it happens, they've seen it happen plenty of times. That's the moment where it just filled me with hope for the future. (patient from Inverness, November 2005)

> This really was the last grab, hoping that I could get back to a normal life if my consultant says 'I'm sorry, there is nothing more we can do for you'. (patient from Essex, April 2006)

> I'd lost hope. Now I've got some back, and it makes a fundamental difference to your outlook… I had more strength in my arms to push myself up… I am relishing the way things are progressing, and continuing to improve (patient from High Halden, May 2006)

> Initially I got results, and then when it stopped, I was saying to my husband 'oh it's a con, it's a real con'. But then thinking back there has been some

> improvement, even if it's very slight... So I don't regret going, I just feel sorry for the people that hoped a lot more than I did. (patient from Hythe, September 2006)

Such media stories were of course not bad for business at the PMC with headlines like "MS woman in stem cell therapy hope", "Stem cell therapy helps MS woman" and "Stem cells offer hope to MS man". But they also led to closer scrutiny of claims being made and clinical practices being used. In May 2006, Jack Price went on record saying:

> What concerns me is the companies who are offering stem cell treatment commercially are not conducting proper trials… You can't judge this kind of therapy by this kind of anecdote even if there were 10 or 20 or 100 people who said they felt better. A company that takes anyone who can afford the treatment is simply never going to tell us the proper answer. (cited in BBC News Online 2006b)

And a few months later, a number of UK-based scientists wrote an open letter to *The Times*, one of the main daily newspapers, stating that:

> Extravagant claims have recently been made of success for 'stem cell' treatments available only abroad… We advise those who are desperate for cures or attracted to cosmetic therapy to be wary of claims being made by clinics offering these treatments. (Henderson 2006)

By October 2006, the Netherlands Health Care Inspectorate (*Inspectie voor de Gezondheidszorg*) temporarily stopped PMC's stem cell treatments following the concerns that had been raised by scientists in the Netherlands and abroad, but also following reports that a patient had suffered a "serious acute allergic reaction" after stem cell treatment at the clinic (Sheldon 2006). According to an Inspectorate report the clinic acted irresponsibly[3] in regard to patient safety since it was "unable to demonstrate the origin, suitability, and safety" of its stem cells (van der Plas-Huisken 2006). Indeed an investigation by the BBC television show Newsnight showed that these stem cells were actually 'research grade' umbilical cord blood cells "not intended for use in humans" ordered via a company in California. Presented with this information, Chief Executive of the Medical Research Council in the United Kingdom, Colin Blakemore said:

> I'm shocked. I am taking what you tell me as true, and my first concern is for the patients, very vulnerable, obviously desperate for treatments and that desperation is being exploited by charlatans it seems to me. (in Watts 2006)

[3] As stated in the 1996 "Care Institutions Quality Act", "institutions must provide 'responsible care' i.e. care that is characterized as being of a good level, effective, suitable, patient oriented, and geared to the real needs of the patient" and "must make clear what they are doing to achieve and maintain that 'responsible care.'" Furthermore, they "must systematically protect and, improve the quality of care they provide", and have to "publish an annual report that elaborates the quality control policies they have applied and reports on the quality of care they have delivered" (Ministry of Health 2006a).

So, how had PMC been able to treat so many patients over the course of more than a year? An official from the Ministry of Health in the Netherlands explained:

> According to the legislation there was no easy way to prevent that. The CCMO is not involved in that, because those companies will give cellular treatment as accepted treatment or experimental treatment but they do not present it as research. […] The way they present it, the way they present it to the patients and how they present it to the authorities. If it is research, they have to write a research protocol and it has to be approved by the Central Committee. If they present it as a treatment, it is more difficult: the Central Committee is not involved and the only thing legislators and Inspectorate of Health can do is to check whether the physicians are qualified, whether the material, documents in terms of quality control is ok, and this is what they did. They went to those companies and clinics, private clinics, and did an investigation whether the material is ok, whether the source was ok, whether the quality control was ok and if it is not, they can close it. And that is what they did. (Interview with regulator at the ministry of health, May 2007)

In January 2007, the government issued a ban on application of stem cell therapy by private clinics which came into effect in January 2007, not so much because of the claims being made, but more because of the fact that the "safety and quality of the stem cells used […] cannot be established" (Ministry of Health 2006b).

"Improving quality of life"

In additon to PMC in the Netherlands, there are at least another 30 clinics/companies providing stem cell therapy worldwide, with numbers constantly rising (Enserink 2006, see Table 1). Many of these can be found in China, which is seen as having one of the fastest growing patient markets in the world thanks to extensive public and private investment and a booming health biotech industry. Whereas the wealth gap is widening and millions of people in China are excluded from the healthcare system, it is suggested that the health biotech industry offers excellent R&D options, reportedly experiencing growth rates of around 30% a year since the turn of the millennium (Frew, et al. 2008; Goodall, et al. 2006).

Shenzhen Beike Biotechnologies Co. Ltd. (http://www.beikebiotech.com) was floated in July 2005 by Beijing University, Hong Kong University of Science and Technology and Shenzhen City Hall. The company is heavily subsidised by public money in the form of research grants and government investments. In translating stem cell research from the laboratory to the clinic, the company works together with universities in Beijing, Hong Kong, Zhongshan, Guiyang and Zhengzhou. At the end of 2007, the company announced the establishment of a global research hub with a GMP (Good Manufacturing Principles) facility dedicated to stem cell engineering, somatic cell nuclear transfer, reprogramming and monoclonal antibody work, located at Shenzhen Graduate School Campus at Tsinghua University. According to CEO Sean Hu, the company is "already helping thousands of patients with our current umbilical cord stem cell treatments, but this ultra high-tech lab will bring us even closer to our goal of helping millions of patients improve their quality of life and will

ensure that we have more advanced products in our pipeline four to five years out" (Xinhua 2007).

The treatment package consists of the administration of umbilical cord blood, bone marrow or peripheral blood stem cells by injections (either intravenous or into the spinal cord fluid). According to interviews with Beike representatives and the company website, treatable conditions includes Alzheimer's, arteriosclerosis, ataxia, autism, diseases of blood vessels, amyotrophic lateral sclerosis, muscular dystrophy, brain trauma, cerebral palsy, Guillain-Barre, multiple sclerosis and spinal cord injury (Goodall, et al. 2006). Beike provides only the "therapeutic stem cell technology" for hospitals; company technicians and researchers prepare the cells, which are then administered by local physicians under company guidance at a partner hospital. Currently, Beike has eleven partner hospitals (Haikou, Qingdao, Hangzhou, Shenyang, Shenzhen, Beijing) in China (www.stemcellschina.com) and one in Thailand (http://www.stemcellguidance.com) under contract. Since 2005, the company has also opened branches in Europe (www.beike.ch), Turkey and the US to facilitate access to the global stem cell therapy market.

In October 2007, Beike announced that their treatments were both safe and efficacious based on their experience with more than 2,000 patients treated. According to Kirshner Ross-Vaden, the vice-president of the company's foreign patient relations:

> Beike's greatest strength, and what differentiates it from other research groups, is that Beike specializes in clinical applications… There are many people in countries around the world who could have a better quality of life and live longer with this technology, but they don't have the chance because of politics, religion and bureaucracy. (The St. Augustine Record 2007)

This is the promise of stem cells, that they will not just prolong life, but (perhaps more importantly in the case of degenerative diseases, spinal cord injuries or brain trauma) also improve the *quality of life* of patients. The distinction between quality and longevity is crucial. In the Dutch cases discussed above as well as in the cases discussed here in a Chinese context, it is clear that patients have travelled not so much to lengthen their lives as to "get something back" or to "get back to a normal life". The promise of regeneration concerns exactly this, improving the ways in which sufferers of certain conditions experience, cope with and ultimately take advantage of their lives (cf. Wahlberg 2007): to be able to *live* a 'normal life'.

Beike's main website for recruiting prospective foreign patients is www.stemcellschina.com which contains a number of patient testimonials using patient diaries as well as footage of interviews before and after treatment which can be viewed online. Patients have travelled to China from America, Canada, the United Kingdom, Switzerland, Hungary and more. Again, individual cases have been reported widely in the media including that of a young man from Montana, America disabled in a car crash in 2004. Having paid $20,000 with borrowed money for stem cell injections at a Beike hospital in China, he claims to have regained use of his left hand as a result: "I just wanted something back, no matter what it was" (Bodeen 2008). His father wrote on their patient blog: "you gave us more than medicine, you

gave us hope, you gave us memories, and you gave us friendships" (China Stem Cell News 2006).

A couple from Florida also recently made the trip to China to get five injections of stem cells at $23,000 for their daughter who suffers from optic nerve hypoplasia:

> None of [our] specialists had heard of the stem cells, of what they're doing here. They didn't believe it would work. They told me not to expect anything to happen out of it. (Lim 2008)

On their final day in China, following the treatment, the parents wrote an excited entry into their patient experience blog:

> TODAY IS OUR LAST DAY WE WILL ARIVE[4] HOME ON FRIDAY AT 7:30 AT NIGHT. ALSO WE HAVE GREAT NEWS THAT CAME ON OUR LAST DAY!!! THIS MORNING THE DOCTORS CAME IN TO DO A FINALE CHECK UP ON [OUR DAUGHTER] WE HAD JUST WOKEN UP AND WAS FEADING [HER] WHEN THE DOCTORS CAME IN THEY BEGAN THERE LIGHT TEST WHEN [SHE] STARTED FOLLOWING THE LIGHT INSTEAD OF HER PUPILS JUST REACTING AND THATS ALL NOW SHE WAS FOLLOWING THE LIGHT THE DOCTORS GOT EXCITED STARTED SAYING SHE CAN FOLOW THE LIGHT AND I WAS IN TEARS SHE COULDE ACTUALLY SEE THE LIGHT AND FOLLOW IT. I IMEDIATLY STARTED PRAYING THANKING HIM. SO WHEN THE DOCTORS LEFT THE ROOM [WE] TURNED OFF THE LIGHTS AND GOT OUT THIS BALL THAT WE HAD GOT FOR HER THAT LIGHTS UP SO WE PUT IT TO THE SIDE OF HER AND SHE TURNED TO LOOK AT IT I CANT EXPLAINE THE WAY THIS MAKES ME FEEL. (China Stem Cell News 2008)

These are of course anecdotal cases, yet Beike's CEO Sean Hu is adamant that they are providing foreign patients with a responsible and ethical service: "In the clinical areas, we know there are improvements. We don't know the mechanism behind it... [but] I can say I changed the life of these patients. Now they get their vision back. They went from completely blind, now they can see stuff. You think that's ethical or nonethical [sic]?" (Bodeen 2008).

Nevertheless, there is also scepticism about claims being made by Beike and many other companies offering stem cell treatments. In China, so-called "innovative therapies" do not require approval from the SFDA although they do require institutional ethical review board approval. Jing Naihe, a member of the Chinese Academy of Sciences has suggested that "money is mainly behind [these treatments]" (Lim 2008) and Hu Qingli, a member of the Ministry of Health's Ethics Committee has highlighted concern that a number of companies are "commercialising unsubstantiated medical claims" (BIONET 2009).

[4] This is a direct quote from the patient blog, we have left spelling and syntax as is.

Governing new therapies

In both China and the Netherlands, indeed in most countries, the policy field with regards to new stem cell treatments remains uncertain and has thus opened up the possibility for private companies to offer "experimental treatments" as established clinical applications. This raises numerous ethical issues since it is not clear in which circumstances it is in a patient's best interest to offer him/her an experimental therapy. Since experimental therapy is not research, it falls out of the purview of research ethics review. Instead, clinicians are left to make judgements in their consultations with patients, many of which, as we have seen, will suffer from 'untreatable' conditions.

Another set of ethical issues emerges from questions around how stem cell therapies – as 'live', biodynamic therapies – should be regulated. It is clear that when it comes to clinical application of therapies, national regulatory systems have primarily been built up around pharmaceuticals. The templates for Good Manufacturing Principles as well as safety, quality and efficacy requirements are in large part being derived from pharmaceutical legislation. But there are of course substantial differences between dynamic, living cells and stable, standardisable chemical compounds. New regulations are being developed, for example, in the United Kingdom, France and at the European Union level (European Commission 2007; Sheridan 2006). Also, standardisation initiatives such as the UK Stem Cell Bank are working "to enhance the safety of biological medicines through the provision of reference materials for assays, by development of underpinning research on product safety and quality and finally by batch-release testing of products" (2008). Still, numerous open questions remain: how should stem cell lines be defined, what makes a stem cell line 'safe' and of 'high quality', how should mechanisms of oversight be organised in a context of global movement of biological samples, etc.?

The example of PMC showed how authorities did not act until there was certain evidence of problems of safety, and als evidence that clinical services did not comply with the standards included in local laws. In the Dutch case, the key issue at stake for regulators was not the claims being made by doctors at PMC, rather it was guaranteeing patient safety by ensuring that the quality of the cells used in therapy were clinical grade. There seems to be a balancing of the patient's right for access to new therapies when available on the one hand, and ensuring safety and quality of the offered treatments on the other.

Indeed, the European Commission's recent *Regulation on Advanced Therapies* is primarily concerned with the safety and quality of 'investigational medicinal products' (such as stem cell lines), much more so than with evidence of efficacy. There is an interesting parallel to be drawn from negotiations about the status of 'traditional herbal medicinal products' in the European Union a few years earlier. After much debate, it was finally agreed by Member States in Directive 2004/24/EC that clinical trials are not needed to back up claims of traditional use "in so far as the efficacy of the medicinal product is *plausible*". At the same time, it was also maintained that "even a long tradition does not exclude the possibility that there may be concerns with regard to the product's safety… the quality aspect of the medicinal product is independent of its traditional use so that no derogation should be made with regard to the necessary physico-chemical, biological and microbiological tests" (European Council 2004). Similarly, the EC argues that while there may be some

exceptions as regards to evidence of efficacy and modes of action for stem cell therapies, there should be no such derogation with regard to the safety and quality of stem cell lines.

As we have seen, it is very often argued that, since innovative therapies will often (almost by definition) be developed for hitherto untreatable conditions, desperation can make patients very vulnerable targets for those whose motives may not be medical. Follow-up studies on stem cell tourists have suggested that experimental therapies advertised by private companies based on anecdotal patient experiences often do not hold their promise as to the actual long-term effects of the treatments (Dobkin, et al. 2007; Dobkin, et al. 2006). Currently ongoing clinical trials using injection of cord blood stem cells target solely leukaemia and other blood-related diseases, yet companies claim to treat a broad range of very different conditions with the same clinical procedures. What is more, even if some kind of clinical effects can be documented, stem cell therapies are of course not miracle cures. Some doctors have suggested that a 'placebo effect' triggered by intense feelings of hope may account for a large part of any treatment effects: "We can give people a sugar pill and tell them it will get rid of all their pain and they'll insist that it works, so I'm highly doubtful of testimonials. If I just spent $30,000 on a procedure, I would want to say it worked too" (White 2007). And finally, very little is known at this stage about possible adverse effects which may result.

Another issue in governing global stem cell therapeutics is linked to "overcoming the barrier of hope" while at the same time ensuring that scientific and clinical practice is not subject to fraud and misconduct. Claims of scientific breakthroughs and miraculous therapies can fuel the pressure put on governments by desperate patients, yet they can also turn out to have been based on unproven or even fraudulent data (Gottweis and Triendl 2006). Moreover, such practices can lead to undue advantages in scientific competition, drawing funding or policy into a direction that makes "good research" more difficult and raising an atmosphere of suspicion against science in society. Regulators are charged with attempting to find a balance between promoting therapeutic innovation and ensuring that vulnerable patients are protected.

Finally, the commercialisation of pharmaceutical research is by now well-documented. Similarly, it is fair to say that those 'translated' stem cell therapies that are on offer to patients willing and able to pay for them today are provided by commercial enterprises in the form of treatment packages. However 'personalised' or 'tailored' to individual patients it is claimed that these therapies are, in reality stem cell therapy today consists of a rather 'crude' course of 3-5 injections at high prices. And although companies will often reassure patients that their stem cells are of high quality, there are no guarantees, especially since regulatory frameworks and oversight mechanisms are as yet not in place although general principles of best practice can provide orientation.

Conclusions

Global stem cell tourism is a reality. As we have shown here, it is fuelled by a combination of patient desperation, hopes, regulatory uncertainty, low cost travel and the emergence of biotech industries eager to translate laboratory research into therapy and revenue. Stem cell research is a field saturated with hope and promise for millions of patients who suffer from untreatable diseases and injuries. This is evident from

patient accounts as well as the marketing tactics of companies. Yet, therapy is considered by most scientists to be "a long way off", notwithstanding that it is on offer today to any one who is willing and able to pay for it.

As a result, stem cell research is a field also surrounded by fears and sober scepticism. A good part of these fears (and controversies) have related to the use of human embryos as well as human-animal hybrids in research. Yet, with somatic stem cell therapy increasingly available around the world, these fears now also concern the vulnerability and safety of desperate patients.

Just as health tourism is transforming the global landscape of healthcare, so too is it becoming apparent that national regulatory solutions cannot stop citizens from travelling to other countries to get access to treatments that are not available or allowed at home. Desperation, it seems, travels.

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Research in Humans in China: The Role of Industry in Governance and Protection of Research Participants

Detlef Niese[1]

Introduction

More and more frequently globally operating pharmaceutical companies move research and development activities to countries in Latin America, Eastern Europe and Asia which in the past were less often involved in global development programs. In Asia, specifically India and now even more China appear to attract the clinical research departments of pharmaceutical companies in the US and Europe. There are multiple reasons for companies to expand their research to these regions and countries including access to large, untreated or "treatment naïve" patient populations [2], increasing cost pressure in "traditional" regions, changing living conditions and disease epidemiology, with the consequence of increasing use of Western type medicines, a large talent pool for R&D as well as incentives by governments for drug developers (taxes, occupational cost). This development receives increasing attention by the public and is subject to growing concern with ethicists, journalists, regulatory authorities and the interested public at large [3] [4]. There is broadly held concern that the lack of an appropriately developed legal and regulatory framework for clinical research as well as economic and societal pressures may leave research participants in China and other emerging economies less protected than in the traditional research sites in Europe and in the US. As research related costs tend to be substantially lower in such countries, there is particular concern that companies may exploit the perceived weaknesses of the legal and economic systems for the benefit of cost saving and increasing profits. It is also being argued that industry would use emerging economies to cheaply develop products for the Western markets and that benefits from such research would not be fairly shared with the research participants who contributed to making them possible. Western regulatory authorities such as the US Federal Food and Drug Administration (FDA), the European Medicines Agency (EMEA) and the Competent Authorities of the European Member States have noticed this development as well and have expressed concern regarding the validity of data generated by research sites which are perceived to be less experienced. They intensify inspections in those countries and also the interaction with regulators such as the Chinese State Food and Drug Administration (SFDA). Amongst other countries the US FDA

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[1] Disclaimer: This article represents solely the views of the author. It does not necessarily represent the positions or views of Novartis Pharma AG or any other Novartis company, its management or employees.

[2] Sax PE et al.: Should resistance testing be performed for treatment-naive HIV-infected patients? A cost-effectiveness analysis Clin Infect Dis. 2005 Nov 1;41(9):1316-23. Epub 2005 Sep 23.

[3] Studdert DM & Brennan TA: Clinical trials in developing countries: scientific and ethical issues MJA 169: 545-548 (1998).

[4] Glickmann SW et al: Ethical and Scientific Implications of the Globalization of Clinical Research N Engl J Med 360;8:_816-823 (2009).

recently established local offices in Beijing[5]. The Chinese government implemented the standards of Good Clinical Practice for Clinical Research during the 1990s and today requires that hospitals to be state certified if they wish to engage in clinical research. In contrast to the perception by the critical public, globally operating pharmaceutical companies also have a strong interest in an ethically and scientifically sound conduct of their clinical research programs.

With the emergence of new scientific and clinical disciplines such as Pharmacogenetics and Translational Medicine over the last decade, the drug development process has changed substantially. The completion of the Human Genome Project gave rise to expectations that a deepened understanding of the molecular mechanisms of disease would help to identify new targets for medicines and would allow to tailor medicines to the individual patient. Such research requires access to large collections of biological samples and related personal data of the donors, so called "Biobanks". While many principles for conducting clinical research also apply to studies with identifiable human samples and data, large biobanks represent actors, including pharmaceutical researchers, with specific ethical, legal, and quality assurance challenges. Therefore, governance and quality assurance as well as training and education of clinical researchers involved in their programs are of significant importance for development organizations in pharmaceutical companies.

China is on the move

Is there need for China and Chinese patients to participate in clinical trials with Western medicines? Like many other emerging economies China is undergoing fast and substantial societal and economic change from an agricultural to an urban, industrial society. More and more of its citizens live under the same conditions as their counterparts in industrialized countries, have access to high quality food and are able to buy and use cars. As a consequence, many diseases which were considered "Western Diseases" or diseases of the developed world are now a growing health threat to the Chinese population. Such diseases include hypertension, vascular disease including myocardial infarction and stroke, diabetes, obesity and depression. At the same time, the use of Western medicines is steadily increasing. With 56 different ethnic groups and a population of 1.3 billion, China is not only a huge country but it is also ethnically and genetically highly diverse. Therefore it cannot always be expected that medicines can be used solely on the basis of data generated in Europe and the US (see also ICH guideline E5 on Ethnic Sensitivity)[6]. Infectious diseases like tuberculosis and hepatitis B continue to be major concerns for the public health care system. While China has a steadily growing demand for Western medicines, Chinese scientists and clinical researchers are joining their colleagues in the US, Europe and other parts of the world in their search for more effective and safer medicines.

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[5] Food and Drug Administration: Human Health Services: HHS Preparing to Open FDA Offices in China, India, Europe, and Latin America (October 16,2008) http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm153679.htm

[6] International Conference On Harmonisation Of Technical Requirements For Registration Of Pharmaceuticals For Human Use Guideline E5(R1): Ethnic Factors in the Acceptability of Foreign Clinical Data http://www.ich.org/LOB/media/MEDIA481.pdf retrieved 5.October 2009

Governing clinical research ethics in China

It takes efforts from all partners in health care including but not restricted to doctors, nurses, industry, politicians, regulators, ethicists and the media to ensure that research in human beings is conducted to internationally agreed ethical and scientific principles. Such principles are commonly described as "*Good Clinical Practice (GCP)*". They were first formulated as a reaction to the cruelties in the name of science during the Second World War, with the *Nuremberg Code*[7] in 1949, later further developed in 1964 by the World Medical Association in the "Declaration of Helsinki" which was last revised in 2008[8], the *Belmont Report* in 1979[9], the "Bioethics Convention" of the Council of Europe from 1997[10], the CIOMS/WHO Clinical Trial guidelines from 2001[11] and others. The Declaration of Helsinki also formed the basis for the GCP guideline (1996)[12] of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). This guideline was transposed into drug regulations in many countries. However, clinical research governance is not only a responsibility of the regulators, ethicists and law makers, clinical investigators and sponsors. Rather, whether and how research participants are well protected and whether the results of human research studies are scientifically robust and credible also depends on the quality and structure of the health care system in general and how access to health care is organized for those who need it.

The concept of GCP was introduced to China as a consequence of the opening of the country to foreign clinical researchers and pharmaceutical companies and with the increasing number of clinical trials conducted by these parties. With the amendment

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[7] The Nuremberg Allied Military Court: The Nuremburg Code: in Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10, Vol. 2, pp. 181-182.. Washington, D.C.: U.S. Government Printing Office, 1949. Reprinted on http://ohsr.od.nih.gov/guidelines/nuremberg.html retrieved September 23,2009

[8] World Medical Association: Declaration Of Helsinki: Ethical Principles for Medical Research Involving Human Subjects, 8th revision World medical Assembly Seoul (2008), http://www.wma.net/e/policy/b3.htm, retrieved September 20, 2009

[9] The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research: The Belmont Report: Ethical Principles and Guidelines for the protection of human subjects of research April 18, 1979 http://ohsr.od.nih.gov/guidelines/belmont.html retrieved September 20, 2009

[10] Council of Europe: Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine (1997) http://conventions.coe.int/Treaty/EN/Treaties/html/164.htm retrieved September 20, 2009

[11] Council for International Organizations of Medical Sciences (CIOMS): International Ethical Guidelines for Biomedical Research Involving Human Subjects (2002) http://www.cioms.ch/frame_guidelines_nov_2002.htm retrieved September 20, 2009

[12] International Conference On Harmonisation Of Technical Requirements For Registration Of Pharmaceuticals For Human Use: Guideline For Good Clinical Practice E6(R1) (1996) http://www.ich.org/LOB/media/MEDIA482.pdf retrieved September 230,2009

in 1999 of the Drug regulation from 1984[13], the Chinese government required the implementation of quality standards. It also led to the establishment of an independent regulatory authority which later became the State Food and Drug Administration (SFDA) to regulate such standards. The SFDA order No.3[14] defining GCP for conducting clinical trials in China went into force 1 September 2003. Since 19 February 2004, only GCP-certified hospitals are authorized to conduct clinical trials, Further, ethical review capacity continues to grow and Chinese ethicists and researchers engage in dialogue with their partners abroad[15] [16]. Capacity in ethical review of research proposals is critical to ensure quality and ethical conduct of research projects in human subjects. The National Center for AIDS and STD prevention (NCAIDS) of the China Center for Disease Control (China CDC) published its first guidelines for Ethics Committees in 2003[17]. In 2005, a Chinese delegation, consisting of members of Chinese Ethics Review committees, visited Europe and the US and met with EC's and IRB's in these countries to learn about their processes. The Peking University Institute for Medical Ethics organized a Workshop which was held in Shanghai in 2006. Members of more than 60 Chinese Ethics committees, representatives of FERCAP, the Asia-Pacific Forum of the Strategic Initiative for building Capacity for Ethical Review (SIDCER), the EMEA, the FDA and the Chinese SFDA participated in this conference.

The role of the pharmaceutical industry in governing research ethics

In contrast to widely held positions, pharmaceutical companies as sponsors of clinical research have a vested interest in adherence by their staff and their partners to internationally agreed GCP principles. Western pharmaceutical companies together with Western academic researchers were indeed major drivers for introducing such principles to China. Only through the compliance of their development programs with strict ethical and quality standards, can they expect regulatory authorities in the US, Europe and Japan to accept data from such trials proving that their products are safe and effective. Major scandals involving respected academic institutions in the US and Chinese partners were strong evidence that dual ethical standards would not be accepted. Still, there is widespread public perception that the pharmaceutical industry

[13] National Peoples Congress China: Law on the Administration of Drugs. Adopted September 20, 1984 at the 7th meeting of the Standing Committee of the 6th National People's Congress, Amended Feb.28, 2001 at the 20th meeting of the Standing Committee of the 9th National Peoples' Congress Presidential Order No.45. Retrieved from James M Zimmermann: China Law Deskbook, A legal Guide for Foreign Invested Enterprises Second Edition (2005) www.abanet.org

[14] State Food and Drug Administration: Order No. 3 on Good Clinical Practice (2003) http://www.bioon.com/drug/chemdrug/243155.shtml retrieved September 20,2009

[15] BioNet: A Chinese-European Project on Research governance in china: Final Report http://www.bionet-china.org/pdfs/BIONET_Final_Report.pdf retrieved 5.10.2009

[16] Hennig W., Bioethics in China: Although national guidelines are in place, their implementation remains difficult EMBO Rep. 2006 September; 7(9): 850–854. retrieved from http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1559670 October 5, 2009

[17] Ministery of Health, China: Ministry of Health Procedures for Ethical Review of Human Biomedical Research (Provisional)(2003) retrieved from www.chinaaids.cn/worknet/irb/doc/t6_en.doc 5.October 2009

would compromise research quality and the well being of research participants for the benefit of higher profits. It is for this reason that the expansion by internationally operating pharmaceutical companies of clinical trial activities to countries like India and China gives rise to ethical concerns. Sure, costs in these countries are much lower, the patient base is much larger and access to treatment naïve trial patients is much easier than in the traditional trial sites in the US, Europe and Japan. Major hospitals in the big centers around the country can conduct clinical trials according to the same scientific and ethical standards but for much lower cost than in most Western countries. Patients in the big cities are as well educated as their Western counterparts. However, with a rapidly growing need for testing new drugs needed by Chinese patients, more and more hospitals with less experience and training will have to become involved in clinical trials. These hospitals often recruit their patients from more rural areas who often are less educated. Such expansion of clinical research requires significant investments and precautions by industrial sponsors to ensure that high scientific and ethical standards are maintained.

While there is broad agreement internationally on many fundamental principles of clinical trial ethics, ethical values are not necessarily global. Rather, they have their roots in local culture and history. In a huge and ethnically diverse country like China there may even be some differences from region to region. Also the medical tradition in China differs substantially from the West. Western companies conducting clinical trials in China are therefore well advised if they work closely with Chinese experts to better understand the impact of local culture and to adjust the development programs to the needs of Chinese people where necessary and to the extent possible. Typical examples of such differences are the importance of consultation with the family as part of the informed consent process and the impact of the Chinese one child policy on pediatric development. While there is a need to pay respect to local culture and values, such respect should not serve to justify disregarding individual rights and internationally accepted principles of Good Clinical Practice.

Protection of research participants in industry sponsored trials

Until 1984, a comprehensive regulatory framework for medicinal products did not exist in China and clinical research according to Western standards was unknown to Traditional Chinese Medicine (TCM). However, following the introduction of the Chinese Drug law in 1984, and its amendment in 2001, a legal and regulatory framework for conducting clinical trials in China was rapidly implemented and more and more adapted to existing internationally agreed standards. Nevertheless, the concept of quality management in general and Good Clinical Practice specifically do not have a long tradition with clinical investigators in China. A reasonable number of hospitals received GCP certification from the SFDA. However, healthcare according to Western standards is still primarily found in major cities and hospitals. Respect to the confidentiality of personal health information and privacy have a different tradition in China compared to most Western countries. Further challenges include restrictions for exporting biological samples, unclear accountability of investigators, insufficient training of local staff, lack of qualified/experienced clinical trial monitors and project managers, limited logistic support, and local medical practice, as well as cultural and language barriers. Such challenges led major Western regulatory authorities like the US FDA and the European regulatory authorities and the European Medicines Agency to question the validity of clinical trial data generated in China and other emerging countries. Increasing inspection activities and the opening of an office

in China by the US Food and Drug Administration are consequences of such concerns. Indeed, competition is growing for the limited number of research sites with state of the art experience in clinical research conduct and new and less experienced sites have to be recruited for the growing number of clinical trials in China. Therefore, it may not be enough for internationally operating pharmaceutical companies to only comply with the legal and regulatory requirements in China. In addition to strictly complying with legal requirements they may decide to apply their own global policies and Standard Operating Procedures which reflect the internationally accepted principles of Good Clinical Practice even if not all of them are stipulated by local law. This will ensure that research participants are well protected and that the conduct of research lives up to US and EU standards. Such best practices include careful selection of research sites and investigators, pre-trial audits, training programs, and continued professional education of their international staff (see Table 1). Those responsibilities also apply to contractors who may assume responsibility for some or all tasks of the trial sponsor.

Quality in clinical trials and ethical review

Ethical review of research studies in human beings has existed in China since the 1990s. A provisional guideline for Ethical Review Committees of the Ministry of Health was implemented in 1998. In 2005, a delegation of the State Food and Drug Administration, along with representatives of major Ethics committees, visited US, European and international organizations to learn more about existing guidelines and processes for ethical review. Support was obtained by the Strategic Initiative for Developing Capacity in Ethical Review (SIDCER) and its Asia-Pacific Forum (FERCAP). Following a workshop in Shanghai in 2006 with participation by major Chinese Ethics Committees, SFDA, European and US GCP inspectors, and a small industry delegation a Chinese Forum for developing Ethical Review Capacity was established. This process is ongoing and is of significant interest to the pharmaceutical industry as well. Ethical review committees have an important role to play in the protection of research participants, assurance of quality in clinical research, and hence in the credibility of data generated by such research.

Self regulation: filling regulatory gaps

Despite many international efforts to harmonize the regulatory requirements for conducting clinical trials, the regulatory standards and requirements continue to differ between countries. For globally operating companies it is important to be able to include in their clinical development programs patients from many countries and regions. Participants in such research programs should enjoy the same level of protection regardless of the country where they are living. For this reason, companies and industry associations have developed global codes, policies and guidelines which should ensure that members of those associations and associates of companies follow common ethical principles and business standards while at the same time obeying the national legislation of those countries where they work. This implies that in case legal requirements for a certain issue are missing in a country like China, or less stringent than the industry or company code, the latter would be followed unless expressly required by local law. Though disclosure of clinical trials is recommended in China, it is still not legally required, therefore IFPMA member companies have, for example, committed themselves by a Joint Industry Position to publicly disclose protocol information of confirmatory phase 2-4 trials, and the results of such clinical trials,

after the products are approved in at least one country. Table 2 provides examples of typical issues which could be subject to self regulation.

Respect to Chinese culture and ethics

In addition to the existing differences in the regulatory systems between China and Western countries, economic conditions, social values and ethical standards also may differ. A variety of approaches were developed to raise the awareness of such differences with clinical researchers and to adapt the conduct of trials to such requirements. In addition to the routine review of research proposals and protocols by independent Ethics Committees, companies may consult with local ethics experts on new research methods, policies and principles of conduct of research and business. This may be done on a case by case basis or by the establishment of a standing committee. An important example is how valid informed consent is obtained. Companies face particular challenges if research subjects are uninsured, do not comprehend the research matter or are under pressure from their family. The Nuremberg Code requires that "*The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision"*. This makes expansion of trials to the rural areas challenging because of a less educated and economically still underprivileged population. In addition to having to adjust the information material to the language and level of understanding of potential research participants (without reducing the content or skipping any important information), the process for informed consent may also require modification. In China there is a strong need for the family to become involved in the decision making in addition to the views of the potential research participant. This may require giving a potential research participant more time to consult with the family. Still, the principle of voluntary informed consent requires that the interest and free will of the potential research participants should prevail.

Benefits to Chinese patients

It is obvious that trials can only be conducted where patients can be found who are suffering from the disease which is targeted by the study drug. This is in fact an important reason for expanding clinical trials to a certain area. However, not all participants in a clinical trial may directly benefit from their participation. Article 33 of the Declaration of Helsinki therefore requires that "*At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study and to share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits"*. Therefore, clinical trials should only be conducted where trial participants would at least have a chance to benefit from the developed product once safety and effectiveness were demonstrated. This is of particular importance if the medicine will be used for serious or life threatening diseases, and where no safe and effective alternative exists. It can never be guaranteed that every medicine which is tested on Chinese patients may eventually reach the Chinese market. The drug may fail, may not be safe or effective in the Chinese population or may otherwise not be approved by Chinese authorities. Nevertheless, if certain principles are followed (see Table 3)

the expansion to China by international pharmaceutical companies of their clinical research activities offers many important benefits to Chinese patients including:

- Evidence of safety and effectiveness of Western medicines in Chinese patients
- Further development of high quality clinical research and clinical medicine in China
- Strengthening global cooperation amongst scientists, medical professionals and regulators for the benefit of patients including in China

Research involving biological material of human origin

During the last decade global drug development underwent a dramatic change. New technologies became available such as genomic sequencing and micro array technology. Genetic technologies gave rise to the expectation that a thorough understanding of the function of the genome of the healthy and diseased organism would finally allow an understanding of the molecular basis of disease. Different patients often respond very differently to the same treatment. Now scientists expect that a molecular understanding of disease would allow tailoring treatment to the needs of individual patients. This concept is known as "*Personalized Medicine*" and requires a very large number of biological samples to be analyzed together with an array of health and personal data of the sample donors. Such collections of human biological samples and related personal data are called "*Biobanks***".** Biobanks and genetic technologies stimulated a new ethical debate which involves researchers worldwide including in China. Chinese researchers are now among the world's leading genetic scientists, and China is establishing large population biobank projects. Research biobanks may be used for other purposes than research as for example to help insurance companies limiting their risks or for criminal investigations. This was well demonstrated when the murderer of the Swedish Minister of External Affairs Anna Lindh was identified in a research biobank in 2003. Also Health insurers are attracted to such research because genetic analyses finally may help to rationalize their risk management. Large population biobanks covering the population of a whole country like Iceland gave rise to specific concerns and triggered the development of several ethical guidelines. In 2004, the European Commission published a report and "25 Recommendations" of an Expert Group on the "Ethical, Societal and Legal Issues of Genetic Testing"[18]. Over the last two years the OECD developed "Guidelines for Human Biobanks and Genetic Research Databases" which are expected to be published in November 2009. Protection of the sample donors is among the most important ethical challenges addressed by all guidelines. Whether, when and how informed consent should be obtained triggers further debates. Article 1 of the Declaration of Helsinki (last revision October 2008) states: *"The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data"* and article 25 more specifically requires

[18] The Independent Expert Group: 25 recommendations on the ethical legal and social implications of genetic testing. European Commission, Brussels 2004 http://ec.europa.eu/research/conferences/2004/genetic/pdf/recommendations_en.pdf retrieved September 20, 2009

that *"For medical research using identifiable human material or data, physicians must normally seek consent for the collection, analysis, storage and/or reuse. There may be situations where consent would be impossible or impractical to obtain for such research or would pose a threat to the validity of the research. In such situations the research may be done only after consideration and approval of a research ethics committee."* Studies using identifiable human biological samples or human health data should follow the same principles as other research on human beings. If samples are anonymized to protect the sample donor, it may not be possible at a later time to ask the donor for consent with research which was not included in the original consent. This situation led to the development of the concept of "*broad consent*" to allow that a precious biological sample may be fully exploited for the benefit of future patients (see also Nuffield Council on Bioethics: Pharmacogenetics Report[19]). *Broad consent* implies that not all details of the future research are defined but may include restrictions (e.g. for criminal investigations or military research). Broad consent should not be confused with a "General Consent" and may be acceptable only under well defined conditions such as anonymisation of samples, and adherence to any restrictions imposed by the sample donor (like restriction of the research area or exclusion of research objectives like military research). Genetic data may be of relevance not only for the sample donor but also for members of his/her family. Such concerns stimulate specific regulations and guidelines for research involving genetic information (see [20]) even if a "genetic exceptionalism" may not be justifiable from a scientist's point of view.

Biobanks as research tools in the pharmaceutical industry

Biobanks are powerful research tools not only for academic research. Pharmacogenetic and genomic research is also expected to address important issues in drug research:

- Identification of biological markers for safety, efficacy or mechanism of action
- Search for disease specific molecular targets
- Identification of defined patient populations
- Understanding the molecular mechanism of diseases

The growing interest of the pharmaceutical industry in genetic/genomic technologies have led to a rapid increase in investment in these technologies by the pharmaceutical industry. Researchers began collecting biological and genetic samples from clinical trial participants and established biobanks within pharmaceutical companies. Detailed personal health data on the trial participants are available from the clinical trial database. The data generated from the biological samples can be combined with the clinical trial data, and allow the identification and development of biological markers of safety and efficacy. Such biomarkers are now being used to further improve

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[19] Nuffield Council on Bioethics**:** Pharmacogenetics: Ethical Issues(September 2003) http://www.nuffieldbioethics.org/go/ourwork/pharmacogenetics/introduction retrieved September 23 2009

[20] World Health Organization Executive Board: Genomics and World Health: Report of the Advisory Committee on Health Research. 112th Session, Agenda Item 4.2. April 2003.

clinical trial designs and to target medicines to patients who are likely to benefit. From very early on researchers from pharmaceutical companies cooperated with regulators and with scientific and ethics organizations like the Nuffield Council on Bioethics in an effort to develop best practices for protecting sample donors while at the same time advancing science.

Regulators like the FDA and later the EMEA recognized the potential of genetic and genomic data collected in the context of clinical trials. In 2003, the FDA issued a *Guidance to Industry* describing a process for voluntary submission of genetic/genomic data[21]. More recently the FDA and the EMEA issued a Joint Guideline on the same topic.[22] Both agencies now cooperate in the interpretation and use of this information. More regulatory agencies are likely to follow.

Governing biobanks in pharmaceutical research

Most biobanks in pharmaceutical companies include samples which were collected in the context of a clinical trial. Table 4 provides an overview on the most important principles to be applied. Two different scenarios may be considered:

1. The biological samples are an essential component of the clinical research protocol (e.g. a validated biological marker for safety or efficacy or the study is conducted to validate such a biological marker)

2. The sample is collected for further research purposes independent of the clinical research protocol

As a general principle, research participants should be informed that with their participation in the clinical study they will also contribute a sample to a biobank. This sample will be used for research which may result in the generation of genetic, genomic, proteomic or other biological information. The type, methodologies and objectives of the planned research should be disclosed. The research participant should also be informed, how the sample is stored, how his/her personal and genetic data are protected, who has access to them, how long they will be stored and what happens to the results generated with his or her sample. Participants may withdraw consent for future research at any time and also withdraw their sample from the biobank. As the sample is contributed to clinical trial data, it is however not possible to eliminate any data already in the database. In scenario 1) the consent to the clinical trial protocol should also include consent with the storage and any research conducted on the sample as part of that protocol. In scenario 2) the patient should be given the opportunity to consent with the participation in the clinical trial separate from the consent to collecting and analyzing samples. It is an important principle of Good Clinical Practice that informed consent is specific as to the research objectives and methodologies. However, science develops fast and not all research questions may be known at the time informed consent is obtained which may eventually be answered

[21] Food and Drug Administration USA: Guidance for Industry: Pharmacogenetic Data Submissions. Docket No.2003D-0497. 68 Federal Register 62461-62463 (2003)

[22] Food and Drug Administration USA, European Medicines Agency, European Commission: Guiding principles Processing Joint FDA EMEA Voluntary Genomic Data Submissions (VGDSs) within the framework of the Confidentiality Arrangement (2006)

with the help of this sample. In case unforeseen additional research is planned the sample donor should be asked again for consent. If this is technically not possible a Research Ethics Committee may be asked for a waiver. Research results are usually not validated and do not allow for disease diagnosis, quantfying disease disposition or making treatment decisons in the clinical context. Rather, such data are important for formulating new research hypothesis, designing future trials or improving understanding of biological processes. While researchers are obliged to share with research participants the outcome of the research, individual patient data should not be shared as they can be misleading and may cause undue distress. In rare circumstances, a clinical trial may produce validated health information on a research participant. In such cases the information should be transmitted to the treating physician together with all relevant information regarding the clinical validity of the data. The physician will have to ensure that the results are properly communicated to the patient and other necessary steps are initiated. The participant's right to know and not to know should be respected**.**

Data protection

In principle, key coded information is identifiable. Specific precautions may have to be applied to ensure that individual genetic information or associatiated data are not accessible to non-authorized individuals or organisations. All data from a clinical trail are coded before being submitted to the sponsor. The code is held by the treating physician or institution. Yet, the computational power of modern computers allows combining data from many sources very quickly and efficiently. This increases the risk that even key coded data could be abused as demonstrated by a scandal in the information industry in 2006 when AOL released key coded search data of 500,000 users[23]. Therefore, technical precautions must be applied to avoid an individual's data being accessible to unauthorized individuals. Such provisions include secure transmission of data from the research site and back, encryption of all data on the data storage devices, prevention of downloading of data by unauthorized individuals as well as storage of clinical and genetic/genomic information on separate servers. Clinical data and genetic or other information generated from the samples should only be accessible by computer. Only aggregated data should be accessible to all researchers. Retrieval and removal of a sample should be automated in case a research participant withdraws consent. All processes and technical installations used for storage and retrieval of biological samples need to be covered by proper Standard Operating Procedures**.**

Access by third parties to samples and data

Public biobanks should be accessible to the general research community. Usually, this involves anonymisation of the samples and data to minimize the risk for the sample donors, and to allow optimal scientific use of the samples. The conditions for access to the samples in a biobank and to related data should be defined in the informed consent document and agreed by the sample donor. As long as the biobank holds identifiable samples and data the sample donor may withdraw consent or samples or restrict the access to his/her samples/data at any time. Industry biobanks are usually

[23] McCullagh D; CNET News.com: Search history gives insight into lives of AOL users (August 8,2006) http://news.zdnet.co.uk/communications/0,1000000085,39280576,00.htm retrieved September 26,2009

set up to support development of new medicines. Therefore they are mostly closed, key coded and do not allow access to samples and data other than to the researchers in the company, to trial monitors, and regulatory authorities. Regulations require that all data included in an application for market authorization are fully auditable and traceable. Therefore, it is not possible to anonymise a biobank containing submission data. Under well defined conditions, a company may open a research biobank to selected consortia of researchers or even the public. This does require, however, obtaining consent by the sample donors and if possible should include anonymisation of samples and data**.**

International cooperation

Exchange between scientists of samples and related data is essential for any research collaboration in academia and industry including collaborations between Chinese researchers and colleagues in other parts of the world. While collaborations involving human biological material or data are usually less challenging within a country, transport of human material or data across borders is subject to a highly diverse legal and regulatory framework which can be an insurmountable hurdle and a real obstacle to fruitful scientific cooperation. A functioning and practical international regulatory framework based on shared ethical principles is urgently needed which serves the research participants, the researchers and the interests of the countries involved alike.

Conclusions

The protection of the well being and the rights of research participants is the most significant responsibility of any sponsor of clinical research regardless of whether the sponsor is a public institution or a private company. The international pharmaceutical industry sponsors the majority of clinical trials conducted worldwide, and therefore has a particularly large responsibility. The pharmaceutical industry is committed to conducting clinical trials to internationally agreed ethical principles. Beyond obeying national laws, sponsors of clinical research should have global policies in place which ensure a consistent ethical framework for their global research operations. Internationally agreed principles like the Declaration of Helsinki, CIOMS guidelines, ICH guidelines and the Belmont Code form a solid basis for such policies. This will ensure that research subjects enjoy the same level protection independent of where they are living, and that the ethical and scientific conduct of research lives up to US and EU standards.

Respect to cultural preferences and values is essential when conducting clinical trials in any foreign country. Research protocols should be adjusted as much as possible to such values. However, such consideration of local values and cultural preferences should not be used as an argument to violate fundamental rights of research participants.

Biobanks and Genetics offer new opportunities for pharmaceutical research. A solid trust basis between science and society is essential for efficient application of new research technologies. This trust depends on respect for research subjects' autonomy. The Declaration of Helsinki provides guidance for conducting research with identifiable samples and data. Relevance for the patient of medical information depends on its content, not the technology used to obtain it. However, the specific risks associated with genetic information may be assessed differently by researchers,

research participants and other stakeholders and in different cultures. Those differences in perception need to be respected.

China is a large country, which is ethically as well as genetically diverse, having an economy and an epidemiological profile that are rapidly changing. Expanding high quality and ethically responsible pharmaceutical research into China therefore serves the interest of Chinese patients.

Appendix: Tables

- **Careful selection of research partners and trial sites**
  - Pre-inspections and audits
  - Track record of investigators, CROs
  - Training and certification of clinical trial staff on site
- **Training and development of own staff and contractors**
  - Training and certification of monitors and other clinical research staff
  - Continuous review and adjustment of policies and procedures
  - Close cooperation with clinical sites and regulators
- **Quality assurance systems**
  - Application of same, global quality standards and ethical principles
  - Post-trial audits, evaluation of trial post-mortems

Table 1: Ensuring quality and ethical conduct: the commercial sponsors role

- **Code of Conduct of Industry Associations e.g.**
  - **International Federation of Pharmaceutical Manufacurers and Associations (IFPMA)**
  - **European Federation of Pharmaceutical Industries and Associations (EFPIA)**
  - **Pharmaceutical Research based Manufacturers of America (PhRMA)**
- **Company policies on key aspects of clinical research**
  - **Code of Conduct**
  - **Conflict of interest in research**
  - **Disclosure of Clinical Trial Protocols and publication of Results**
  - **Pharmacogenetics and biobanks**
  - **Privacy with specific consideration of health data**
  - **Professional standards in working with health care professionals and patient organizations**
  - **Global Conduct of Clinical Research**

Table 2: Examples of self regulation in the pharmaceutical industry

Do

+ Adapt trial portfolio to local medical needs
+ Apply same ethical principles worldwide
+ Enroll Chinese patients in global trials

Don't

- Run trials where it is not planned to make the drug available
- Implement protocols which would not be acceptable elsewhere
- Disregard societal and cultural context

Table 3 Some practical recommendations for conducting clinical trials in China

- Research on identifiable human samples is research in humans[1]
- The sample donor should be asked for consent based on full information about the research she/he is participating
- Information should be as specific as possible
- Unforeseen research may require to ask the donor for new consent
- Under well defined conditions[2] "broad consent"[3] is an acceptable option and may ensure that a precious sample can be fully analyzed
- Where it is not possible to obtain informed consent the vote of an independent Research Ethics Committee should be obtained
- Family / Community consent should also be considered where culturally expected or if the family may be affected by the research

[1] Declaration of Helsinki 2008
[2] Anonymization of samples, strictly defined research area or other safeguards
[3] See definition by Nuffield Council for Bioethics :Pharmacogenetics" 2003.

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Table 4: Principles for protecting the autonomy of sample donors

Clinical Trials: The Indian Perspectives

R. Kishore

Introduction

In August 2008 (a month before the presentation on which this chapter is based) there were media reports of 49 children dying during clinical trials conducted by India's premier medical institution namely the All India Institute of Medical Sciences, New Delhi. According to an eminent opposition leader the poor Indian citizens are being used as "guinea pigs" by multinational pharma companies and that "the consent is driven by vulnerability due to poverty or sometimes because they believe it is conditional for the treatment for which they went to the hospital".[1] Such reports are not the solitary instances. There have been many reports of serious injuries and loss of human lives due to unethical clinical trials, violating all the three basic ethical principles governing biomedical research namely "respect for persons", "beneficence" and "justice".[2]

Notwithstanding such ethical miscarriages, it ought to be appreciated that clinical research is an essential part of scientific advancement aimed at ameliorating human suffering. In today's world of fast advancing technology, increasing quest for well-being and wider human interaction, it is not possible to perceive a world with circumscribed geographical or political boundaries and no country can afford to live in isolation. A country like India passing through economic transformation is a major stakeholder in the emerging global pursuits and opportunities. Clinical research is an essential expression of contemporary health care strategies. "If we don't carry out research, the blood of those who die will be on our hands".[3] There seems to be no difference of opinion between India and other parts of the world as regards the value and utility of clinical trials but the perceptions differ with regard to areas of research and the methodologies to be adopted in view of India's characteristic socio-economic and cultural milieu as compared to rest of the world. The strategies evolved by the Western world, including consensual paradigms, have to be suitably modified – at times fresh approaches have to be evolved – in order to protect the interests of persons belonging to vulnerable sections of the society.

It is significant to note that more and more international entrepreneurs are attracted to India for conducting clinical trials on the Indian population. According to one report "there has been a 10-fold increase in research in the last five years".[4] It is estimated that "contract research business in India may go up to Rs 13.2 billion (about US $ 281

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[1] Brinda Karat, CPM leader, Hindustan Times 20 August, 2008: 7.
[2] Ethical Principles and Guidelines for the Protection of Human Subjects of Research, The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, April 18, 1979, the *Belmont Report*.
[3] Joshua Lederberg, Nobel Laureate, former President of Rockefeller University (Quoted by Daniel Callahan, Presentation, before the President's Council on Bioethics, July 23, 2003).
[4] Sandhya Srinivasan "Indian Guinea Pigs for Sale: Outsourcing Clinical Trials" India Resource Center September 8, 2004 (http://www.indiaresource.org/).

million) by 2010 – perhaps Rs 44 billion (about US $ 950 million) if regulatory hurdles are "streamlined".[5]

In this paper I seek to analyze the Indian milieu, identify the country's major concerns and suggest the course to be adopted by the sponsors of clinical trials in order to attain their meaningful role in this important socio-scientific activity.

Why is India an attractive destination?

"India is fast emerging as a favoured destination for clinical trials in new products by multinational pharmaceutical companies."[6] Various factors for India's popularity may be summarized as below.

- Easy access and availability of research subjects
- Diverse and therapy naïve population
- Vast gene pool
- Lower operational costs
- Large pool of highly trained physicians, nurses and technical personnel
- Wide spread and world class medical facilities
- Well developed and advanced IT structure
- Favourable IPR environment after signing of the WTO
- Use of English as primary medical and business language
- Softer regulatory framework

It is well documented that the average costs of doing Phase I/II/III drug trials in US are $20/50/100 million respectively whereas in India they are 50-60% less and could be up to 75% faster. (Table I) The cost of Phase-II and Phase-III clinical trials in India "may be as low as 60% less than the average cost in the United States of America".[7]

Cost of clinical trials in the US vis a vis India

Study	Average US cost (in millions)	Cost in India
Phase I (Normally tests on small groups of healthy humans)	$ 20	50% less than the average cost in US
Phase II (tests on individuals afflicted with the condition for which the drug is developed)	$ 50	60% less than the average cost in US
Phase III (Tests on large groups of afflicted patients)	$ 100	60% less than the average cost in US

[5] *Ibid.*
[6] Bindu Dey and Payal Dey "Clinical Trials - Commerce versus Ethics", published in PHARMABIZ.com Wednesday, May 04, 2005.
[7] *Ibid.*

For the above several drugs companies have generated data in India on their products to be used in developed countries, as shown in the following Table.[8]

US FDA New Drug Application data generated from India

Drug Company	*Molecules Researched*
Alcon	Vegamox
AstraZeneca	Merenem
Cangene	Hepatitis B Vaccine
Eli Lilly	Alimta Gemcitabine (breast cancer) Cialis (erectile dysfunction) Xygris (Septicemia)
Glaxo	Lamictal
Jannsen	Resperidal
Novartis	Tegaserod
Pfizer	Voriconazole
Roche	Peg-Interferon
Santen	Quixin
Wyeth	Influenza A Vaccine

The Indian milieu

Characteristic features

In order to evolve ethically sound paradigms relating to clinical research in a country such as India it may be worthwhile to study some of its characteristic features, which are enumerated below.

- **Fast growing population**, leading to problems of resources, planning, implementation, distribution, management and control.
- **Social Inequalities**, based on birth, family background, castes, economic capability, trade, educational status, employment, religion, tribe, and ethnicity.
- **Religious Multiplicity**, with variable beliefs, practices and affiliations.

[8] *Ibid.*

- **Cultural Pluralism,** leading to diverse value concepts, convictions, traditions, living styles and mindset.
- **Linguistic Barriers**, due to multiple languages being spoken and written in certain countries like India.
- **Economic disparities**, contemplating heterogeneous research designs, consistent with the economic status of the research subjects, and cost subsidization.
- **Illiteracy**, calling for specialized and effective educational and counseling skills.
- **Poverty**, prohibiting the research subjects and their community from meeting the consequences of research induced injuries and depriving them of enjoying the benefits of the developed product.
- **Genderization**, manifesting as a deeply rooted bias against women and female children.
- **Infrastructural constraints**, lack of Institutional set-up, organizational capability, communication, transport and medical facilities, industrial base, and adjudicational mechanisms.
- **Legislative inadequacy**, leading to conceptual and functional ambiguity, non-protection of the rights of research subjects, denial of statutory safeguards, and difficulties in enforcement of ethical guidelines and standards.
- **Different priorities**, namely, population containment**,** safe drinking water, nutrition, housing, sanitation, waste disposal, prevention of communicable diseases, primary healthcare and education.
- **Vulnerable sections**, like, poor, illiterate, women, pregnant women, female children, minors, elderly, mentally disabled, unemployed, labourers and socially backward.

Major concerns

In view of the aforesaid characteristic milieu, India's concerns are manifold and the sponsors must ensure that the clinical trials are consistent with the following perspectives.

1. Choosing the right field of trials keeping in view the relevance of the research product for the host population.
2. Proper selection of trial subjects keeping in view their socio-economic, cultural, religious and family profile.
3. Due care in obtaining free and informed consent of the trial subjects.
4. Maximum care and precaution for safety of subjects during the trial.
5. Adequate care of the subjects in the event of trial induced injuries.
6. Equitable sharing of burdens and profits between the researchers and the host population.
7. Accessibility of the research product to the host population at reasonable terms.
8. Ethical review of the research protocols by the host country in order to ensure scientific, social and ethical compatibility.
9. Availability of infrastructural and administrative capability in the host country to effectively deal with incidental and consequential aspects of the trial.
10. Consistency with host country's socio-economic, cultural, religious and demographic realities.
11. Protection of vulnerable sections of the population.
12. Confidentiality and non-stigmatisation of the trial subjects.

The policies and programmes concerning clinical research should be consistent with the above major perspectives in order to attain social credibility and acceptance.

Informed consent

Consent is a vast expression, embracing profound meaning and expectation. It must be appreciated that legal incompetence because of minority or mental impairment is not the only barrier to free and informed consent. There are a host of other factors, which may impart consensual incapacity to an individual. The problem of free and informed consent therefore has to be handled at the individual, community and societal level. At the individual level, because reliance on proxy consent by community heads may cause gross ethical miscarriage to the trial subjects leading to non-cooperation on their part which may result in premature termination of the clinical trial. At the community level, because the religious leaders and community heads are the big power centres capable of frustrating the research in the event of any communication gap. At the societal level, because the state's public policy, founded on socio-economic imperatives, political expediency and religious beliefs may come into conflict with scientific pursuits. It may therefore be worthwhile to understand the major impediments in free and informed consent in the Indian context, which may be enumerated as below.

- Ignorance and Illiteracy
- Economic dependence
- Power Centres
- Material inducements
- Gender bias
- Linguistic barriers
- Superstition
- Allurement of therapeutic benefit

In a social order as heterogeneous as India, a unitary consensual paradigm may not be workable. The consent requirements are linked to the nature and class of the trial subjects. In this context, the following four categories can be identified in the Indian population.

A The educated, advanced and economically sound sections where individual, free and informed consent can be obtained after adequate enlightenment.

B Educated/semi-educated and economically weaker sections, living in a traditional setting where the decision making process is a collective exercise with dominant participation of the father or husband and the individual's choice is subordinated to family perspectives or even to extraneous considerations. This constitutes the majority group and is often referred to as the middle or lower-middle class in Indian society

C Uneducated, economically backward and primitive groups where the head of the tribe or the religious seer commands authority even in matters relating to an individual's private life and it is not possible for the individual to give free and informed consent

D The impoverished and deprived whose only concern is to safeguard his survival and free, informed consent does not carry any meaning to him. He can be lured into any kind of intervention by extending small material considerations.

Thus, for the purpose of clinical research, the composite socio-economic profile of the Indian population does not allow for any single consent strategy. The consent procedures are to be adopted according to the class characteristics of the trial subjects.

Proper selection of the trial subjects

In the process of selecting the research subjects, it is necessary to give adequate appreciation to their socio-economic, religious and cultural status, nature of occupation, and family circumstances, including the extent of dependence of the family members and the amount of prejudice likely to be caused to them in the event of adverse outcome. Guideline 10 of the International Ethical Guidelines for Biomedical Research Involving Human Subjects, prepared by CIOMS, *interalia*, states "Special justification is required for inviting vulnerable individuals and, if they are selected, the means of protecting their rights and welfare must be particularly **strictly** applied".[9] Furthermore, "Ethical obligations to vulnerable individuals in the research enterprise will often translate into **special procedures** to protect their interests".[10] (*emphasis added)* In view of prevailing circumstances in developing countries, namely, economic constraints, limited administrative capability, inadequate medical facilities, and inherent social bias against certain sections of the population, it may not be practicable to "strictly" observe and "translate into special procedures" the required care and precaution. As such, the inclusion of vulnerable sections of the population in the research is questionable. An assessment of the subject's ability to understand the nature and implications of research is also essential. This in turn requires an objective evaluation of his mental capacity. "Incorrect capacity determinations are problematic because of their consequences".[11] In order to ensure equitable distribution of benefits the research subjects should be selected after due publicity of the research projects.

The characteristic Indian milieu and the incapacity of a large section of population to give free and informed consent creates a need to take special care and precaution in the selection of trial subjects and it is an essential obligation of the sponsors to study the following aspects of the life of potential trial subjects before exposing them to clinical trials.

- Physical fitness
- Sex and age
- Marital status

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[9] International Ethical Guidelines for Biomedical Research Involving Human Subjects, 1993, prepared by CIOMS in collaboration with WHO, Geneva. P29

[10] "Ethical Conduct for Research Involving Humans". Tri-Council Policy Statement, issued by Medical research Council of Canada, Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research Council of Canada, August, 1998.

[11] Rebecca Dresser, J.D. Research Involving persons with mental disabilities – A Review of policy Issues and Proposals. Commissioned papers by the National Bioethics Advisory Commission, Vol.II, May, 1999.

- Reproductive profile
- Size of the family
- Economic status
- Nature of employment
- Place of residence
- Nature of class/tribe

Implementation

In order to ensure protection of trial subjects against coercion, exploitation or unwarranted consequences and to safeguard the interests of the family, community, and the researcher it is necessary to understand the nature and extent of care and precaution required at each stage of clinical trial and the responsibilities the process casts on various agencies. The clinical trials involving human subjects pass through the following four stages.

Stage-I (pre-interventional)

- Review and approval of the research project by the ethical and scientific committees of the host country.
- **Exclusion of vulnerable groups:** Poor, prisoners, minors, female children, migrant labourers, dis-empowered women.
- Elimination of undue influence due to paternalistic forces, financial allurements, economic dependence, religious taboo, job temptations, etc.
- Assessment of the subject's competency to understand the nature and consequences of the proposed intervention.
- Briefing the trial subject about moral foundations of the intervention and the exact nature of the procedure, its consequences, possibilities of therapeutic benefits, if any, and the options available to him.
- Informing the trial subject about the agencies involved in the research or trial, their antecedents and past performance, and the obligation and liability of each of them in the event of any complication. It must be remembered that, "Academic institutions that create alliances with industries to conduct research require a strong review process to probe possible conflicts of interest between researchers' scientific responsibilities, and business interests (e.g., ownership or part-ownership of a company developing a new product)".[12]
- Informing the subject about his/her entitlements and incentives and the particulars of the agencies and authorities whom he/she should approach in the event of need.
- Information about the provisions of law governing the research or trial.
- Due respect to the subject's religious and cultural sensitivities.

Stage-II (interventional)

- Evaluation of physical fitness of the research or trial subject to undergo the procedure.
- Complete knowledge on the part of the researcher about the safety, efficacy, and the side effects of the drug.
- Absolute care and precaution in administering the drug or any other procedure.
- Respect for the subject's privacy during the intervention.

[12] International Ethical Guidelines for Biomedical Research Involving Human Subjects, 1993, prepared by CIOMS in collaboration with WHO, Geneva: 29.

- Availability of all necessary measures including medical support in the event of any complications.

Stage-III (post-interventional)

- Close follow-up of the trial subject in order to monitor the effects and consequences of the intervention.
- Observance of complete confidentiality about the emerging information relating to the trial subject.
- Providence of all measures necessary to combat any adverse consequences attributable to the research intervention.

Stage-IV (utilizational)

- Rehabilitation of the subject in the event of disability attributable to the intervention.
- Measure to check stigmatisation and discrimination against the subject.
- Availability of the developed product at subsidised and affordable cost to the subject and his/her community.

Relevant areas of clinical trials in the Indian context

In a developing country like India, with a large population, changing socio-economic profile, rising expectations and entry of the private sector in the health delivery system there is great scope for clinical research and trials. The country's population already exceeds 1 billion, but a safe, reliable, cheap, acceptable and easy to use contraceptive is yet to be discovered. Communicable diseases are still the major killers and they cannot be combated in the absence of effective vaccines. Nutritional disorders, owing to poverty, continue to constitute a substantial cause of morbidity. The country possesses a rare knowledge preserved in tradition, which can be exploited if subjected to modern scientific examination. The country has a rich biodiversity, which requires research and experimentation for its utilisation. In view of limited economic capacity of its people the country needs to develop techniques of mass production of drugs, with indigenous resources, at low infrastructural and operational costs. The areas which are most in need of clinical research and trials may be enumerated as below.

- Ideal contraceptive for population containment
- Eradication of communicable diseases
- Control of nutritional disorders
- Exploitation of traditional knowledge
- Better use of indigenous resources
- Production of cheaper drugs
- Improvement in storage and preservation techniques

Legal framework in India

In India legal provisions with regard to clinical trials involving human subjects are contained in the Drugs and Cosmetics Act, 1940 and the Environment Protection Act, 1986. Two other documents that are also relevant are, the Indian Council of Medical Research (ICMR) Guidelines (2000) and the Good Clinical Practice (GCP) Guidelines developed by the Directorate General of Health Services (DGHS) (2001). Only the former two, being legislative enactments, possess statutory force.

The Central Government amended the Drugs and Cosmetics Act, 1940, by incorporating Drugs and Cosmetics (IInd Amendment) Rules, 1995, which came in to effect on January 20, 2005. In the amended rules the earlier Schedule Y has been substituted with a new Schedule Y, which contains provisions relating to permission and conduct of clinical trials in India. An examination of the amended Rules show that they are not capable of addressing the challenges emerging out of clinical trials on human subjects in India, for the following reasons, inter-alia.

i. There is no provision to restrict clinical trials conducted by foreign sponsors only to those areas where the research product is of use and is available to the Indian research subjects and the population at an affordable price. This is contrary to the interests of the Indian population and reduces them to the status of laboratory animals. This also constitutes a violation of paragraph 19 of the Helsinki Declaration.

ii. There is no effective provision relating to the selection and recruitment of trial subjects thereby leaving vast scope for conducting research and trials on the poor, illiterate, socially disadvantaged, unhealthy, ill, dependent and voiceless segments of the population, incapable of giving informed consent and also not in a position to manage research induced injuries.

iii. There is no provision to protect the above vulnerable sections of the Indian population against material inducements and temptations extended by the sponsors of trials thereby making the provisions of informed consent a meaningless proposition.

iv. There is no effective provision to ensure reasonable and speedy compensation to the research subjects in the event of trial induced injuries, nor is there any provision for their rehabilitation thereby placing the subjects and their family members in a position of extreme vulnerability.

v. There is no specific provision in order to govern clinical trials using placebos.

vi. The appointing authority in respect of Ethics Committees and the manner of their appointment is not defined.

vii. Specific and effective provisions are not laid down regarding the monitoring and auditing of the research protocols and designs by independent and objective authorities.

viii. Eligibilty and qualifications of the Contract/Clinical Research Organizations (CROs) are not defined and there is no provision for their registration in India before they are permitted to initiate clinical trials in the country.

ix. There is no provision for establishing a centralized registry/database having relevant information concerning ongoing clinical trials in India and as such the people are unable to know about the unethical activities on the part of sponsors and investigators of trials. This is not consistent with the principle of accountability and transparency.

x. Effective and deterrent penal provisions are not laid down in order to punish the sponsors and investigators who subject the Indian population to unwarranted and unethical clinical trials.

Differences in the milieu of developed and developing countries

S. No.	Developed Countries	Developing Countries
1.	Better understanding and appreciation of scientific pursuits leading to easy rapport between the researchers and the population,	Limited perceptivity of scientific promises and the nature of innovation and research, generating communication gaps and misunderstanding.
2.	Less risk of research subject exploitation owing to higher economic capability, education, wider interaction among various actors in society and independent oversight.	Greater risk of exploitation because of poverty, illiteracy, linguistic barriers, social inequalities, cultural practices and lack of communication among different sections of the society.
3.	Minimization of adverse consequences by virtue of better health status of research subjects, effective healthcare facilities, greater health consciousness and better partnership.	More possibilities for adverse effects because of poor health status of research subjects, inadequate health-care facilities, lower level of health consciousness and lack of coordination.
4.	Better operational atmosphere because of advanced infrastructure i.e., Institutional set-up, organizational capability, communication, transport, industrial base, and adjudicational mechanisms.	Difficult and unfriendly operational atmosphere due to deficient infrastructure casting additional stress and burden on the researchers.
5.	Higher accessibility of research products owing to more affordable, user friendly procedures, and improved supply and distribution mechanisms.	Lower accessibility of research products because of cost constraints, cumbersome procedures, and inadequate supply and distribution mechanisms.
6.	Higher funding capability of the sponsors, research institutions and the state leading to use of advanced techniques and methodologies and lesser flexibility and higher freedom of choice and decision making.	Lower financial support and the consequent compromise on the use of advanced procedures and methodologies, curtailment of choice and discretion.
7.	Higher engagement of health policy makers in the area of research and innovation and integration of research into healthcare system leading to evolved legislative approaches and regulatory mechanisms, consistent with ethical and orderly conduct of clinical trials.	Lesser engagement of health policy makers in the area of research and innovation owing to different priorities, leading to legislative inadequacy, and deficient regulatory mechanisms, thereby increasing the risk of exploitation of research subjects.

Sponsor's essential obligations

In the contemporary milieu of economic liberalization and increasing privatization researchers ought to realize that they carry vast moral commitment and institutional responsibility to achieve the highest ethical, scientific and financial standards with a

view to protect the rights, welfare and dignity of research participants. It is worth remembering that clinical trials are not merely a scientific pursuit. They are a social pursuit, embracing in their fold the concepts of right and wrong. Values therefore assume predominant role.

1. Non-exploitation

- Excluding the poor, illiterate and voiceless from the trials because they are not capable of exercising free and informed consent.
- Abstinence from making false claims and promises and from extending allurements, temptations and inducements.
- Respecting confidentiality, privacy and security of the data.
- Protection of vulnerable sections of the society.
- Respecting the rights, welfare and dignity of the trial subjects.

2. Integrity

In an area where an agency is tuned to human beings in flesh and blood who are dependent on the agency's superior power and resources integrity assumes the foremost importance. It implies the highest degree of:

- honesty,
- commitment,
- responsibility
- accountability.

3. Self-regulation

- Enlightened, committed and motivated leadership at the top, with conviction and belief in values,
- training and sensitization of the personnel engaged in trials,
- periodic review and close monitoring,
- regular interaction with the people's representatives and the state authorities,
- knowledge of ethical codes, guidelines and the host country's policies, rules and regulations,
- appreciation of differences between the circumstances and perspective of developed and developing country's,

4. Transparency

5. Safety

6. Accuracy

7. Effective rapport with the front line actors of the civil society leaders

8. Availability of adequate resources

9. Publication of findings and results in a candid and timely manner

Conclusion

The goal of all clinical trials is to ameliorate human suffering by discovering the promise of science and technology. The best way to achieve this goal is integrity and self-regulation on the part of the sponsors. Good governance means exploring scientific promise with minimum risk to research participants. The process requires great degree of social insight, ethical commitment and operational acumen Clinical trials involve many stakeholders – from present to future generations – and, at times, the stakes are vast and deep. Clinical trial is a pursuit where scientific, socio-economic, legal, ethical, moral, cultural and religious contexts co-exist. Research "is a moral good to be weighed against other human goods, but not an overriding moral obligation".[13]

In a developing country like India, having a big market for foreign investors, the individual and the community have to be protected against undue experimentation and its consequences. "The background fear is a breach of distributive justice, since products that disadvantaged populations bear the burden of testing are likely to be marketed in affluent countries and be unavailable to populations of poor countries that serve as testing sites".[14] At the same time, policy makers ought to realize that clinical research is an essential part of the country's health delivery system as it carries vast promise in addressing many difficult issues by indigenisation, innovation, cost-effectiveness and optimization of resources. It has the potential of galvanizing the country's national health programmes by discovering vaccines, drugs and devices at affordable costs for mass use and may even provide an answer to the country's nutritional crisis.

[13] Daniel Callahan, Director, International Programs Hastings Center, Presentation, before the President's Council on Bioethics, July 23, 2003.

[14] Ethical and Policy Issues in International Research: Clinical trials in Developing Countries. Report and Recommendations of the National Bioethics Commission, Bethesda, Maryland, April 2001, Vol. II: a-7.

CONCEPTUAL REFLECTIONS

Does Chinese Culture Constitute Challenges to Informed Consent?

Zhu Wei

Abstract
The principle of informed consent, since its appearance in China, has become a topic of controversy. Many doubt its adaptability in the context of the Chinese cultural background. They claim that in China it is often the family (not the patient) that makes the decision in real clinical practice or research. Besides, from the point of view of cultural tradition, Chinese culture does not seem to be compatible with the principle of informed consent. As a result, many scholars conclude that Chinese culture presents challenges to the application of informed consent in China. This paper attempts to show that such claims are unjustified.

Over the past several years, doubt has been raised as to whether or not the principle of informed consent – an idea which orginated in the West – could be integrated efficiently and effectively into Chinese practice. This doubt is largely based on the following two points: Firstly, what is often seen in medical practice or clinical research in China is that it is the family (not the patient or research subject) that makes the decision when the need for such a decision arises. Secondly, from the perspective of cultural tradition, the Chinese culture does not seem to be supportive of the practice of informed consent.

Let us try to look at the two above-mentioned claims and decide whether they really constitute a challenge to the principle of informed consent. To begin with, it is quite true that we find many cases in which the family plays the major role in decision-making. For example, if a patient is to receive a special medical examination or treatment or an operation, often the physician will let the family members know first, trying to ask for their opinion, and hiding the information from the patient himself or herself. Even when the physician decides to share the information with the patient, he will choose to get permission from the family members first. It is generally agreed that the heavy involvement of the family in the decision-making process is important and necessary because they share a fundamental common interest with the patient. And often the patient himself or herself would seek to depend on their family for decision-making.

In research work, this is also the case. According to Article 26 of the “Law on Medical Practitioners” issued in 1998, “The physician is obliged to describe the case objectively with the patient and the family. In the meantime, he should try to avoid any possible negative consequences on the part of the patient while revealing the information. In case of trial clinical treatment, it is necessary to obtain permission from the patient or his/her family members”.

The second claim is related to Chinese cultural traits. Some scholars hold that the dilemma of the principle of informed consent in China is caused by the focus on collectivity in the Chinese culture. Such focus on collectivity (or lack of individuality), when seen in the context of medical practice, naturally means that once a patient finds himself/herself in the hospital, he/she should leave the decision-making

responsibilities and other treatment-related matters in the hands of the physician and the family. The patient has complete trust in the physician and the family members and knows that their decision will be in his/her best interest. But in Western culture, individuality is often emphasized, and the theory of informed consent, which was developed in the West, naturally tends to place greater emphasis on the role of the individual. This, in turn, is the root cause of why the application of the principle of informed consent becomes difficult in China. There is a major difference between the East and the West at the cultural level.[1]

At this point, some key issues have to be addressed. For example, does the fact that family consent is common in China mean that family consent is as important as or even more important than individual consent? And is the difficulty involved in the application of the principle of informed consent really caused by the lack of individuality in the Chinese culture? To seek answers to these questions, we feel it is of utmost importance to decide whether or not family consent is justifiable in the context of the Chinese culture, and whether or not there is a lack of respect for individuality or autonomy in the Chinese culture.

First, there is the issue of family consent versus individual consent. Is it true to say that individual consent may be ignored because of the prevalence of family consent? Here is a case that may serve as an answer to this question. A woman about to give birth to a baby died of difficult labour because her husband refused to give his consent for operation, which was the only possible way to save her life at the time.[2] And the reason for the refusal on the part of the husband, quite ridiculously, was that he knew his wife would give birth to a girl. In this tragedy the obstetricians and the hospital should be held responsible for improperly handling of the situation (They should have intervened since it was obvious that the husband's decision was against the best interests of the wife). But undeniably, it was the overemphasis on family consent by the obstetricians and the hospital that resulted in the death of this poor woman. Here we see the conflict of interest between the woman and her husband. From the point of view of the wife, who is struggling for life, survival is her sole and only concern. Yet the husband, who is expecting a boy (but not a girl), does not see why he should give his consent for operation. This is a typical case which shows that family consent, common as it is in China, is not justified under all circumstances.

As a matter of fact, many studies show that it is only when the family's interest echoes that of the patient that family consent can be justified. And, many times, this is what actually happens in Chinese medical practice. This form of family consent is not only necessary but also conducive to the restoration of the patient's health.

It is worth pointing out again that family consent is desirable only when the interest of the patient and the family overlap. Should there be a conflict of interest between the

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[1] See Chen Fajun, Fan Jia: "Issues on Informed Consent in Clinical Practice", Medicine an Philosophy, Vol. 1, 2003, p111-13; Wang Deye: "Informed Consent and Trails on Human Subjects", Journal of Dialectics of Nature, Vol.1, 2004, p15-21; Fan Ruiping "Self-Determination VS. Two Incommensurable Principles of Autonomy", Bioethics, 1997, 38 (11): 4.

[2] Tu Liyan, Guo Zhaojiang: "Principle of Informed Consent and its Cultural Context", Chinese Journal of Medical Ethics, Vol. 5, 2001: 30-31.

patient and his/her family members, then family consent would not be the best choice because there would be the risk of not safeguarding the patient's best interests in the decision-making process. Nowadays, amidst huge social shifts and the disappearance of the traditional families, the value standards and orientations among family members may grow radically different from each other. Against such a background, the stress on uniformity in opinion and family consent is quite suspicious, particularly for women, who have long been the victims in the traditional family whenever conflicts occur.

According to surveys recently conducted in Shanghai, family consent becomes the choice usually when revelation of the information to the patient may negatively affect the patient. The fact that family consent is common does not mean that it is always the best choice. In recent years, in many hospitals in Shanghai, family members are not allowed to make any decision for the patient unless they present a signed informed consent form. Taken together, this indicates that family consent and individual consent complement each other in Chinese medical practice, and family consent is accepted only when family members are authorized to do so. Still, there exists, to a considerable degree, the need for independent and autonomous decision-making.

Now from the perspective of culture, it is true that Chinese culture, which is rooted in Confucianism, does not clearly put forward the idea of autonomy. But if we study Confucianism carefully, we will discover that it does not deny autonomy either. Individuality, creativity and freedom – core values inherent in the notion of autonomy – may also be found in the spirit of Confucianism. For example, Confucius once said, "An army may lose its commander-in-chief, but not the will power of an individual soldier to win the battle".[3] Here "the will power of an individual soldier" is equivalent in meaning to dignity, self-respect and independence in Western culture. "One may be in danger of losing one's life, but the sense of freedom of choice is not to give up".[4] In this statement by Confucius, the Master is reiterating the importance of freedom of choice, which, for him, is a right endowed upon every individual being by Nature. And Mencius also pointed out that "One is not to show arrogance when rich, not to resort to self-pity when poor, and not to yield to power when threatened".[5] These quotations are enough to point to the fact that in Confucianism there is also the stress on autonomy and autonomous decision-making.

From the point of view of Confucianism, saints and gentlemen should set an example for the rest of the society in holding on to freedom, independence and individuality. Both Confucius and Mencius emphasize the importance of "goodness" if a person is to deserve the title of gentleman. And to realize this "goodness", one is required, first and foremost, to be faithful to his real "self". When this "self" remains the same, and with him throughout life, then he will know what to do even though he may be in different life situations. He will help others when he becomes a success; and he will still spare no effort to improve himself even if he fails to achieve success in his career.[6]

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[3] Confucius: The Analects, Book Nine.
[4] Liji (Book of Rites), Ruxing (Conduct of the Scholar).
[5] Mencius, Tengwengong 2.
[6] Mencius, Jinxin 1.

As discussed above, in Confucianism we find no direct reference to "autonomy" or "autonomous choice". But there are ample examples which show that Confucianism is not against the notion of autonomy. Instead, it is quite progressive towards autonomy and autonomous choice. The only difference between Confucianism and Western Culture is a matter of degree. In the context of Chinese culture, the importance of an individual is seen through the way he is related to others around him. Self-perfection, career achievement, and a sense of responsibility for all members of the society – these represent the best qualities in a "good" man. And with this in mind, one is able to cultivate strong will power, individuality, and a sense of love for all under the sky.

Historically, the idea of autonomy has been accepted in China since the late Qing dynasty. Viewed as a word synonymous in meaning to right, autonomy was initially almost equated with national autonomy and national sovereignty. Because of China's loss of economic interest and other national interests in its dealing with Western powers, and because of the signing of unfair treaties, the Qing dynasty government and its officials realized the importance of "rights"and national autonomy or independence[7]. Later, some intellectuals also tended to equate autonomy with rights when they wrote about the importance of maintaining individual autonomy. In a book that came out in 1899, the authors claimed that "The nation flourishes when each individual is guaranteed his own rights; and the nation is doomed to fall apart if its people are deprived of their rights"[8]. Also, some intellectuals, influenced by Darwin's theory of evolution, attempted to justify the fight for individual rights. In their opinion, the protection of individual autonomy was good for competition, and competition would help promote the development of the nation.

As time progressed, in the late 1980s, with the establishment of the market economy, the urge for autonomy and individual rights entered into a new stage. The role of individuals in the society became further strengthened. Such pursuits as fringe benefits and the realization of personal worth were seen as healthy aspirations. And everywhere in the whole society "autonomous choice, competition and success" was encouraged[9]. People came to see that it was only through autonomous choice and daring efforts that they could manage to secure a better place in the world.

Ordinary people's earnest desire for the protection of their rights and autonomous standing was realized in the "Law on the Protection of Consumers" that went into effect in 1993. In this law, it was stated clearly for the first time that members of society and institutions have the right to information as consumers. According to Section 1 of Article 8 of this law, "Consumers have the right to know the actual status of the goods they buy and the service they pay for". Although this was only a law in the area consumer protection, it had symbolic meaning in China's effort to protect individual rights. Ever since this law was issued, other laws in other areas were

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[7] Jin Guantao, Liu Qinfeng: "Evolution of the Concept of Right in Modern China", http://www.cc.org.cn/newcc/browwenzhang.php?articleid=1655. "On the Spirit of Individualism in Confucianism", Qilu Journal, Vol.5, 2005.
[8] He Qi, Hu Lihuan, "New Encouraging Learning, Commentating New Policy"---- Collection of Works of He Qi and He Lihuan, Shengyang: Liaonin Press, 1994, p142.
[9] Zhao Xiuyi: "Consciousness as an Agent and His Rights", Journal of East China Moral University, Vol. 4, 2003, P7-12.

drafted and enacted. And the awareness of rights' protection and individual autonomous choice among people in the society became firmly established.

In the field of medicine, the publication in the 1990s of the book "The Right of the Patients" was an unusual event, because in the book the authors first explicated the importance of honouring and protecting the patient's rights[10]. Thereafter, the Ministry of Health of P.R. China, formulated a series of laws and regulations, endeavouring to tighten measures in the protection of patient rights. "Hospital Management Guidelines", "Law on Medical Practitioners", "Regulations on the Handling of Medical Misconduct", "Population and Family Planning Law", "Law on the Health Care of Mother and Baby", "Law on Pharmacy Control" came out one after another. Above all, individual rights and autonomy have been sought after many years in China. It is closely related to the growth and development of the nation; and the faster the society moves ahead, the stronger the sense of autonomy is in the society members. Today, China has entered into the age of the market economy, and the field of medicine itself has become marketized. Under such circumstances, it is inevitable that the patient's best interests will not always coincide with that of the family, as it may have 20 or 30 years ago. Therefore, stress on autonomous choice and decision-making becomes more important because this is an effective means to safeguard the best interests of the patient. This is also why in medical practice and research programs a considerable amount of attention has been paid to the protection of autonomous choice and decision-making.

Now that we have laid out all the facts, it is time to weigh the points and try to work out some solutions. Firstly, we are interested in the difficulties involved in the application of the principle of informed consent. It is true that we encounter many difficulties in the process of applying the principle of informed consent in China. But this phenomenon is certainly not only seen in China. Other countries in the West have similar problems in this respect. For example, when Chinese scholars assert that it is a cultural difference that results in the lack of individuality or autonomy in the patients or subjects, Western scholars are also puzzled by the same embarrassing situation with their patients and subjects. And, when our scholars claim that autonomy is an idea borne out of Western culture and is not compatible with Chinese culture, Western scholars are also troubled by the problems associated with autonomy. For example, many Western scholars alse argue that the idea of autonomy overemphasizes freedom of choice and decision-making on the part of the patient/subject, but ignores, to a large extent, the responsibility of the physician/researcher. Thus it leaves the impression that the theory of informed consent protects the rights of the physician/researcher more than that of the patient/subject. Obviously, culture or cultural difference is not to be blamed for such difficulties.

Secondly, it may help to take a close look at how autonomy and informed consent are related to each other. Autonomy in the West was originally a political concept. Later, Immanuel Kant extended the use of the word "autonomy" to philosophical discussion. As a result, autonomy began to gain new meaning, and it was used to refer to self-governance, the right to freedom, privacy, individual choice, free will, autonomous action, etc. But autonomy in bioethics has a narrower meaning. It means that medical

[10] Qiu Renzong, Zhuo Xiaoqing and Feng Jianmei: The Rights of Patients, Beijing: Peking Medical University Press and Peking Union Medical college Press, 1996.

professionals have the obligation to respect the patient's autonomous choice and should allow the patient to make his own independent decision. Autonomy in medical practice is reflected in the principle of informed consent. Autonomy carries with it a sense of being independent, rational and cautious. But it does not automatically negate influences from the outside. Whether in the West or in China, the principle of informed consent requires that we respect the patient's rights, reveal enough information, and allow him to make his own decision because we know no better means than this to safeguard the best interests of the patient.

Of course, we admit that there are times when the patient may not be able to make a sound decision or repeat mistakes in the process of decision-making. If this should happen, we would seek to intervene because we know, both in the West and in China, that our ultimate goal is to protect the patient and to promote his well-being. We do not care about autonomy for the sake of just caring about it. This is why we feel it is important and necessary to help those who are incompetent, mentally handicapped and those who have lost consciousness temporarily and children to make the decision. This is also why we have to intervene when there is a suicide attempt within our family or among our friends.

By now it must be quite clear that there actually exists no real difference between the West and China in the matter of informed consent. We all agree that in informed consent the highest principle is the assurance of the best interests of the patient/subject. To do this, sometimes individual consent is required; but at other times, family consent may be expected. It is ridiculous to try to offer an explanation in terms of cultural differences. Rather, in my opinion, we should turn to look at the operational measures in real medical practice and decide whether they help contribute to the smooth and successful implementation of the principle of informed consent. This is where our efforts should be directed in our work, now and in the future.

Concerns and Principles
Bioethics and the Challenge of Cross-Cultural Biopolitics

Christoph Rehmann-Sutter

European-Chinese collaborations in biomedical research bind scientists, doctors, patients, administrators, citizens, industrial managers and many other participants from at least two countries together. They build more or less extended, topical and transient, bi- or multinational institutions, which are often called 'projects', 'partnerships', or 'consortia'. The 'ethics' of such transnational research, like all research ethics, is not a given set of rules or criteria that has been adopted internationally and formulated in international conventions once and for all. Innovation and changing circumstances give rise to novel questions or new aspects, which cannot all be anticipated. Research ethics must therefore be seen as a dynamic process of continuous reflection and learning. This process necessarily involves the exchange of particular experiences and locally meaningful ideas across those cultural domains that are represented by the participants. Biopolitics has increasingly become transnational (Zhang 2008). How can *bioethics* – this engaged and systematic reflection about the moral issues involved in the practices of research, medicine, biotechnology and regulation – be transnational as well? Is bioethics always bound to a particular 'cultural system' of shared beliefs and a tradition of ideas? Is it different in other cultures? Or – worse – is bioethics itself the expression of one cultural system that would not emerge in others? Experience during the three-year collaboration between Chinese and European scholars under BIONET has impressively demonstrated that bioethics is *not* just a 'Western' invention, even if many prominent approaches and theories have their origins in 'Western' philosophy. There are 'Eastern' approaches and theories as well, rooted in the rich resource of Chinese cultural history and philosophies. Theories and methods might differ but the concerns are widely shared: the exploitation of the vulnerable position of patients who trust that they will get the best possible treatment is, for instance, one such shared concern. We share many concerns, but we may explain them with reference to different moral principles, which may overlap to a certain degree.

Here I want to ask what is meant by ethical 'concerns' and 'principles', and how principles and concerns are related to each other. How are they used and enacted in practice? Principles mostly appear as parts of a moral judgment about a course of events. And judgments can be considered to be right or wrong. If bioethical work were to focus mainly on principles it would be essentially about finding the right judgments and sorting out wrong ones. Ethical concerns, on the other hand, are the expression of a personal commitment to a course of events. They do not necessarily judge, but they express what somebody sees as crucially important and relevant in this situation. Or they express what somebody sees to be ethically problematic in such circumstances. Concerns and principles both have a history, but on different levels. Principles rely on a history of theories and beliefs, whereas concerns refer more to moral experience and a continuous practice of reflection.

These questions seem interesting philosophically also because of their anthropological implications. The 'self' that uses moral principles and the 'self' that expresses and discusses ethical concerns represent different cultural constellations of subjectivity, or we can say that they represent different *forms* of the moral Self with regard to social reality. Concerns have a different kind of appeal to other people, with whom we live, than principles. Concerns ask people to look by themselves and see what happens, whereas principles ask them to check the consistency of a proposed system of rules that are applied, enacted or violated in a certain case. Concerns can be seen as more or less pertinent, they may be shared or not shared, sometimes they can prove groundless; but they cannot in the same sense be said to be wrong, as principle-based judgments can. This is a hunch I have that needs to be discussed on the basis of examples.

The underlying question is: can bioethics be based around concerns rather than principles? What would be the implications of a concern-based bioethics for intercultural or global ethical discourse, as opposed to a principle-based bioethics? This touches on some larger philosophical questions that will not be solved in this short piece. I try to elucidate two questions, which are less ambitious. (i) Does it make a difference whether bioethics sees itself as grounded in principles or in concerns? (ii) Could a concerns-based bioethics have advantages in a transnational public sphere? Obviously these questions depend on the bigger ones. They presuppose that it is at least not nonsense to think about the possibility of basing bioethics around concerns rather than principles.

I start with a case example that should explain more concretely what I mean by concerns and principles.

Example: iPS to mice

At the time of writing (Summer 2009) the world media reported the groundbreaking success of two Chinese stem cell research teams working with iPS cells. They could prove that 'induced pluripotent stem cells', which were derived from differentiated body cells (e.g. from the skin of an adult animal) and then induced by biochemical means to become pluripotent stem cells like embryonic stem cells, can give rise to a whole animal again. The experiments were conducted in mice, and the technique applied is known as 'tetraploid complementation'. The iPS cells were implanted in a blastocyst embryo whose cells had been made tetraploid. In this environment the iPS cell was able to divide and differentiate in such a way that the body of the foetus consisted of diploid cells derived from the inserted iPS cell, whereas the placenta and the chorion grew from the tetraploid cells. The mice that were born were living normally, had been able to grow up, and at least one had become a fertile adult.[1]
Two completely contradictory ethical interpretations of this experiment have been suggested. One has been included in most of the media reporting on the experimental success of Shaorong Gao and Qi Zhou's groups. The experiment was seen as proof that iPS cells are equivalent to embryonic stem cells, and that this technology therefore can be developed further to replace embryonic stem cells, which are regarded as morally controversial because they can only be derived from human embryos. iPS cells do not rely on the destruction of embryonic human life, hence they

[1] Zhao (2009); Kang (2009).

are morally permissible. The reasoning behind this interpretation is based on a moral principle: the principle that it is morally wrong to end the life of a human embryo. It can be called the principle of 'sanctity of embryonic life'.[2]

The other ethical interpretation goes in the opposite direction and says that these experiments show that it is morally wrong even to use iPS cells for research or medicine, because the experiment proves that the iPS cells are totipotent. It also refers to the principle of sanctity of embryonic life. The question is why embryonic life is different from the life of the cells of the human body. Both are in a certain way human life. But, so the answer goes, embryonic life has the potential to become a human person, whereas a body cell lacks this potential. According to the principle of sanctity of embryonic life it is the potentiality to make a human person that makes one human cell type morally considerable and the other morally neutral. The basis of the view that the life of embryos needs to be protected is the 'principle of potentiality', which refers to the developmental potential as a descriptive category in the first place. This can be seen as vindicated for iPS cells by the experimental demonstration of tetraploid complementation.[3] Given the appropriate circumstances, an iPS cell is able to develop into an adult. Therefore, human iPS cells contain the potential to develop into persons and, according to the principle of potentiality, they fall under the principle of sanctity of embryonic life like zygotes and other totipotent cells of the early embryo, and it is wrong to kill them.

Which application of the principles is the right one here? Which one has priority, the principle of sanctity of life (applied to human embryos) or the principle of potentiality (applied to totipotent cells)? This seems difficult to say.

But there is a third interpretation of the same experiment. What it demonstrates is the possibility of presumably every body cell of an adult being reprogrammed into a functioning embryonic cell at the blastocyst stage. (This does not apply to erythrocytes, because they lack a nucleus.) The manipulations that are necessary to realize this potential of adult body cells are, however, quite complicated and intense and would never happen in nature. They include firstly all the steps applied in the laboratory to turn skin cells into iPS cells, and secondly all the steps applied in the laboratory to make an iPS cell divide in the way a cell of a blastocyst embryo does. Among many other, perhaps less dramatic, biochemical stimulations, it needed a second existing embryo at the blastocyst stage when the iPS cell was inserted. Only there, in this artificial context and after considerable biochemical and physical manipulation, could the cell perform its potential. But it still could, and this is indeed remarkable. It proves that body cells retain the potential to act like embryonic cells, if they are stimulated, manipulated in the proper way, and inserted into the right multi-cellular environment. The role a cell plays, we could say, not only depends on its inner constitution (its genome, its shape and composition), but significantly also on the cellular environment in which it is placed. A developmental potential (that can be said to 'unfold') is not an inner propensity of a cell but a result of complex interactions. The reality, which makes what a cell signifies ethically, is therefore a function of the total structure of the organism in which the cell is placed. This reality,

[2] The principle of sanctity of life can of course be used in different senses, applying only to people, or to all organic life (Glover 1977).
[3] See Hans-Werner Denker (2008, 2009).

together with its ethical significance, is malleable. What a human person is, and why a human person matters ethically, does not depend on its genome and the potentiality that is inherent in every human cell, starting with embryonic cells. It rather depends on the reality of an embodied human person itself. And the capacities of the body's cells have just been demonstrated to be more amazing than we previously believed. Perhaps, knowing this, we look at our own bodies differently.

The principle of sanctity of embryonic life, the principle of potentiality, and the principle of embodiment (let us so call it) are all moral principles in a certain way: standards that recommend types of action (cf. O'Neill 2001, 2009). Now we need to ask: what are the possible ethical concerns here? One concern is that the technique could be applied to produce human progeny. Children born through this technique would be at risk of developing malfunctions and diseases of many kinds. They would be embodied human 'guinea pigs', exploited as objects of a medical experiment, who were never asked to give their free and informed consent. This concern does not result in an ethical condemnation of experimentation with iPS cells, nor even of experiments with tetraploid complementation in humans, if the experiments are terminated at an early embryonic stage, and if no embryos are implanted into the uterus of a woman. This experiment is not immoral, the concern tells us, because it violated a principle. The concern is that a human child would be harmed, used and exploited for interests that are not her or his own. Another concern is that a woman may be forced or talked into accepting such an embryo being inserted into her uterus. These concerns tell us that there is a need for a tight regulatory framework that prevents the application of this technique for producing children. Children are the most vulnerable here.

The choice of my example could be said to be unfair, because not every application of principles leads to contradictory results. There are other cases where the application of moral principles leads to an unambiguous moral judgment. I admit that this element of my case discussion is rather contingent and is bound to the choice of my example. I will *not* base my argument for ethical concerns and against the exclusive role of moral principles in bioethics on the fact that in this case principled arguments have led to a contradiction.

Principles are used and concerns arise

Principles and concerns in bioethics are related concepts, but if we observe how we use them we see that they have different implications, can be used under different circumstances and with different rules. In a word, they have a different moral grammar.[4] For instance, we can say that somebody 'applies' a principle or 'uses' a principle. But we cannot say that somebody 'applies' or 'uses' a concern. On the other hand we can say that in a situation concerns 'arise' or 'are raised', while it does not make sense to say that principles 'arise' or 'are raised' in a given situation.

While the most elaborate principles work in a top-down way, lay out a rule (it might be only a loose one and it may allow exceptions), refer to substantial philosophical justification, and stand for a system of ethical judgment, concerns may be more direct,

[4] For a discussion on the use of principles in ethics see also the July-August issue of *The Hastings Center Report* 2001 and the 3rd issue of the *Journal of Applied Philosophy* 2009: O'Neill (2001, 2009), Little (2001), Benjamin (2001), Brownlee (2009), Archard (2009).

personal, work bottom-up, express the commitment of the speaker who emotionally cares for a course of events, and they may raise an important problem that asks for a more serious discussion. Some principles may be mere 'rules of thumb' and lack elaborate philosophical background. But all principles are (or contain) claims of knowledge applied in a judgment. Concerns, as Charles Taylor puts it, 'incorporate a sense of what is important to us in our lives as subjects' (Taylor 1985, 60).[5] In some cases a concern indicates that some practices or affairs are ethically questionable. Principles also tend sometimes to exclude other principles, while concerns are not denied because somebody else has other concerns.

If people do not share the same principles, there will be a discussion about which principles are the right ones, or better than the others. People do not always share the same concerns either. But in such a situation the discussion has a different character. Concerns can very often be explained by bringing up the facts of a case, by bringing in testimonies of people with first-hand experience, and by establishing 'the true story' (or variants of it depending on the perspectives). Principles, on the other hand, need to be explained by their implications and justifications. These properties of concerns and principles may be important for international bioethics. Principles may depend on the choice of an ethical theory or on the acceptance of a certain cultural tradition, while excluding some other ethical theories, or elements of other cultural traditions. Because they carry no theoretical baggage, concerns may be more easily shared, even between advocates of different ethical theories, and they can possibly also be shared by different cultural traditions, which would not agree on all of the key principles.

Principles are general statements about what makes actions morally justified. In other words, they appear in the context of moral judgments. Moral judgments, however, are not the only way of ethical thinking. When we characterize ethical thinking with words like 'to justify', 'judgment', etc., we use the analogy of law and court. It is the 'judge' who makes a judgment about the case. The question is, which action was justified or not justified. If I make a moral judgment about a case, I position myself in the role of a moral judge. The judge – legal and moral – is (hopefully) an impartial, independent, insightful and reasonable person. These virtues make her or him a good judge. Ethical thinking can, however, be different from the practice of judgments in law and court. When we explain how and why we care for a patient in medical practice, we explain a relationship of responsibility for the patient who is dependent on us. And such explanations may refer to the concrete needs of the patient here and now and to our own practical involvement. When we do this we are not positioning ourselves in the role of a detached observer. We are not even impartial, because with determination we may take the side of the patient. And as care givers we are ourselves essentially dependent on the other in the relationship of care.[6]

Principles are widely used in biomedical ethics. Tom Beauchamp and James Childress have developed a very influential account of four principles: respect for autonomy, beneficence, nonmaleficence and justice. These principles have been derived

[5] Margaret Archer (2000) has developed an elaborate account of human agency that is based on concerns as social emotions.

[6] Such an ethics of care, which is based on the acknowledgment of dependency as a key experience, has been suggested by Eva Kittay (1999).

reconstructively from a wide acknowledgment of reflected moral common sense in medicine and biomedical research (see Beauchamp/Childress 2001). Their key advantage for practitioners is that they are not bound to a particular ethical theory like Kantianism or Utilitarianism, and they integrate a wide range of moral intuitions. But their list of principles for bioethics is not comprehensive. There is also wide discussion about the 'principle of utility', the 'principle of universalizability' or about a 'precautionary principle'. The Danish philosophers Jacob Rendtorff and Peter Kemp (2000) have suggested an alternative list of four that are intended to be a European alternative to Beauchamp and Childress' 'American' principles: the principle of respect for dignity, the principle of respect for integrity and the principle of respect for vulnerability, together with the principle of respect for autonomy. And of course, we use many arbitrary moral 'principles' to explain our moral thinking in certain practices. There is, for example, the claim for 'reproductive autonomy'. Or I say that my own principle as a teacher of biomedical ethics is to build on my students' own moral experiences.

Concerns cannot so easily be enumerated in an abstract form, because they refer to a situation, a course of events, a piece of history, an aspect of real society. In the example of iPS cells that have been used to grow a mouse, the concern was that children could be made and suffer from the side effects of this manipulation, or that a woman could be exploited to provide her uterus for experimental purposes. Such concerns can only be explained together with the situation they belong to. But there are also more general concerns that refer to the moral difficulties in human societies: for instance the concern that somebody who is innocent is harmed by collateral consequences of decisions that seem rational. That harmful consequences may be hidden behind good and reasonable intentions is a quite general concern.

If we look at the use of principles more closely, we also see connections between principles and concerns. One is that principles too can be inspired by concerns. Take the precautionary principle. It contains the concern that we have just mentioned: the concern that unintended consequences, perhaps unforeseeable effects (or effects of effects), of a technological application may cause harm. The principle of respect for autonomy contains the concern that others can treat us in an instrumental way, as means to their own ends, and in doing so may not recognize us as equal subjects with our own right to self-determination. Principles are therefore not to be seen as opposites of concerns. Rather we can say that they *encapsulate* concerns. However if the precautionary principle is formulated in an abstract way, the concern is hidden behind the form. Somebody could claim that we are not morally allowed to apply new biotechnologies, unless (1) we know all the possible consequences, and (2) all these consequences, even the least desirable ones, are morally legitimate, and that this is so *because* it is morally required to enact the precautionary principle. In a discussion about this position we would fight over the reasonability of this exceptionally strict requirement in the field of biotechnology, given the fact that the same principle could never be applied to other fields of life (like falling in love, travelling, etc.) where knowledge about all the future consequences of our actions is chronically lacking.[7] The concern, however, which is encapsulated in the precautionary principle, will be shared by many on both sides of the discussion for or against the principle: the concern that we may not be aware of harmful side or secondary effects of a decision,

[7] See my discussion of predictability in Rehmann-Sutter (1998).

and should therefore work towards enlarging our knowledge base as far as possible, or the concern that significant possible harm would be downplayed by a seemingly low likelihood. But to be fair this concern must be applied to *all* options in a decision, also to the option of not developing a certain biotechnology, or to the option to use more traditional means.

A second connection between principles and concerns is that principles may give explanations as to *why* we should be concerned about something (Little 2001). Principles are explanatory. For example, the concern that the child resulting from an experiment demonstrating that human iPS cells are also totipotent would be seriously harmed and wronged, is not just a feeling that this might be so. It is rather a concern that can be explained: firstly by referring to a principle that seriously harming another person always *prima facie* wrong, and secondly by referring to a principle saying that using persons for medical experiments is wrong because the relationship would be exploitative and lack respect.

So, there is no strict dichotomy of principles and concerns. They work on different argumentative levels. But they can still have a difference in style. It is not the same to *start* from principles or to start from concerns. Principles are general arguments used in judgments, while concerns refer more directly to the particular and personal, even if many concerns are also of general importance. Concerns can be contained in or transported with principles and they can be explained by referring to principles. But the general form of principles may hide the force and direct appeal of the concern-based argument. In moral theories principles appear as axioms, i.e. as general first norms that set the beginning of a moral doctrine, whereas concerns are a sort of uneasiness, worries about possible harm, wrong, mistreatment, or injustice. A concern identifies an issue, an ethical concern identifies a moral issue in a situation. To raise doubts about the soundness of a principle is not the same as to ignore a concern that was raised.

Principles are clearly at the top of the positive side in the list of our moral terms. They express what is desirable, or what makes something ethically acceptable. Concerns are frequently on the negative side. They express what is undesirable or wrong in a certain constellation of actors, and should therefore be changed. But principles and concerns are not symmetrical terms just on the positive and the negative side of the vocabulary of ethical language.

One characteristic of principles and concerns can be seen if we see how principles and concerns can be rejected. If a concern is given up during conversation, thanks to better insight, it is not deconstructed as wrong but as groundless. We may say convincingly: ‘See, no need to worry’. But it does not make sense to say: ‘Your concern is wrong’. But we do say: ‘I don’t share your concern here’. In such a case we have the burden of proof to demonstrate that there is no reason to worry, and the concern in reality is indeed groundless. Concerns can be seen as more or less pertinent, they may be shared or not shared, they can sometimes prove groundless; but to say ‘groundless’ does not mean that they are ‘wrong’. The person who was concerned was perhaps right in her concern, but the concern was not necessary *in this situation here*. The descriptions that are given of the situation are, however, statements that can indeed be true or false.

If we succeed in demonstrating that a concern is groundless, we do not claim that the concern was false. What we say in such a situation is something like: 'I understand your concern, but the problem that you see is solved or will not arise'. Or, if the constellation is the inverse and we are in discussion with somebody who does not share our concerns, then we must explain why we do see a problem. The other could explain why she or he does see a problem. In arguing for this, references to general concepts may have an important role. But we could also refer to those people who are involved in the situation, are affected by the issue that we see and express concerns in their own words. And we could then say: 'If you deny that there is an ethical problem here (e.g. when using people in poor countries as handy test subjects in drug trials), then you disregard their equal participation in the ethical discourse'.

I believe that concerns are truly ethical while principles are moral. This may be surprising. Reading standard bioethics literature it would be more common to expect that principles are 'ethical' and concerns 'moral'. There is, however, no consistent use of those two terms; sometimes they are also used interchangeably. If ethics is a theory of what is moral and immoral and if theory rests on principles as its basis, principles are identified with the 'ethical' side of the relation. But there is a bias in this ordering. One immediately tends to think that concerns, which are 'just' moral, are contingent (i.e. they depend on particular sensibilities and on the local customs), whereas principles carry rational insight and can provide general justification. We should try the reverse.[8] I believe that it also makes sense to say that the concerns contain a moral sensibility and responsibility to those involved and affected, which is genuinely ethical. I prefer to use the term 'moral' for systems of norms and values and equally for a system of rational justification of rules and decisions. Two flagship examples of Western philosophical ethics – with a significant influence on current bioethics – are Utilitarianism and Kantianism. Their methods of justifying rules and decisions (calculating the overall utility or the check by universalizing rules or singular decisions) would, in my terminology, be called 'moral theories' whereas the ultimate matters of concern encapsulated in both moral theories – freedom as autonomy for Kantianism[9] and happiness and wellbeing for Utilitarianism – are concerns with regard to a good and fulfilled life and constitute their 'ethical' basis.

Learning from disagreement

But why does this matter for BIONET and for European-Chinese research collaborations in bioethics? The intuition is that cross-cultural discourses in bioethics may benefit from reformulating the topics in terms of concerns instead of principles. Recollecting the experience from discussions at BIONET workshops and conferences we may say without much hesitation that this intuition is correct, because this experience shows that quite often concerns are more easily agreed upon across cultures than principles. But less clear is whether it is also possible more generally to capture key elements of ethics in terms of concerns. Starting from the observation that

[8] I am encouraged to try such a 'swap' by the terminology used by Paul Ricoeur (1992).

[9] Unlike O'Neill (2002), I see the ethical basis (my sense of the term 'ethical') in Kantianism not in a principled autonomy but in the recognition of others like ourselves as individual subjects of freedom. Freedom is the ultimate *matter of concern* in Kantian ethics. Kantian formalism is an approach to interpreting, realizing and safeguarding personal freedom in social relationships.

principles encapsulate concerns, explain them and bring them to the forum of rationality, albeit with a different accent, I argue that concerns are more fundamental ethically than principles. Therefore, I believe that an ethical discussion that starts from concerns instead of principles can indeed lead to an understanding in the crucial areas with which ethics is concerned. Let us look at an example outside the BIONET.

The striking international disagreement about the moral status of the human embryo can be taken as an instructive case. Difficulties have become particularly prominent since the United Nations (UN) negotiated towards an international ban of reproductive cloning of human beings. These negotiations ended in failure, despite the fact that there was a global consensus (at least among the UN representatives) that reproductive cloning should indeed be banned urgently with effective instruments of international law.

I participated in these negotiations at the UN in New York during 2002 and 2003, as a bioethical expert for the Swiss UN delegation. Negotiations started in an Ad Hoc Committee of the Sixth Committee with a scientific and bioethical hearing. After that, all member state delegations could express their opinions about reproductive cloning. I was struck by the agreement between all the opening statements about reproductive cloning. Not a single nation gave any reason to doubt that an international ban of reproductive cloning was both desirable and ethically relevant. But there was one big disagreement right from the start, which continued throughout the process of three four-day working sessions, several session points in the Sixth Committee assembly, and two session points in the General Assembly. This disagreement was sparked mainly by the US delegation, together with the delegation of the Holy See (the Vatican), and immediately supported by a series of nations with a strong Catholic background. Their argument was that *only* banning reproductive cloning of humans would have serious side effects. It would allow ‘therapeutic’ (or ‘research’) cloning of embryos for generating stem cell lines. And starting from the assumption that human life starts at fertilization and every individual has a full right to life, independent of age, only prohibiting nuclear transfer cloning for reproductive purposes and not also for research purposes would be inconsistent and ‘false’. The expression of a ‘false ban’ has been commonly used. But this move, proposed by the group of nations led by the US under the George W. Bush administration, was impossible to follow for many other countries (like the UK, Sweden, and China), whose legal positions on the moral status of embryos differed. In part, these countries had national legislation in force that explicitly *allowed* nuclear transfer cloning of human embryos for research purposes and for creating therapeutic cells or tissue.

France and Germany, who were in 2001 the authors of the original proposal to initiate a process towards a global ban of reproductive human cloning, were clear about the fact that in their own countries therapeutic cloning was banned. Their proposed approach (backed also by the Swiss delegation, the UK, China and many others) was to proceed pragmatically step-by-step, first deciding about reproductive human cloning, where an agreement seemed easy to reach and most urgent, then, in a second step, discussing therapeutic cloning, and deciding about therapeutic cloning independently. But this pragmatic procedure was made impossible by a powerful intervention on the part of the US delegation, who declared that they would *block* every other solution except a comprehensive ban that included *both* forms of cloning. This was difficult for several reasons: (i) the US is the world’s largest superpower

with a right to veto decisions in the Security Council; (ii) the Sixth Committee should find results by consensus, which then become proposals to the General Assembly of the UN.[10] The disagreement was formulated as a disagreement about procedures and there was much power politics (which is beyond the scope of this paper), but the underlying substantial moral disagreement was on the embryo question: is the zygote – be it the result of a fusion between an intact oocyte and a sperm or between an enucleated oocyte and a somatic cell – already to be considered as (or like) a person with an inalienable right to life and an intrinsic dignity according to the principle of sanctity of life extended to embryos? This was a question about fundamental belief, about the moral axioms from which one was starting.

The process that could have led to a cloning ban ended at the 58th General Assembly on 5 December 2003. The General Assembly decided in this situation of unresolved controversy to take no action at the moment but to reconsider the issue later. In the following year, the discussions were re-opened, not as a process leading to a binding convention, but as one ending only in a declaration, which is legally non-binding. On 23 March 2005, such a statement about human cloning was finally adopted by the 59th General Assembly of the United Nations, with a majority of 84 votes in favour to 34 against, with 37 abstentions.

I know that not everybody will agree with my assessment of this outcome. I maintain that it signifies a striking failure of intercultural bioethics.[11] I see three reasons that let me conclude that the process failed: (i) Despite a general consensus about the urgency of a ban on reproductive cloning (albeit for different, in part mutually supporting reasons that range from human dignity considerations to the protection of the cloned children, who would be at risk of being seriously harmed physically, and who would be instrumentalized morally as research objects) the process ended in a non-binding declaration instead of a binding convention; (ii) the document had only 54% support, which is dramatically weak and undermines the authority of the normative recommendations; (iii) the wording of the statement is ambiguous; it even leaves the main point open to interpretation. I quote the key passage:

> "(a) Member States are called upon to adopt all measures necessary to protect adequately human life in the application of life sciences; (b) Member States are called upon to prohibit all forms of human cloning inasmuch as they are incompatible with human dignity and the protection of human life."[12]

This leaves everything open. One could even imagine a country claiming that reproductive cloning does not infringe human dignity. As several authors (in my eyes convincingly) have pointed out, the argument regarding human dignity is one of the weakest of all possible ethical arguments against reproductive human cloning, because it is purely dogmatic and introduces an ethically problematic form of genetic determinism.[13] Because cloning is not different from the natural occurrence of a homocygotic twin, except that it is artificially induced and temporally retarded, it is

[10] See the summary of the events and votes on www.un.org/law/cloning.
[11] See also the collection of views in Roetz (2006).
[12] The United Nations Declaration on Human Cloning is available on www.un.org/law/cloning, under the number A/RES/59/280.
[13] See Pence (1998) and Honnefelder/Lanzerath (2004).

difficult to defend the position that it is temporal postponement of twinning that makes cloning an infringement of human dignity. In homozygotic twins nothing can be found that is against human dignity. Twins are persons who each have their own distinct personality and possess human dignity like everybody else. The fact that their genetic material is not unique does not change anything with respect to human dignity. Why should it then be counter dignity if the two twins are asunder in time? Time difference in the generation of homozygotic twins can therefore only be irrelevant ethically for their equal recognition as dignified human persons. But if it is not even clear that reproductive cloning is an action that contradicts human dignity, the wording is ambiguous regarding the question of therapeutic cloning too. Given that those advocating it probably believe that it does not infringe human dignity, the conclusion seems unavoidable that the actual UN declaration on human cloning does not necessarily contradict therapeutic cloning. This outcome is embarrassing, to put it modestly. Paragraph (a) of the declaration does not help either, because protection of human life is only required to be "adequate", whatever this means.

What can be learned from this experience? It would be naïve to claim that the negotiations would have been successful if only the discussions had been concern-based instead of principle-based. My interpretation of the failure is that across the dividing lines between the camps, concerns could not be *heard* by those who held the opinions and formulated the strategies, because those with decision-making power were either not in the room themselves or were already committed to very tightly defined principles that did not allow them to be flexible enough. All negotiations at the United Nations are based on a complicated infrastructure of power relations. These power relations always transcend the people sitting as representatives on their country desks in the hall where the negotiations are taking place. The actual participants in the discussions are delegations of states, and depend on more or less strict remote control by their governments. This does not apply to all governments in the same way; not all already had a fixed position before the negotiations started, but some of the most powerful had.

The principles that have been formulated iteratively (often the principles of tolerance, of respect, and with regard to the embryo the principles of potentiality, dignity and sanctity of life) could not convince most of the delegations in the other camps to change their minds or to enlarge their approach. Concerns could have had this power of moving minds and enlarging views in normal face-to-face discussions. But in this setting, concerns were not really heard, or did not reach those with decision-making power, or even did not appear explicitly on those hundreds of written statements exchanged among the delegations during the long negotiation process. The style and framing of the discussion did more to facilitate declarative statements than the asking of others, in order to learn why they maintained their opinions and why they saw their principles as pertinent. Yet it is this approach that would have brought forward the concerns behind the principles and initiated a more cooperative style of decision-making. Is this a sign that in difficult bioethical cases a universal consensus is impossible? Is the embryo issue dividing the world into two moral cultures? Before assuming this somewhat disappointed conclusion we need be look at the concept of the universal once again. What is meant by 'universal consensus'?

Universals and recognition

No distinction was made between *universalization* of ethical principles and their *universalizability*. With universalization of ethical principles I mean the claim that principles, if they are right, should be valid universally, i.e. acceptable for everybody, or accepted by every reasonable person. This claim is not unproblematic in cross-cultural bioethical discourses, because in controversial matters it can be heard as a denial of reasonability of deviant beliefs, which may be seen as perfectly reasonable by members of other cultural traditions. Universalizability, however, is a much more tolerant claim of universality. It is not a requirement that the others participating in the discussion adopt certain beliefs and reject others, but in the first place a requirement of oneself: if a maxim (rule, principle, etc.) should be tenable, I must be sure that it is not arbitrary (or just 'sounds good'). I need to check whether I can find it acceptable that others accept it too. Is it possible to *wish* it to be accepted universally? This version of universality retains the rigor of the well-known Kantian 'categorical imperative' without denying a plurality of moral rationalities, at least in certain respects. I do believe that it is more congenial to what Kant actually had in mind.

Those principles that we have mentioned so far are formulated in a universal language. If the principle of sanctity of embryonic life says that it is wrong to end the life of a human embryo at an early stage, it is wrong to do so for everybody at all places in the world and at all moments in time, independent of how the embryo was generated. Does this mean that *all* principles are problematic because of their underlying generality claim? I do not think so. As Olivia Little (2001) has demonstrated, generality is even defensible for a moderate particularist. Claims can mean 'for the most part' and be porous for exceptions: 'defeasible generalizations […] privilege the conditions or cases in which a certain connection holds', i.e. they refer to a 'default status'. They mean, for example: 'Normally it is wrong to do …'. And in saying so we explain the ethical content of a type of situation; attention is called 'to what is theme and variation, deviance and normality, paradigm and emendation.' (p. 38)

There is a second difference within the concept of universalism. Seyla Benhabib distinguishes between four forms of universalism: essentialist, justificatory, moral and juridical. Her argument is that some forms of universalism are indeed prerequisite and *necessary* for an intercultural moral discourse to be possible. Other forms of universalism, however, may be obstacles. Let me explain her argument in some detail. She first makes an interesting point about the concept of 'culture'. We are tempted to speak of cultures as delineable wholes. This goes back to Johann G. Herder's philosophy, in which he saw a culture as a domain representing the shared values, meaning, language and symbols of one people. Cultural studies have demonstrated that this picture is flawed, because it presumes homogeneity of cultures, their separateness, and a view from outside, which is not possible for somebody who tries to understand the system of meanings. We observe and speak always as participants in a culture, even when we go to a foreign one. We are never non-encultured observers. The Herderian 'culture' also misrepresents the intercultural reality of the modern world. It is normal for many of us to participate in more than one culture at the same time. The narratives and symbols are partially shared, partially contested and dynamic. There are overlaps and partial coherences. All cultures are hybrids and poly-vocal, multilayered, decentred, fractured systems of action and signification. They are far from homogenous and consistent, but contain, in the words of Clifford Geertz

(1973), plenty of contradictions, questionable improvements and tendentious commentaries. Therefore, in international bioethics the question is not how members of two separate cultures as closed systems of meaning can talk together. The discursive context of cross-cultural dialogue is more complex but also less problematic, because cultures are themselves fractured, overlapping webs with partially shared practices, beliefs and significations.

On this basis, Benhabib[14] then distinguishes four different beliefs that can be said to be 'universalisms'. (1) One is 'essentialist universalism': this is the belief that there is a fundamental human nature or a human essence, which defines who we are as human beings. She concedes that there is no convincing concept of such a fundamental human nature or human essence that defines us universally as human beings, regardless of race, gender, sexual orientation, nationality, cultural background, everywhere and at all times in history. We do not need such a concept. (2) A second form of universalism she calls 'justificatory'. It is the belief in the normative content of human reason, in the validity of procedures, of evidence, in the value of impartiality, the possibility of inter-subjective verification of results, argument or data. (3) And there is 'moral' universalism. This is the belief that all human beings, regardless of race, gender, sexual orientation, bodily or physical ability, ethnic, cultural, linguistic, and religious background, are entitled to equal moral respect. (4) Finally there is 'juridical' universalism: the belief that all human beings are entitled to certain basic human rights, which does not necessarily include complete agreement on the content of the list of those human rights.

Benhabib (2007, 13) then gives a nuanced evaluation of these forms of universalism. She argues that:

> 'any political justification of human rights, that is, the project of *juridical universalism*, presupposes recourse to *justificatory universalism*. The task of justification, in turn, cannot proceed without the acknowledgment of the communicative freedom of the other, that is, of the right of the other to accept as legitimate only those rules of action of whose validity she has been convinced with reasons. Justificatory universalism then rests on *moral universalism*, i.e., equal respect for the other as a being capable of communicative freedom. Justificatory universalism, however, need not presuppose a full-fledged theory of human nature or a comprehensive moral, religious, or scientific worldview: an account of human agency in terms of the "generalized" and "concrete" other will suffice.'

The common idea behind these universalisms is 'the recognition of communicative freedom' (ibid.): 'In order to be able to justify to you why you and I ought to act in certain ways, I must respect your capacity to agree or disagree with me on the basis of reasons the validity of which you accept or reject. But to respect your capacity to accept or reject reasons the validity of which you evaluate means for me to respect your capacity for communicative freedom.' (14) I would add: I respect both your *capacity for* communicative freedom and I allow you the space for agency in the discourse, i.e. I recognize you as *real subjects* of communicative freedom. These forms of universalism therefore aspects of a *recognizing* universalism. They do not

[14] Benhabib (2002) pp. 26ff; Benhabib (2007).

claim *what* others should believe, but they claim that the others should be recognized as subjects who accept or reject beliefs on the basis of reasons, the validity of which they accept or reject. This stands in contrast to essentialist universalism, which is a *dogmatic* universalism, because it claims to know what others should believe about human nature, the fundamental principles of ethics, or the like.

International discussions about good governance of research and practice in biomedicine and biotechnologies are comparable to discussions about political justification of human rights (to which Benhabib is referring), because both are normative and both concern regulations in ethically sensitive matters. Also in cross-cultural bioethical discussions, the other must be recognized as a person with agency. This implies that all others are regarded as subjects with an equal right to express their own concerns, with an equal right to be heard, an equal right to claim rights and duties, virtues and ideals. I agree with Benhabib's analysis that without a universal recognition of the communicative freedom of the partners in a cross-cultural setting, i.e. without recognizing them as others with agency, communication would not be possible.

There are certain bioethical principles that are very close to this emphasis on communicative freedom, for instance the principle of 'free and informed consent'. This principle does not claim that the person should accept certain beliefs and reject others. It is just a procedural principle that allows the person a space of agency.[15] For, as an agent, the person needs to be respected in her power to consent or dissent. Therefore the principle of free and informed consent is not one of the problematic principles in cross-cultural bioethics. As the discussion about family consent and the role of trust show, there are different views on the concrete procedures on how to best realize informed consent and on the meaning it should have.

Conclusions

The questions stated in the introduction can be answered as follows: It does make a difference whether bioethics sees itself as grounded in principles or concerns. And a concerns-based bioethics could indeed have advantages in a transnational public sphere. However the picture that has emerged is more nuanced.

(1) If a principle is transparent regarding the ethical concern it encapsulates, and if this concern is shared, the moral principle has a better chance of being understood across cultural differences. Perhaps communicative work in concrete case discussions will lead to a formulation of the principle that reflects language from both cultural contexts, and resonates with both. In other cases, principles may be more difficult to grasp, or even be divisive. One question that could improve understanding across the divides is the question about the underlying ('encapsulated') concerns. I believe that perhaps every moral principle, if it has prescriptive moral force, contains ethical concerns that can be made explicit. It is the ethical concerns that give authority to the principle, not the 'rational', general form. *Principles can be unpacked to deliver the concerns*, which provide them with normative power. Therefore, a concern-based bioethics is not a bioethics without principles, but a bioethics that uses principles in a

[15] Elsewhere I have suggested that allowing agency could replace the old principle of non-directiveness as a better interpretation of the ethical basis of genetic counselling (Rehmann-Sutter 2009).

non-dogmatic way. Principles need to be transparent regarding the ethical concerns that they encapsulate.

(2) It is not the use of principles per se that creates difficulties, but a certain *style* of using them. Principles can be used to make one's thinking clear, explicit and understandable to oneself and to others. As such they are indispensable in ethical language. As such, principles do not imply essentialist universal claims. Or not all of them do. Principles can, however, be used in a way that is divisive. They are divisive if they are not transparent regarding the ethical concerns they encapsulate. They are divisive if they imply a dogmatic universalism. However, both concerns and principles do imply the recognizing form of universalism: all others must be seen as agents with communicative freedom. Shared ethical concerns function as a common ground for starting constructive and engaged cross-cultural bioethical work.

(3) There is an emerging global agenda in bioethics. For philosophers this is a challenge. We should ask which approach to bioethics is *capable* of meeting the demands that arise in such discussions across cultural differences. Which bioethics is capable of contributing to a cross-cultural understanding on ethical issues? Or, in the words of political scientist Amanda Dickins,[16] which bioethics can help to create an 'international space'? I plead for a bioethics that acknowledges that it is also itself actively interfering in the practical domain. Bioethics is the *communicative practice* of generating mutual understanding, not just arguing about issues. As a communicative practice it is therefore not ethically neutral. Bioethics is 'doing things with words'. One part of bioethics must reflect on this and be an 'ethics of bioethics'. Acknowledging this means that bioethics should also critically reflect on how it acts, and on the attitudes it holds at the cross-cultural interface.

(4) Bioethics starts *within* societies and cultures, *among* concrete partners. Bioethicists, even those who express their views in the form of universal principles, reflect on ethical issues *from within* a cultural setting. Bioethics itself contributes a layer in the poly-vocal and hybrid, decentred systems of actions and significations that make cultures. And here, bioethics does not start ethical thinking from scratch. Bioethicists hear and speak concretely with involved others who are also hearing and speaking. Therefore, every ethical statement has an address (Butler 2003); it is directed to somebody who is herself or himself a morally competent and reflecting subject whose communicative freedom needs to be recognized.

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[16] Amanda Dickins (2008).

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PART 2:

STUDENTS' FINDINGS

Introduction

Ole Döring

Over its 3 years of operation, the BIONET was able to conduct an exchange visit program for advanced students from China and European countries. The BIONET students were encouraged not only to visit different sites in their guest countries and explore their research field, but also to embrace the opportunity for cultural learning. Disregarding the short time and limited funding available for this activity, the BIONET's students turned out to be the finest seed produced under this project; with several of them embarking on promising careers as bridge-builders between the continents and the people. Some of the resulting papers have been collected for this volume. They take up and develop topics introduced in chapters above (part 1) and offer examples for the feasibility, relevance and high quality that can unfold under conditions of sound planning and reasonable support.

Chen Haidan, in her report about "Stem Cell Governance in China: From Bench to Bedside?", makes use of inspiration and resources she drew from her studies in Europe, in order to reflect about the governance situation in her home country. She presents three cases from China to illustrate various strategies to bring stem cell science to treatments and commercialization. Chen demonstrates how translational research involves multiple interactions between different actors and requires new modes of governance. In China, as in other countries, the regulatory context for translational stem cell research is fraught with uncertainties. However, the absence of state regulation has not led to a "Wild East" regulatory constellation, but rather to individualized regulatory strategies by a variety of stakeholders.

In a carefully embedded micro-study, "The IVF-Stem Cell Interface in China: Ontologies, Value-Conceptions and Donation Practices of Embryonic Forms of Life", Achim Rosemann investigates the value and status attached to IVF embryos from the perspectives of potential embryo donors in China, and asks, what are the factors that influence patients' decisions to donate? He expressly casts doubt on the widely spread notion of a culturally entrenched ethics of allegedly Confucian origin. Rosemann provides evidence indicating that ideas on the value and the permissibility to donate and use human embryos for hESC research are much more complex and diverse in China than is commonly suggested. Speculation that, as a result of the high abortion rate related to the one child policy, the value of early forms of unborn human life is generally low among Chinese people could not be confirmed. Moreover, assumptions that Confucian-inspired ideas on the starting point of human life are still valid in China were not supported by the participants of this study. In the second part of his study, he describes a varied picture of professional ethics, with a wide range of practices that unfolded between the poles of a strong commitment to professional care and responsibility on the one hand, and forms of occasional deception / manipulation of patients on the other.

In her related study, Anika Mitzkat targets the "Donation of spare embryos for stem cell research: Experiences and views of couples undergoing IVF at CITIC-Xiangya Hospital of Reproduction and Genetics, Changsha, China". In this exploratory pilot study, she follows a qualitative design with a phenomenological approach, with the

goal to understand the processes of ethical decision-making about donation of embryos for hESC in both Chinese and European contexts from different participants' perspectives. Her findings indicate the feasibility and highscientific merit of engaged cultural studies "in the field" in China, and its significant relevance for the bioethical discourse.

In her research project, "The Political Stabilization of Technology: the case of oocyte contribution to stem cell research in California, China and the UK", Megan Allyse applies a new theoretical framework (the Political Stabilization of Technology, PST), which provides reflective, predictive and explanatory insights into policy processes surrounding the State's normative management of emerging scientific and technological developments. She applies it in three national contexts, from a political science perspective and with significance for anthropology and comparative cultural sciences. A major methodological finding is that, we need to understand the distinctions between the multiple social and scientific contexts within which oocyte extraction has come to be employed if we are to grasp how it became contested in three such widely divergent social and cultural contexts.

Joy Yueyue Zhang sets out towards the cosmopolitanization of science. The focus of her study, "The Regulation of China's Stem Cell Research in the Context of Cosmopolitanization", is to examine how the globalization of the scientific community has influenced the regulatory developments in scientific practices within China. According to her insights, the advancement of the contemporary life sciences cannot be promoted solely with a top-down approach, but should involve social agencies and include initiatives generated from different levels. The awareness of dependency was a key factor that promoted the globalization of research, and it is the acknowledgement of interdependence that enables cosmopolitanisation in regard to governace as well.

Wang Chunshui, in her study about "Ethical and Social Aspects in Neuroscience: Focus on Medical Interventions of the Brain" observes that, at present, due attention is not being paid to social and ethical issues of the neurosciences in China. The aim of her long-term study-project is to learn how to identify these new issues, to study the relevant social sciences methodologies, and try to address these issues, especially in the context of China, but with obvious implications for Sino-European research governance.

In her BIONET students' report, Li Rong describes the situation of "Informed consent in the clinical work of ART and the research of stem cells" from her perspective as a clinical gynecologist in Beijing. She focuses in particular in comparative studies of the ways in which informed consent is organised in China, Germany and the UK, and the situation of surrogate motherhood, which is forbidden although practiced in China, legal in the UK and forbidden in Germany. She argues for the need to give greater attention to spending due time and care when taking consent and raises concern about childrens rights and welfare in the context of surrogate motherhood.

Sui Suli argues, in her report on "Comparing the Practice of Genetic Counselling in the UK and China", that the practice of genetic counselling should be seen within the social contexts of different countries. These include economic conditions, distribution of health resources, the medical care system, professional governance, population

policy, and cultures. Although acknowledged in theory, in practice, the ideal of non-directiveness and non-judgement in genetic counselling is hard to achieve. This is owing to the intrinsic heteronomous character of medical practice. Sui observes that more understanding and psychological support for patients are needed in order to improve the relevant capabilities. Within and between China and Europe, more research is plainly needed, to which this study makes a significant contribution.

Finally, Su Yeyang draws our attention to another exciting field of interdisciplinary study. Her article, "Engaging the Scientist's-Public Interaction – Understanding the New Partnerships in Today's Biological and Biomedical Research", focuses on understanding and analyzing contemporary engagement with science and the public, which can be initiated by life scientists. Su reports from interviews that helped gain in-depth perspectives from different stakeholders involed in such engagement. Her findings suggest that, although a scientists-reach-out strategy may have shortcomings, such as conflicts of interest, and participation is limited, such initiatives should be encouraged as the first step towards bridging scientific knowledge gaps. Moreover, science communication is a process. Proper training and education should be provided to scientists and students, who are interested in interacting with the public.

Stem Cell Governance in China: From Bench to Bedside?[1]

Chen Haidan

This article presents three cases in China and shows various strategies to bring stem cell science to treatments and commercialization and the problems encountered in the process. The case studies show that translational research involves multiple interactions between different actors and requires new modes of governance. In China, as in other countries, the regulatory context for translational stem cell research is fraught with uncertainties. However, the absence of state regulation has not led to a "Wild East" regulatory constellation, but rather to individualized regulatory strategies by a variety of stakeholders.

Introduction

On 21 January 2009, just a day after Barack Obama's inauguration as president of the United States, Geron received FDA clearance to begin the world's first human clinical trial of embryonic stem cell-based therapy for acute spinal cord injury in up to 10 patients. This trial has been seen largely as a milestone in the process of translation of stem cell technology from laboratory work to clinical trials (Jeffrey 2009, Pollack 2009, Walsh 2009), and it has set a road map that other scientists, clinicians and regulatory authorities might follow in the future. The Geron trial points to the challenges of how to cope with bio-objects like stem cells and of how to regulate the clinical translation of stem cells.

Biopolitics in Asia is often regarded as a "Wild East" type of politics by Western countries, and Asian countries like China and India tend to be blamed for an assumed lack of regulation and ethical guidelines in experimental medicine (Gottweis 2009). However, I argue that it remains to be examined in empirical detail what the similarities and differences are between China and other countries when it comes to the governance of the clinical translation of stem cell research, how translational stem cell research operates in China, and which regulatory approach is emerging while acknowledging irregularities that could occur during the transition stage in China. Given a series of "known unknown" and "knowable unknown" factors in stem cell research (Eriksson and Webster 2008), this article argues that successful translational research, as defined below, needs to go beyond simple linear translation models and must build a new system of governance, particularly a pattern of combining soft regulation and hard regulation. Myth has it that China is some "Wild East" of stem cell regulation. This article will show that though one can hardly argue that clinical translation of stem cells in China is strictly regulated, the reality of stem cell research does not correspond to the typical clichéd images. As in other countries, the actors involved in translational medicine in China need to pay attention to the complex process of translational medicine and a multiplicity of factors. Public concerns and regulatory challenges are an important part of this constellation. As recent events such as the milk powder scandal in China have shown (The Economist 2008), the Chinese

[1] This article is a modified version of Haidan Chen, Stem cell governance in China: from bench to bedside? *New Genetics and Society*, Vol.28, No.3, September 2009, 267-282.

population is far from being a passive entity, and scientists as well as regulatory authorities seem to have taken this message on board.

In this article I will address some of these controversial issues and in particular attempt to open up the "black box" of translational stem cell research in China by discussing case studies.[1] My first case study will show how the research group led by Robert Chunhua Zhao from the Center of Excellence in Tissue Engineering, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, conducted clinical trials on a stem cell therapy abiding by Provisions for Drug Registration, PRC and which scientific, political, and economic hurdles the group encountered. A second case study will focus on the much-debated stem cell company Shenzhen Beike Biotech (Lim 2008, McCullough 2008, Nelson 2008), and discuss the controversial and greatly criticized stem cell therapies of Beike and illustrate how the company took advantage of the ambiguity of regulatory policy. Finally, I will show the attempt by the city of Tianjin to shape a new "stem cell industry" and which factors have been mobilized to move stem cell science into application. The focus of these three cases has been chosen because they help to analyze the key challenges in the governance of translational medicine (Wainwright et al. 2006), and the complex modes of ordering between biomedical research and the medical-clinical system, industry, society and political regulation in the field of stem cell translational research.

Governing translational research

The term "translational research" first appeared in PubMed in 1993, but it did not attract extensive attention until around 2000 (Butler 2008). The goal of translational research is to bring biomedical knowledge from the laboratory to clinical application and therapeutic products. Given that previous attempts such as "clinical pharmacology" and "experimental medicine" have not been very successful in moving from science to commercialization and the patient's bedside, the latest iteration – "translational medicine" – brings expectations, but it has not been "sprinting off the blocks" (Anon 2008).

The abyss between basic and clinical research is sometimes labeled as the "valley of death," as this particular chasm has existed in the ecosystems of bench and bedside research for over 30 years (Butler 2008, Kraft 2008). Nobel Prize winner, Sydney Brenner argues that "from bench to bedside" translational medical research is based on an incorrect assumption. The focus should be the other way around, he posits, "from bedside to bench," shifting the emphasis to humans and viewing each individual patient as an experimental model (Friedberg 2008). Jill U. Adams (2008) suggests building the bridge from bench to bedside. Other scientists believe two-way dialogue and interaction between scientists in preclinical drug discovery and clinical developers are necessary for effective translational research in drug development (O'Connell and Roblin 2006).

This article argues that translational research is a project that involves multiple interactions between different actors, and I will show that simple linear translation models are insufficient to grasp complex scientific medical realities. Translational research involves new modes of governance, which require both "hard regulation," such as laws, guidelines, and statutes, and "soft regulation" through internalized criteria that shape the comportment of scientists, professionals, and patients (Rose 2008). From the perspective of co-production (Jasanoff 2004), I argue that

"successful" translational stem cell research needs a system of governance, a mode of ordering (Law 1994) that can be understood as a strategy for patterning a network of interaction in a number of different fields, in particular, in the scientific/technological field, the medical/health field, the industrial-economic field, the legal-ethical, and the socio-political field (Gottweis 2010).

The transformation of laboratory-based science into cures does not follow a simple linear model (Tait and Williams 1999). Although intellectual property issues are important in the interaction between academia and industry, recent research shows that the public-private partnership is increasingly perceived as supremely important for the translational effort (Littman et al. 2007). What's more, stem cell treatment as personalized treatment needs a quality control standard, special business models, and particular science and technology innovation systems to bring economic benefits to industry and social benefits to the public, especially to patients. The patients are the objects of clinical trials and recipients of therapeutics. A key issue in this context is the care for the patients, and the compatibility of the healthcare and medical system with public health, so much work must be done to represent stem cells in the public and help the public understand stem cells.

Translational research and Chinese biotechnology

Over the last decade, China has been investing heavily in biomedical and biotechnological research with the aim of positioning itself as a serious competitor in the global scientific and biotechnological market (Salter et al. 2006). China has a large population and is confronted with a broad variety of diseases and health problems in its population. Health is a top priority in the country, and translational research is seen as a promising solution for tackling many human ailments.

The overarching goal of "The S&T Strategic Plan 2006-2020" is to contribute significantly to President Hu Jintao's visions for the development of China such as the "peaceful rise" and the "harmonious society" and to improve progress in the life sciences, especially to address social problems and improve human health (Wilsdon and Keeley 2007). To achieve this last goal, China has mobilized strategies to strengthen the development of the life sciences and biotechnology, for instance, giving more grants to develop biotechnology through a variety of programs.

In China, stem cell research has been defined as an area with great potential for translational medicine. Stem cell projects and cloning research are included in the strategically defined "reproductive and developmental biology" area, one of China's fields identified for major investment in the "2006-2020 strategic plan." Accordingly, the field of translational stem cell research is considered to be a great opportunity for China to compete with other nations early in the process of scientific development (PRC State Council 2006).

The majority of the funding for stem cell research in China comes from the Ministry of Science and Technology (MOST) programs such as the so-called 863 program and the 973 program. Besides MOST, research funding comes from the National Natural Science Foundation of China (NSFC), the Ministry of Finance (MOF), local government, and enterprises.[2] Furthermore, great efforts have been made to attract back overseas talent, some stem cell scientists are recruited by administrative departments at different levels through various projects, such as the Yangtze River

Scholars Program, the Chinese Academy of Science Hundred Talents Program, the NSFC National Distinguished Young Scholars Program. Finally, each region in China tries to fully utilize its own advantages, and different municipal and provincial governments offer favorable policies, financial incentives, and competitive grants in the hope of attracting top scientists to develop better stem cell science in their regions.

Regulatory context

In the United States, the FDA's regulation on stem cell-based therapies were proceeded by a protracted process of negotiation. This was also the case for the European Commission's Regulation (EC) No 1394/2007 on advanced therapy medicinal products. Similarly, in China the passing of the Regulations on Clinical Application of Medical Technology issued on 2 March 2009 by the Chinese Ministry of Health (MOH) took a long time and involved a lengthy decision-making process. Before 2007, stem cell-based products and therapies were categorized as biological products, and applications for clinical trials had to go through the State Food and Drug Administration (SFDA) review according to Provisions for Drug Registration (SFDA Order No.17).[3] However, during the first review processes in 2005 and 2006, the SFDA found it difficult to regulate stem cell-based products and therapies as drugs. On the verge of medical reform in China, the SFDA no longer wanted to be responsible for the review (interview 6). On 11 March 2008 the Chinese government announced a sweeping cabinet restructuring plan that would be put the SFDA under the Ministry of Health (MOH) and the "Super Ministry of Health" would become the manager of areas such as medical service, food, drug, and public health (Xinhua 2008).

After a long negotiation, it seems that an agreement has been reached between the SFDA and the MOH that in the future, regulation of stem cell clinical application would be promulgated and implemented by the MOH. A stem cell application would be applied and regulated not as a drug, but as a new medical technology for clinical application. On 24 July 2007, the MOH put "the Regulations on Clinical Application of Medical Technology (exposure draft)" and "the List of Category 3 Medical Technology (exposure draft)" on its website for more consultation and opinions from the public. This is a new and regular way to generate participatory elements in the development of law in China. In these exposure drafts, stem cell transplantation technology was listed as a category 3 medical technology. Meanwhile, the MOH entrusted the Committee for Medical Technology of the Chinese Hospital Association (MTA) to constitute an expert committee and to draft "the Regulations on Human Stem Cell Clinical Application." On 24 October 2008, the MTA organized a workshop to discuss "the National Regulations on Clinical Application of Human Stem Cell Transplantation Technology (draft)". The participants recommended that the clinical application of embryonic stem cell technology should be performed more cautiously and strictly and follow ethical and moral norms, which is still in the discussion. According to the Regulations of Clinical Application of Medical Technology, which came into effect on 1 May 2009, stem cell medical technology, as all "category 3 medical technology" that are deemed "ethically problematic", "high risk", and "still in need of clinical verification", is under the direct regulation of the MOH. The MOH has designated 5 institutions to review them from 1 May 2009 to 1 May 2011.

To sum up, as in many other countries, the regulatory context for translational stem cell research in China was once fraught with considerable uncertainty. Even with the new regulation, there will still be some uncertainties in terms of its implementation. The selected cases in this article will analyze the different aspects of governance required to support the development of translational medicine in China.

Case studies

From bench to bedside

This case study will show how stem cell research in a university setting starts with ideas in the hope of bringing treatments to patients. It describes the road from in-vitro development to animal studies and the development of control standards for clinical studies. To move from animal studies to clinical trials is a complicated process and depends on the cooperation of research institutes and companies, the settling of ownership and property rights, and the creation of a well-developed business model. Graft-versus-host disease (GVHD) is a common complication of allogeneic bone marrow transplantation used to treat some blood diseases. There are a large number of investigational therapies for GVHD treatment and prevention around the world. After many years of research, Robert Chunhua Zhao and his colleagues from the Center of Excellence in Tissue Engineering, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, demonstrated that allogeneic Flk1+ mesenchymal stem cell transplantation not only has great capacity for differentiating into other types of tissue, including the reconstitution of hematopoiesis (Guo et al. 2003, Fang et al. 2003), but it also can lead to potent immunosuppressive properties and donor-specific tolerance by their immunomodulatory effects on T cells and dendritic cells (Zhang et al. 2004, Deng et al. 2004, 2005). These preclinical studies prompted them to apply to the SFDA for a stem cell therapy on humans in an effort to help patients suffering from leukemia to reduce the degree of graft versus host disease.

The scientists I interviewed found the translation of basic research into clinical application extremely difficult, and they found themselves under substantial pressure to justify their funding for stem cell research (interview 4, interview 6). Even though their preclinical papers had been published and clinical trials had been approved by the SFDA, the risks and uncertainties for such personalized stem cell therapies in the clinical trials are always difficult to assess (Baker 2008). From 2003 on, the researchers from the Zhao lab began to cooperate with the National Institute for the Control of Pharmaceutical and Biological Products, the drug testing institute designated by the SFDA, and worked out the quality control standard for the stem cell-based product. In December 2004, the first Chinese stem cell drug “Bone Marrow-derived Mesenchymal Stem Cell” received official approval from the SFDA to begin clinical studies, and the application conformed to the Provisions for Drug Registration (SFDA order No. 17). During the clinical trials, the researchers in the Zhao lab realized that the main scientific obstacles for translation from the bench were caused by the differences between animals and human beings. The key issue in animal studies is to build animal models in order to simulate diseases in humans and to test the efficacy of a treatment (Sabroe et al. 2007). However, the Chinese case showed the drugs that tested effectively in animal studies were not all effective in the clinical trials with humans because the patients’ conditions were much more complicated than simulated in the animal studies, so the researchers had to adjust their protocols constantly to test the efficacy of the treatments.

But Zhao's team was also confronted with other challenges in its efforts of bringing stem cell treatments to clinical application. In November 2005, the Institute of Basic Medical Sciences & School of Basic Medicine, Chinese Academy of Medical Sciences, Beijing, which Zhao's team belongs to, signed a contract with the Tianjin Economic Technological Development Area to initiate a partnership in stem cell product development. In the team's opinion, the success of the Phase III trials depended on sufficient grants from the industry, multi-center effective stem cell trials, and a large-scale preparation of stem cells. The funds of their clinical trials come partly from the 863 program and partly from their collaborative company. The clinical trials in Phase II have further validated the efficacy and safety of the treatment. However, they found developing stem cell-based products and therapies to be much more expensive and complicated than developing conventional chemical drugs. Stem cells derived from bone marrow of different donors were different, and even the same stem cells had various treatment effects on each patient in the clinical trials (interview 4). This variability is a common problem in biological, 'wet tissue' therapies, which are difficult to control. But the regulatory problem is then for agencies to decide how much variation they can accept and still claim to be licensing therapies to an agreed regulatory standard.

The case of Zhao's team is the only case in China whose allogeneic stem cell clinical trials have gotten SFDA approval and approached the the end of Phase II trials. But overcoming the hurdles between animal models and humans was not enough. For a research institute to be able to do translational research from bench to bedside, it had to cooperate with hospitals for clinical trials, and for later stage trials and product development. Taxpayers' money was not enough to support its work. Thus a partnership with industry was envisioned to efficiently address the financial problem. Finally, the case of translational research from bench to bedside shows that Zhao's team had made a deliberate effort to go through a strict regulatory procedure, a process the Zhao group considered essential for it to achieve acceptance and legitimacy. But they were worried that, if the future regulation of stem cell therapies was under the MOH, the post-2007 regime rather than the previous SFDA, they would lose the advantages of their translational research done before this date. Also Zhao´s general approach is fraught with considerable uncertainty, including the establishment of the new regulation on clinical application of stem cells in China and their impact on the team's translational research.

From bedside to bench?

"Looking for the cutting edge of stem cell science? Instead of Stanford or Cambridge or Singapore, consider Shenzhen." On 31 March 2006, BusinessWeek reported the influence Beike Biotech would exert (Einhorn 2006). In the following section, I focus on the case of Beike Biotech, the company which attempted to bring stem cell research to patient treatment in China. My case study will show that Beike Biotech mobilizes a special business model to accelerate stem cell applications in hospitals. Although the local government of Shenzhen is in support of Beike, there are other voices who argue it is unethical to apply experimental therapies to patients and that Beike's proof of treatment effects mostly rely on patient testimonials through blogs on the company's website, but the treatments have not yet been proved by published scientific literature (Lau et al. 2008). The company's strategy for translational stem cell research seems to consist mainly of constructing a platform to link scientists,

clinicians, research institutes, and healthcare institutions in an effort to create cooperation.

Beike Biotech was set up in Shenzhen, the first special economic zone of China on 18 July 2005. It collaborates with hospitals and treats patients in the hospitals and then shares the resulting profits. Until 2008, Beike cooperated with 13 hospitals, 6 centers were added in 2008, and 5 new centers will be initiated in 2009. According to Xiang Hu, the Chairman of Beike Biotech, doing translational research from bench to bedside and developing stem cell medical products would involve an average investment period of more than 10 years and could amount to roughly 100 million US dollars (cited from He 2006). So, Beike's strategy was to start the business "the other way around." The company mainly uses umbilical cord blood and autologous bone marrow-derived stem cells to treat patients by lumbar puncture or IV infusion. In 2007, treatments totaling approximately 2,640 injections of stem cells were performed, and by the end of November 2008, the number had reached 8,283 (interview 3). According to Beike, many of the people approaching the company for treatment are facing death because of their health condition. As long as stem cell therapies are safe, effective, and controllable, they can be used as experimental therapies for patients who have no alternative methods to be cured (interview 1). This incurs a mass of controversies and criticisms.

The core of the controversy around Beike is the ethical issue of unproven therapies with stem cells being marketed directly to patients who are vulnerable and in despair. Hyun and his colleagues (2008) have pointed out the importance for stem-cell-specific experts to assess the risks of abnormal product function and tumor development and to be involved in the scientific and ethical review at each step along the translational research process. In its "translational model", Beike meets none of these criteria. The International Society for Stem Cell Research (ISSCR) addresses in its position on stem cell regulation that scientists and clinicians should not participate in commercial purveyance of unproven stem cell interventions as a matter of professional ethics. Regulators should prevent illegitimate therapies from being used on patients, as these therapies lack scientific transparency and professional accountability (ISSCR 2008). But Beike's representatives hold a different view. They reason, "Since stem cells are there and might bring patients some hope, is it ethical not to treat patients with stem cells when they suffer from incurable diseases and are dying?" (interview 3). Another view: "Controversies raised by experts focus on the fact that there is no strict evidence theoretically, but in my personal view, this is a scientific chauvinism. In reality, they [stem cell experimental therapies by Beike] have helped to treat many incurable diseases, but in theory, we can't disprove it or prove it, there is something science can never solve… We think at least it is good for society and solves people's real pain." (interview 2)

Before 2 March 2009, the Chinese government's policy toward experimental therapies was ambiguous. First of all, no regulations existed for the kind of activities Beike was pursuing. Beike Biotech got the approval for its trials from the ethics committees of their collaborating hospitals, and it kept the records of the stem cell treatments at local healthcare authorities. One Beike representative argues that the tension between patients and doctors in China has never been more intense than now, so if there were any serious problems in Beike's stem cell treatment, the company would not have survived because of lawsuits. However, he remains concerned that the central

government might shut down Beike at any time. In his view, the company has constructed a stem cell research and development platform by gathering first-hand data from clinical research and application, thereby attracting better scientists and clinicians, healthcare institutions, and research institutions for cooperation and further research. Talent, technology, and capital are essential factors for industry, but he feels the most important elements that will decide the future of the industry are favorable policy and regulation (interview 1).

The Beike case demonstrates clearly the considerable complexity of translational stem cell science in China. The long debates on whether stem cell therapy should be defined as a drug or as a medical technology, and whether the SFDA or the MOH should be responsible for the regulation led to an ambiguous regulatory context in the country. Far from operating independently in some sort of regulatory vacuum, Beike's activities were inseparable from a variety of political, social, and economic developments in China. While the Beike model has been severely criticized as undermining patient rights and interests, I have also shown that the management of the company is aware of these critiques and its implications for its further operations, and tries to deal with them through web-based communities like patients' blogs. Furthermore, it seems to be the case that the Chinese government is no longer willing to accept the existence of stem cell clinical application as it took swift action with the new regulation.

However, the Beike model remains highly unusual and controversial. It started its business by administrating stem cell treatments and hoping to feed the findings from clinical research and application back to basic research. This step should be followed by working out Beike's own standard, and this would eventually lead to the application for the MOH's approval of stem cell clinical application. Thus, its model challenges the traditional "from bench to bedside" strategy. Needless to say, the criticism focuses on the fact that more research is needed to validate the substantial safety and efficacy of translational medicine before it is applied to patients. As FitzGerald (2005) has pointed out, when more attention is placed on applied research than on basic research, and the workforce is engaged in drug development and has not received training in both basic research and clinical research, the acceleration of the drug development into Phase III clinical trials comes at the expense of a thorough understanding of the mechanism of new drugs and a sophisticated approach to dose selection. As a result, the early emergence of stem cell therapies into the healthcare market and resulting global stem cell tourism is fueled by a combination of patient desperation, regulatory uncertainty, and the emergence of industries eager for translational medicine (Wahlberg and Streitfellner, forthcoming). With the new regulations on clinical application of medical technology, all the central aspects of the Beike model will undergo a thorough test and it remains to be seen how viable the Beike model will be in the future.

Bench and bedside interaction

The following case study of the Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College is to show how the city of Tianjin hopes to take full advantage of its research institutions' strength in hematopoietic stem cell research and application by establishing a company to run a stem cell bank and building a hospital for stem cell clinical research and application.

In Tianjin, the National Industrial Base of Stem Cell Technology and the National Center of Stem Cell Engineering and Technology gradually developed. Simultaneously, scientists, clinicians, and investors made great efforts to represent stem cells in the public, let the public understand and accept the new technology of cord blood stem cell banking, and persuade the local and central governments to support their stem cell industrialization. The Tianjin business model for stem cell research kept this project ahead in stem cell research, however this case illustrates the ways in which issues of healthcare system and physician-patient relationship, the intellectual property and other commercial conflicts of interest, produce obstacles for translational medicine.

It is a well-acknowledged fact that it is almost impossible for academicians to procure sufficient competitive grants to bring a drug or a test to the clinic and comply with all the testing necessary to meet regulatory requirements (Hörig et al. 2005). Hence it has become a strategy to invite industry to get involved earlier in the translational research process. The Institute of Hematology and Hospital of Blood Diseases, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, are national institutions for hematology. Within this "tissue economy" (Waldby and Mitchell 2006), the banking of the umbilical cord blood of newborns as a source of stem cells began in 2000 as a new field of hope in the emergence of regenerative medicine (Brown and Kraft 2006). Benefiting from the advanced technology from the Institute and the Hospital, in 2001, the Union Stem Cell & Gene Engineering Co., Ltd. (the Corporation) was jointly founded by the Institute of Hematology and Blood Diseases Hospital, and Shanghai Wangchunhua Group, a private firm. Each partner shared the stock of the Corporation, which has a public and private hematopoietic stem cell bank (Tianjin Cord Blood Stem Cell Bank) with a network service system.

According to Weissman (2002), the public's understanding of stem cells is important for developing and legitimating stem cell science. Since 2002, the Corporation has engaged in a variety of activities to inform the public about what stem cells are and why newborn babies' umbilical cord and cord blood need to be collected and stored for future use by offering courses for pregnant women and their families. On the Corporation's website, for example, there is a special section giving information about stem cells and cord blood stem cells in particular. As one leader of the Institute of Hematology and Blood Diseases Hospital explained (interview 8), these efforts are significant, as, in the view of the company, Chinese citizens gradually understand profound scientific knowledge with pictures and easy language that these promotional activities use. The Corporation's state of operation showed that a portion of the citizens accepted the idea that for the benefit of younger generations and other people, cord blood and umbilical cords should be donated or stored, while some of them still doubted the practice because it had potential risks and uncertainties associated with stem cell banking.

As my interview partners emphasized, the government's support is extremely helpful for bench and bedside bidirectional interaction and for developing stem cell industrialization (interview 5, interview 7, interview 8, interview 9). The Corporation's business model brought much social and economic benefit; meanwhile, it has been sharing with the government the importance of developing stem cell research to gain their financial support. In 2000, the National Industrial Base of Stem

Cell Technology was ratified by the National Development Planning Commission, and two years later, the National Centre of Stem Cell Engineering and Technology was ratified by the Ministry of Science and Technology. In 2004, with the support of the National Development and Reform Commission, the National Engineering Centre of Cell Products was created. Its commercial arm, the Tianjin AmCellGene Engineering Co., Ltd., was registered in the Tianjin Economic Technological Development Area. As my interview partners say, though they have very good facilities of laboratories and hospitals for stem cell basic research and clinical research in their locality, it does not mean that the researchers in the Institute of Hematology could just go out of their doors and carry out clinical studies in the Blood Diseases Hospital around over the corner. Concerning the influence of the Institute of Hematology and Blood Diseases Hospital in China, researchers do everything in compliance with the rules (interview 5, interview 7, interview 9). With the reform of the healthcare system, the physician-patient relationship in China is getting worse, which impedes researchers' enthusiasm to do innovative translational research. That China has not promulgated clear regulations early enough has already affected the advancement of stem cell translational research and industrialization in the city of Tianjin (interview 11).

While the Tianjin model improved significantly, the lowering of the traditional barriers between academia and industry is accompanied by conflict-of-interest issues. For example, the division of earning created conflicts between collaborative partners, as one of my interview partners informed me: "In the national industrial base of stem cell technology, Wangchunhua Group owned 38% stocks, the Institute of Hematology owned 30% stocks, the research team owned 20% stocks, and the East China Union Stem Cell & Gene Engineering CO., Ltd. owned 12% stocks, but later one of the team leaders took away 32% stocks of the research team and the East China Union Stem Cell & Gene Engineering CO., Ltd. as his own property and ran them as a family-owned enterprise. He broke the heart of his research team members; we felt our hard work was not respected." (interview 10).

The Tianjian case demonstrates again the multi-faceted aspects of translational research and its interaction with society and politics, with particular relevance for governance. Based on its advantages of hematopoietic stem cell research and transplantation, the Institute of Hematology and Blood Diseases Hospital has become a leader in stem cell industrialization in China. At the core of their strategy was setting up the Corporation to run the business of cord blood banking, helping the public to understand the stem cell field, and later persuading the government to build a national industrial base and a national center of stem cell technology. Most obviously, as in all other cases mentioned in this article, central challenges for translational issues did not only come from intra-scientific developments and obstacles, but also from society and the economic context. Linking science with society and business through the creation of the stem cell bank as a boundary object (Star and Griesemer 1989) was a key intervention in this case. All of these institutions in the same network made bench to bedside interactions possible, but conflict-of-interests remained a problem for cooperation and affected the stability of the network. Again, the phenomenon of the rising importance of the patient in the Chinese biomedical system turned out to be a key factor in the operational mode of the emerging Tianjin model of translational research.

Conclusions

My case studies on translational stem cell research in China show that the protracted debates about regulatory regimes gave rise to ambiguous policies, and different actors in different regions of China tried to imagine future regulatory approaches in the context of translational medicine. From the analysis of the cases, the article shows that the linear translation model fails to reflect the complexity of the translation processes illustrated in the three cases above, as there are still many risks and uncertainties as well as a variety of scientific hurdles and regulatory issues in the process of translational stem cell research, which involve a complex interaction among different stakeholders such as scientists, clinicians, investors, regulatory officials, lawyers, ethicists, patients, and the public. Translational research needs two-way or multi-way dialogues between scientists and clinicians, and co-operation between academia and industry. Those translation investigators who are dually trained in scientific laboratories and clinical settings are very important personnel to link the information both from bench and bedside, but they are a "rare species". To construct platforms to bring all these actors together plays a tremendous role in translational research. Concerning the particularity of stem cell-based products and therapies, effective business models and innovation systems are beneficial for translational medicine. Finally, social and ethical dimensions have to be taken into account in the clinical translation process, as patients' and the public's rights should be protected. As the case of China shows, the absence of state regulations in the field of clinical stem cell research and application has not led to a "Wild East" regulatory constellation, but rather to broad variations in often individualized regulatory strategies by a variety of stakeholders. The emergence of the new regulations of clinical applications of medical technology is a crucial step in creating viable, efficient, legitimate, and internationally accepted strategies in bringing stem cell science to clinical application. We would expect the Chinese state to introduce more coherence in the implementation of the regulation in the future.

Notes

1. This paper uses the method of interview first to get the overview of stem cell research in China, and then goes indepth into three cases by interviewing people, attending meetings and reading documentation. The quotations of interviews are transcripts from tape-recording and my translation from Chinese to English.
2. The 863 program (the National High-Tech R&D program) and the 973 program (the National Programme on Key Basic Research Projects) are two core programs of the Ministry of Science and Technology, PRC. The National Natural Science Foundation of China (NSFC) funds basic research in China.
3. The Provisions for Drug Registration (SFDA Order No. 17) issued by the State Food and Drug Administration on 28 February 2005 was repealed at the same time The Provisions for Drug Registration (SFDA Order No. 28) went into effect as of 1 October 2007.

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The IVF-Stem Cell Interface in China: Ontologies, Value-Conceptions and Donation Practices of Embryonic Forms of Life

Achim Rosemann

Field of interest
Donation of embryos for hESC research; the perceptions and experiences of donors; donation procedures in the context of the IVF clinic[1]

Guiding questions
(1) What value and status do IVF embryos have for potential embryo donors in China? What factors influence patients' decisions to donate?
(2) How is the value of embryos defined in the context of the IVF clinic? How is the donation of embryos for hESC research initiated and carried out in China?

Methods
The data presented here were gathered in February and March 2008, in five IVF clinics, and six stem cell centres in various cities in South-East and Central China. Research methods comprised the analyses of documents, semi-structured open ended interviews with 15 stem cell scientists, 15 IVF clinicians and 15 embryo donors, as well as a quantitative survey, which was conducted among 74 patients of IVF clinics, 230 students from a medical faculty and 246 students with a non-medical study background (N total = 550 participants). In the survey the underlying procedures, purposes and prospects of the use of IVF spare embryos for hESC research was explained in detail. The survey included multiple-choice and open-ended questions to which respondents could provide handwritten comments. Data analysis was carried out with the use of SPSS 14. 220 survey participants provided handwritten comments and explanations of their viewpoints. The comments were translated by professional translators in China from Chinese Mandarin to English.

Main-findings part 1

The embryo's value for (potential) donors and factors that influence donation decisions
In the majority of Western societies, with the UK as a major exception, hESC research has been slowed down by continuous debates on the ethical and legal permissibility of the destruction and use of human embryos. Such public and political debates seemed largely absent in the context of China, where a permissive regulatory

[1] The original analytical focus of the research project on which this contribution is based was actually considerably broader than the aspects discussed here. Situated in the institutional, cultural and socio-economic contexts of Mainland China, the research formed an analysis of the transformation chains of the value, status and meanings attributed to human reproductive tissues, from their harvest to the moments of their donation, use and circulation among researchers in China and elsewhere, and as perceived from the viewpoints of donors, clinicians and scientists. A selection of topics has been made here to highlight issues that are relevant for the BIONET agenda.

approach was introduced within a short time, by and large following the UK example. As Chinese and other East Asian political leaders have repeatedly pointed out in this context, ethical or religiously based scruples as they have dominated debates on the usability of human embryos in the West do not exist in their societies (Sleeboom-Faulkner and Patra 2008).

In China, to some extent at least, such ideas are reflected also among philosophers and bioethicists. According to bioethicist Qiu Renzong (2000, 2007), for example, the traditional Confucian view that a person comes into being only at the moment of birth, is still valid in China. The human embryo, from this perspective, is a betwixt and between entity. It is neither a person, with corresponding moral status, nor is it inanimate matter, without any moral status. For professor Qiu, therefore, the embryo is best described as a precursory person: a form of human biological life that due to its forebearing role deserves due respect, but that can be destroyed or manipulated if there is sufficient reason, and such reason is provided amply by the strong therapeutic potential of hESC research.

A third, less philosophic, explanatory approach to the observed lenient regulatory situation of hESC research in China has been provided by Cookson, who has connected the overall support for embryo research to the one child policy (2005). The underlying assumption here is that, as a result of the high numbers of abortions carried out during the last two and a half decades in the context of the national and provincial birth politics programmes, early forms of human life are generally valued low in China, and that therefore a permissive regulatory environment would easily be accepted and introduced.

A striking feature that unites these diverging positions is that they are formulated entirely in the absence of the voices of those who in reality are confronted with the decision to donate their embryos for hESC research: women and couples undergoing IVF treatment. What value do these persons ascribe to their embryos, and what are the assumptions and concerns that influence their decisions to refuse or accept donation? These are the questions that shall be discussed in the first part of this contribution. Of interest here is that the very few empirical studies that tackle questions of the value and status of early forms of unborn human life in the context of China (Nie 2005, Cong 2007) arrive at a much more heterogeneous and complex picture, than the perspectives introduced above.

Narratives of life, death and value

My own research findings clearly confirm this complexity. It shows that the attitudes among providers of embryos are much more variegated and multifaceted, than commonly suggested in political and philosophical debates on the issue. The notion, for example, that ethical scruples regarding the use of human embryos do not exist in China, cannot be upheld in the light of the following data. While among the 550 participants of the survey the overwhelming majority (97.5%) regarded hESC research as making meaningful contributions to medicine and the sciences, only 45.7% of all survey participants indicated that they would actually agree to the donation of their embryos for hESC research, while 53.4% made it clear that they would refuse donation (0.9% remained undecided).

Among the latter group, 52.9% (28.8% of all respondents) rationalized their refusal, by supporting the statement that 'using the embryo is the same as consuming a life' – an assertion that actually echoes one of the key complaints against the use of embryos for hESC research in many Western societies. The issue was qualified in several of the survey respondents' handwritten comments[2]:

> To donate an embryo to research is equal to killing a life. I think life cannot be destroyed casually. (Student, Medicine, female, 25 years)
>
> The embryo is the descendant of me and my wife. It is an organism and it can't be killed. (Student, Financial Engineering, male, 23 years)
>
> It is a moral matter. The embryo is also a life and has its right to live. (Student, Medicine, male, 21 years)

An underlying reason for the widespread support of the declaration that using an embryo for hESC research is equivalent to terminating a human life, might be that, quite contrary to Confucian-based interpretations, by far the majority of the survey respondents indicated that in their view the life of a human being starts already at the initial stages of embryogenesis: 56.8% of all respondents selected in response to the question 'when do you think does the life of a human being start' the answer option 'at the moment of fertilization', and another 31.4% opted for the moment 'when a fertilized egg cell has evolved to an embryo'. Altogether, only 10.8% of all 550 respondents conceived of the starting point of the life of a human being as being situated at a later moment during gestation: 3.3% opted for 'the development of the nervous system', 3.6% argued in favor of 'the development of the organs' and solely 3.9% provided support to the perspective that 'the life of a human being starts at the moment of birth' (1.0% of the total remained undecided).

These findings suggest that lines of ethical reasoning that depart from the Confucian-inspired idea that a person comes into existence only at the moment of birth, do not correspond to the ideas of the overwhelming majority of research participants in this study. Accordingly, debates or regulatory approaches that depart from this line of reasoning fall short in accounting for the rich plethora of meanings and actual needs of the persons confronted with the decision to donate their embryos in China. To depart from the actual values and forms of reasoning of these people should be a central matter of respect.

Assessing the emotional impact of donation

That a more donor-centered perspective is required in debates on the use of human embryos for hESC research, which accounts for the subjective, embodied and emotionally charged perspectives of the women and couples who are actually confronted with the decision to give away their embryos for research, came to the fore also in the response patterns to survey questions that addressed the (anticipated)

[2] The relative young age of these respondents can be explained by the over-proportional high number of students who participated in the survey. In fact, in some of the IVF clinics I encountered some serious bureaucratic obstacles, when asking for permission to carry out the survey. In the universities, in turn, I encountered no problems when asking for permission to carry out a survey among students.

psychological and affective impact of embryo donation. Interestingly, 31.4% of all respondents here endorsed the statement 'I expect some psychological or emotional difficulties after the donation of my embryo'. And a sub-group of 37.9% of the 293 respondents who had specified that they would refuse the donation of their embryos provided support to the statement: 'I do not donate my embryos because I am afraid of emotional or psychological consequences' (these are 20.2% of the total number of survey participants). Such fears were also reflected in several of the handwritten comments of survey participants:

> It [embryo donation] may have consequences for people in a spiritual and psychological sense. Also it may bring conflicts with morals and ethics. (Student, Chinese Literature, female 23)

It may hurt the person who donates mentally. (Student, Computer Science, male, 21)

That women are likely to build up a stronger emotional bond with their embryos can be seen also from the following excerpt of an interview with an IVF patient. Just before our conversation the women had heard that she was in the first phase of pregnancy:

> I want to keep these (frozen surplus) embryos for a long time. I really cannot consider giving them away now. Maybe later, when my child is four or five years old […] but also then I would not like to give them away all. I still would like to keep some. (IVF patient, 29 years)

That this expression of affection toward super-numeral IVF embryos was not just a singular exception can be seen also in the following: 34.7% of all respondents provided support to the statement 'I have strong feelings for my embryos', while another 29.0% indicated to 'have some feelings for my embryos'. Only 19.7% indicated to 'have low or no feelings for my embryos' and 16.6% remained undecided.

The embryo as part of the family and kinship group

A final aspect that should be highlighted addresses assumptions about the entwinement of IVF embryos in the web of social, bodily and emotional relations of the family and wider kinship group. To whom the embryo belongs is actually an ambiguous matter and among a certain segment of potential embryo donors in China the opinions of family members seem to play an important role in decision making processes:

> Such a decision [to donate the embryo] must be discussed with the family as a whole and the opinions of the others must be respected. If there is a member who disagrees, I will think about this. But it really depends on the attitude of this person. If his or her opinion is very strong, that means, opposes donation very strongly, I would not donate. I do not want to hurt the relationship between family members just because of donation. (Female IVF patient, 32 years)

Such patterns of inter-familial respect and obligations appear to be closely intertwined with culturally mediated conceptions of the human body and notions of physical interrelatedness between the generations. As one of the researchers I interviewed explained it to me:

> You know, in Chinese cultural tradition people regard their bodies as coming from their parents, and it is seen as very precious, so we have to take good care of our bodies, we cannot give any part of it to others. So in the Chinese tradition it is forbidden to give away… to donate your tissues or organs to others, including your cells, your gametes, which include oocytes and sperm. Therefore, [many] people cannot agree, if their embryos shall be used for research.
>
> I: What would happen if someone believes in these ideas but would still donate?
>
> This would be an activity that means that you do not respect your parents. Your parents gave you your hair, your body, your organs, this…, the whole of you. The parents gave this to you and you did not take good care of it, you gave parts of it to others. So you don't respect your parents.

From this perspective, donation of embryos without prior consent of the donors' parents forms an obvious violation of culturally mediated social norms and represents a serious act of disrespect and disloyalty. This way of thinking is reflected also in a larger number of handwritten comments of survey-respondents:

> From a Chinese traditional point of view 'we get our bodies from our parents', so we can't give it away casually, not to mention a new life. (Student, Medicine, female, 25)
>
> The traditional concepts (sayings) tell us it is unsuitable to donate the embryo. I'll give up the donation for the principle of filial piety. (Student, Accountancy, male, 24)
>
> The aged ones tend to pay more attention to life. As to Chinese people, parents and grandparents care always much about their children and usually will not agree to donate the embryo, which possibly can be a child. The traditional and conservative thoughts are a critical reason for their disapproval. I'll respect their opinion. (Student, Human Resources, male 22)

Discussion

Taken together, these findings suggest that attitudes and perceptions of the value and of the permissibility to donate and use human embryos for hESC research are much more varied and complex in China than is commonly suggested. Claims that ethical concerns regarding the donation and use of embryos for hESC research were something typical for Western societies, but absent in China, can not be upheld on the basis of the data presented above. The decision making process for the contribution of super-numeral IVF embryos to research seems, at least among a larger proportion of individuals in China, to be characterized by careful reflections on the nature and value of these human biological resources, and on an introspective assessment of the

psychological and emotional consequences of the act of donation, as well as of its permissibility in the light of inter-generational patterns of respect and obligations. Accordingly, lines of ethical reasoning that depart from the Confucian-inspired dogma that the life of a human being starts only at the moment of birth seem to fundamentally mismatch with the ideas and perceptions of the majority of the population of potential donors in China. They fall short in accounting for the rich plethora of meanings and needs put forward exemplarily by the participants of this study. Equally flawed, however, appears the assumption that the value of early forms of human life, as a result of the high number of abortions that have been carried out in the context of the one child policy, is generally regarded low in China. Instead, as the above introduced data suggest, forms of embryonic life in China, are entangled in a rich web of overlapping and sometimes contradictory layers of meaning, value, values, emotions and social relations, that analysts, policy makers, researchers and clinical staff should well be aware of (*cf.* Cong 2007; Dikötter 1998; Nie 2005; Greenhalgh and Winckler 2005). In the next section, I shall continue with the exposition of findings that provide some insights into the manifestations of clinical practice through which the donation of embryos is initiated and carried out.

Main-findings part 2

Clinical practices: the value of embryos as defined in the IVF clinic and the ways in which donation is initiated and carried out

For persons who undergo infertility treatment the in vitro fertilized embryos signify a profound source of hope and value. After the diagnosis and experience of infertility the creation of these embryos constitutes an important source of 'reproductive capital' that embody the promise to re-render the long cherished but recurrently discouraged dream to have one's own child, back into the realm of the possible.[3]

Whatever the initial outlook of infertility patients on their embryos may have been, however, in the course of the IVF treatment these ideas and feelings are subjected to considerable changes. Exposed to new forms of expertise and explanations and to the rigorous testing of their embryos' quality and reproductive viability, these persons learn to conceive of the characteristics, properties and value of their potential offspring in previously unheard and unimagined ways; a process that forms a considerable cultural challenge for many lay-people. These restructuring processes of attitudes, mental pictures and ideas about their embryos, do clearly facilitate the attempts of clinicians or stem cell researchers to motivate IVF patients to donate their spare-embryos for research. This is so, not only because created IVF embryos get evaluated and categorized along parameters of reproductive potentiality, but also because they allow for the overcoming of alternative understandings of life, value, ethics and sociality, such as defined by common sense, tradition or religion. While I cannot discuss these points here in detail, I shall provide a number of examples that

[3] It should be noted at this point that the desire for a child is, in comparison with other societies, likely to be even more pronounced in the context of China, where infertility is often stigmatized, and the moral and filial duties of children play a vital social function in intergenerational patterns of reciprocity, in which children shoulder the responsibility to provide moral and financial support for their aging parents (and grandparents).

offer insights into the concrete ways through which the donation process of embryonic tissues is initiated and carried out in the context of the IVF clinics I visited.

Exploring clinical practices

The ways and routines through which the donation of embryos was carried out in the visited clinics varied considerably, across but also within different institutes. Overall, especially among senior IVF clinicians (who in many instances are also stem cell researchers), a highly developed consciousness of responsibility for the needs and concerns of patients was expressed. The requirement to stick to ethical principles such as informed consent and the right for a voluntary and autonomous decision were unanimously endorsed in this group:

> They [the patients] have the right … their behavior is totally voluntary not under any pressure from the researchers or the doctors and […] no matter how they will decide, their clinical treatment will not be influenced at all. (Senior IVF clinician 7)

> We have to explain to them, we have to offer different options, and then the patients make a decision by themselves. (Senior researcher 4)

> We have to protect the rights of the patients, so that they receive all the embryos they need for a successful pregnancy. Then we have to give information to donors about our research […]. We have to inform patients, also if we want their low quality embryos. (Senior researcher 3)

Many more examples could have been provided here. However, it should be noted that the overwhelming majority of these statements were from clinicians (or clinicians/researchers) in highly organizational functions, who would only sporadically deal with the practical sides of donation procedures in person.

Not too surprisingly, at the immediate level of clinical practice a more varied picture emerges. The sense of responsibility displayed in the quotations above was reflected at this level in a clearly less consistent way. While a large number of the clinicians and researcher who were involved in the facilitation of informed consent (IC) procedures, seemed really to do their uttermost best in informing patients, in answering their questions patiently, in offering time and the opportunity to discuss things with friends or family, so that a genuinely independent and voluntary decision can be derived at, others would carry out IC procedures in less mindful and patient-friendly ways.

As the following example shows, ideas such as ‘the right to be informed’ were sometimes handled in superficial and rather unsatisfactory ways:

> I: When you ask patients to donate their low quality embryos for hESC research, what information do you provide to them?
> R: Information? (Laughs)… Not much information. Just these words written down on this paper here, not much more information.
> [She points to a multiple-purpose informed consent form that lies on the table in front of her, which has to be filled in and signed before the onset of the

treatment; most of the issues that were covered here refer to the risks and procedures of the infertility treatment itself; the donation of low quality embryos for hESC research was only one issue among many, and dealt with in two sentences. It is specified that the donated embryos shall be used for research and that they will be destroyed in the process and can not be reclaimed.]

I: But the woman [an IVF patient] we spoke to this morning, she didn't know anything about stem cell research. Don't you have to explain it to her?
R: It is just a brief, a brief explanation. It doesn't have many details.
I: But does that happen often that a woman is asked to sign a form and she does not really know what for, I mean, for what kind of research the embryos are given away?
R: But they… most of the patients do not care about what research we are doing. They just focus on… if they can get successfully pregnant (laughs). […] You know, most of them just don't have any questions about it. They just go over it. They agree or disagree and then talk about other things. They don't focus on this… this is not their focus. (Junior IVF clinician 5)

Especially younger clinical staff members appear to carry out informed consent procedures in careless and sometimes highly irresponsible ways. Occasionally, the conversations that accompanied the IC process appear to be characterized by the calculated handling of silence, that is, the facilitation of 'choice' through strategic games of information concealment and disclosure. In some cases the conversations with patients also included elements of overt deception and the making of untenable promises:

I: How many percent of patients want to provide their embryos after you have talked to them?
Dr 1: Mm, maybe 75%.
I: Oh, that is a lot!
Dr 2: Yes but that is because we encourage (鼓励/guli) them, we persuade (说服/shuofu) them.
I: How do you do this?
Dr 2 (laughs and points to Dr 1): She is good at this (laughs again). She is doing this very well, to persuade patients.
Dr 1: I tell them that it is useful for scientists and useful for mankind, in the future, probably… And, ok, I will make sure that the donated embryos will not be given to other people, so that they know they will not have another baby.
I: And what else do you tell. How do you try to persuade a patient so that she really…
Dr 1: If patients come to our hospital their purpose is to have a baby, they do not care too much about the remaining embryos. […] I tell them that the stem cells [derived from their donated embryo] can maybe be used for their children, in case they have a disease that can be cured in the future.
Dr 2: If their child has leukemia for example, maybe our research would help to cure these diseases. Maybe the patients if they hear this they think it is better for their child [if they donate], so many times they will agree. (Junior IVF clinicians 1 and 3)

Similar tactics of leading patients to believe that stem cells derived from their donated embryos might directly benefit the future health of the donors or the donor's child could also be observed in another clinic. As a clinician in a senior position told me, occasionally he would tell patients the following:

> If in the coming days, there will be the necessity that you use the stem cell line [established from your embryo] for medical purposes, we will check whether your embryos have become a cell line, what and where the cell line is today, and whether it is possible to use this line for you. If in the future there is a technique you are the first to use this technique. You have the privilege to use the stem cells. (Senior IVF clinician 2)

Discussion

While I do not want to preclude that such promises may – at least partly – be based on good intentions, or at least on a genuinely optimistic attitude towards the medical potential of stem cell research, it is clear that these conversations with patients contain elements of deception and manipulation. In addition to that, from a legal perspective, such claims remain entirely unsupported. In the consent forms that patients sign, it is unmistakably specified that with the act of donation the donor gives up all future rights on the embryo, including all claims to get access to future therapies or economic gains derived from research for which donated embryos have been used.

Summary and take-home lessons

Summary

In this contribution I have highlighted two different aspects related to the donation and use of human embryos for hESC research in the context of China: perceptions of the value of donated embryos among real and potential donors (1), and an exploration of the ways through which the donation of embryos is initiated and carried out at the level of clinical practice (2).

Research findings to the first of these two thematic clusters have suggested that attitudes and ideas on the value and the permissibility to donate and use human embryos for hESC research are much more complex and diverse in China than is commonly suggested. Claims that the donation and use of embryos in China goes without any form of ethically based concerns or scruples could not be maintained. Also speculations that, as a result of the high abortion rate related to the one child policy, the value of early forms of unborn human life is generally low among Chinese people could not be confirmed.

But also assumptions that Confucian-inspired ideas on the starting point of human life are still valid in China were not supported by the participants of this study. Almost 90% of all survey respondents had indicated that in their view the starting point of the life of a human being is located at the earliest stages of the gestation period. While it may be, that on an intuitive level Confucian-based ideas on the starting point of the life of a human being, find a higher level of support among people in China, than was expressed in this survey, it seems to me, that the specific procedures of the IVF treatment, through which patients are confronted with new ideas, insights and images of their embryos, clearly favor perceptions in which the starting point of the life of human beings is seen to be located at much earlier points during pregnancy.

Taken together, these insights highlight how important it is, actually, to depart from the situated, embodied and emotionally charged perspectives of potential embryo donors. Only then can the impact of the process of embryo donation for hESC research be understood in a really nuanced way, so that culturally or socio-economically determined complexities can be accounted for, and clinical and governance procedures can be developed that correspond to the needs of potential donors in a convincing way.

In the second part of this contribution I provided a range of insights into the contexts and communication processes through which the donation of embryos is facilitated in IVF clinics in China. A highly varied picture emerged here that offered insights into a wide range of practices that unfolded between the poles of a strong commitment to professional care and responsibility on the one hand, and forms of occasional deception / manipulation of patients on the other. Variance could be shown to exist not only across different clinics, but also within particular institutions. On average, and with notable exceptions, strong differences in attitudes and practices could be noted between clinicians and researchers in lower and higher professional positions. These gaps between promoted principles of good practice at the top level and *actual practice* indicate a lack of adequate ethical training of clinical staff or researchers. Or, as might be the case in some clinics, they refer to the absence of a true interest for responsible donation procedures, so that bioethical principles get reduced to officially proclaimed lip service, with a layer of ignorance and malpractice underneath.

Take-home lessons

1) Approaches of ethical governance of stem cell research need to depart from the situated, embodied and emotionally charged perspectives of the individuals or collectives who are actually confronted with the decisions and dilemmas brought about by these new technologies, be it in the context of tissue supply, or with regard to forms of patient recruitment and treatment in emerging forms of stem cell based clinical trials and commercialized experimental stem cell therapies.
2) Independent social science research, especially qualitative research, or a combination of qualitative and quantitative research methods, as in the presented study, is best equipped for such an analysis, so as to derive situated, practice oriented and cross-culturally informed insights through which ethical debates, regulations and governance approaches can be informed.
3) Statements of politicians or government officials, who claim to speak on behalf of the ethical attitudes and values of whole nations or continents, should be met with caution. These declarations emerge in relation to wider geopolitical interests, strategies and identity politics and are likely to lack insights of the variegated and concrete perspectives and needs of those who are actually confronted with the decisions and dilemmas brought about by new technologies.
4) This objection applies also to purely philosophically based lines of ethical reasoning, or to sweeping forms of theorization that discount the assumed effects of major biopolitical projects such as China's birth politics. The validity of such speculations should first of all be treated with sober skepticism; at least as long there is no solid empirical evidence that supports these ideas.
5) With regard to the issue of the donation of reproductive human tissues for stem cell research, studies that might provide such evidence have to account for the rich web of overlapping and sometimes contradictory layers of meanings, value,

values, emotions and social relations in which these tissues are embedded in, in the context of China, as elsewhere.

6) In the final two points I shall comment upon the facilitation of informed consent procedures as encountered in some of the visited IVF clinics. While a cross-culturally informed type of bioethics recognizes that there are variations in the ways in which social phenomena and processes are categorized and problematized, my understanding is that some of the practices I encountered, did clearly transgress the (admittedly difficult to define) borderlands of mutual respect and the positive recognition of difference. The observed ways in which patients were mislead, by some clinicians, are intolerable, according to Chinese as well as international standards. (While such cases of malpractice might also happen in the UK, it is clear that controls and rule transgressions are handled there in a more consistent and strict fashion.)
7) Collaborating partners in China and Europe should be well aware of these problems, as well as of the possibility that conscious compliance to these conditions might backfire in the future. On the other hand, continued and more collaborations, in tandem with the ongoing efforts to improve the situation, by scientists, bioethicists and the media in China, as well as by the Chinese government, seem a promising way to work toward a better future, by promoting more and better forms of ethical training of medical staff, as well as more consistent forms of ethical governance that includes the introduction of more reliable regulatory structures and of a legal and institutional infrastructure that is able to control, monitor and sanction transgressions of valid rules and standards.

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Donation of Spare Embryos for Stem Cell Research Experiences and Views of Couples Undergoing IVF at CITIC-Xiangya Hospital of Reproduction and Genetics, Changsha, China

Pilot study report

Anika Mitzkat

A BIONET student exchange project

Field work in China at CITIC-Xiangya Hospital of Reproduction and Genetics, Changsha, Hunan Province, P.R. China, March 10th – April 26th 2008

Background and aim of the project

One of the key questions tackled in the BIONET project concerning the ethical governance of Chinese-European research collaborations is "how can *vulnerable patients* who are in a desperate situation (as is often the case with both ART and stem cell therapy patients) be safeguarded against risks of inducement and exploitation?" (BIONET 2008). Such a description meets many of the characteristics of the situation of IVF (*in vitro* fertilization) patients who are asked to donate spare embryos for embryonic stem cell research. These women, together with their partners, have to decide whether they agree to donate for research or not, and what is to be done with a spare embryo in any case. The experience and the perspective of the women concerned are of particular interest for bioethics, for evaluating the regulations that are in place, and for reviewing the practice of informed consent and decision-making.

There are a few qualitative empirical studies either still ongoing or recently completed that give evidence of the patients' perspectives: One is being conducted by Lene Koch and Mette Nordahl Svendsen in Copenhagen, Denmark, a second by Erica Haimes and co-workers in Newcastle upon Tyne, UK, and a third by Jackie Leach Scully, Rouven Porz and Christoph Rehmann-Sutter in Switzerland. In China, where IVF is practiced in several state-of-the-art clinics around the country in high numbers, and where several centres also do stem cell research, no systematic study of the patients' experiences, views and ethical concerns has been conducted so far. On the basis of the studies in the UK and in Switzerland (Scully et al 2004, 2008; Haimes et al 2008), I conducted a pilot study in Changsha, one of the largest IVF centres in central China. The BIONET student exchange scheme allowed me to do field work in Changsha for this project during seven weeks, to establish the methodology and the local network that was necessary for then conducting and interpreting 5 qualitative in-depth interviews with IVF patients about their views on embryo donation for embryonic stem cell research (ES).

As regards the ethical implications of in vitro fertilisation (IVF) and embryonic stem cell research (hESC), a vast quantity of theoretical literature can be found. Beyond that, there is a lack of empirical knowledge, which could substantiate the ethical points of view in the perceptions and understandings of those involved. Data from the ongoing European studies underline that the specific situations, understandings and experiences of couples undergoing IVF are morally significant and, in some ways, differ from what bioethicists find on the basis of theoretical considerations. One area

of particular interest is related to the so-called "spare" embryos and to the option of stem cell donation. Starting from this perspective, the initial questions of the study whose results will be reported below, were:

> *How do involved persons (clinicians, nurses, scientists and the patients and potential donors themselves) experience the impacts of IVF and the possibility of donation of embryos for research?*
> *What are their perceptions and considerations concerning "spare" embryos and about decisions on what should happen to them?*

The aim of this study was to provide insight into the experience of couples undergoing IVF treatment who are directly involved in these kinds of decision-making. The short-term objective of the project was to obtain a better understanding of the individuals' situations and the decisions of the interviewees.

Methods

The project can qualify as an exploratory pilot study. It follows a qualitative design with a phenomenological approach.

The interviews with Chinese interviewees challenge language and cultural differences. The most important methodological consideration was that of "opening the field". From the beginning, establishing contact with the couples undergoing IVF and building up a trustful relation for the interviews took place under recognizably difficult conditions. Prior to starting interviews with the patients, two steps were necessary to obtain familiarity with the setting. These consisted of expert interviews and participant observations. The interviews were translated by an interpreter bit by bit in both directions, audiotaped, transcribed and analysed.

Expert interviews and participant observation

During the first two weeks, I met experts from each department to familiarize myself with their work and their procedures, and also to introduce myself and build up confidence in the aim of the study. Information obtained during this period was put on record by personal notes and protocols. During the following weeks, it was possible to accompany a doctor to meetings with patients for several days at a time.

Patient interviews

Interviews with women/couples who were asked to decide whether they were ready to donate embryos for hESC were conducted *after* their decision had been made. The physician acted as the gatekeeper to the potential interviewees.

The patients who were waiting for their appointment with the doctor were given an information sheet about the project. During the meeting with the doctor, they were asked whether they would agree to participate in our study. If they agreed, they gave their telephone number. Mrs. He Jing, who later acted as interpreter and had a psycho-sociological educational background, gave the potential participants a call. If they still agreed in participating, a date for the interview was found. The interviews were conducted using a semi-structured questionnaire, which was modified from the European studies. On the one hand, semi-structured interviews allowed me to follow

the study goals and, on the other hand, to find new aspects during the course of the informants´ own narratives[1].

The interviews were accompanied by the local interpreter and translated in both directions, from Chinese to English and from English to Chinese. Both the original dialogue and the translations of sections of the conversation were audiotaped and transcribed. Data analysis used a phenomenological method (Giorgi/Giorgi 2003) to identify the major themes that emerged.

Ethical considerations

Couples undergoing IVF are potentially vulnerable persons, because they are a) patients and b) in a situation that might inflict mental tension upon them. The gatekeeper, i.e. the clinician responsible for the treatment of the patient under concern, was instructed to decide, after evaluation, which patients would be able to participate. In addition, informed consent was considered an obligatory measure before the interview took place. In the information material, it was explained to the candidates that the data would be treated anonymously.

Before the recruitment process for the interviews could start, approval of the local ethics committee in the Changsha clinic had to be sought. The ethics committee agreed to all points of the study outline.

It was an advantage for preparing and conducting this study in a complex clinical environment that I was myself trained as a nurse before becoming a qualified nursing scientist. In my previous work and during the studies, I had extensive professional training and experience in conducting qualitative research with patients and relatives in existentially demanding situations. Nevertheless, talking about intimate themes like infertility and the wish to have a baby, with all the implications this wish may have, is likely to cause psychological distress for the participants that could not always be anticipated. Therefore, preparations were also made for psychological support to be available on demand in the hospital.

Results

Features of the clinical setting

The Reproductive and Genetics hospital of CITIC (China International Trust and Investment Company) Xiangya was founded in the beginning of 2003. As of January 2009, 15,935 patients have been treated. The average pregnancy rate is 48.17% and has raised from 40.39% in the year 2004 to 51.79% in the year 2008. (cf. Li and Lu 2005)

Results from the expert interviews and from participant observation

The first step of the observation included visits to each department of the hospital, which were guided by one of the local staff members, and it also included listening to the lectures that are regularly given for patients. Thirdly, it additionally involved walking around to acquire familiarity with the location and the people to obtain a general impression of the people’s habits and everyday behaviour, etc.

[1] For viewing contact forms and questionaire please contact the author.

The Reproductive and Genetics hospital has a clinical department, a genetics center, a reproductive center and a sperm bank. I talked to several physicians in the clinical department. However, as most of them could not speak English fluently, the possibilities of conversation were limited and it was sometimes not possible to ask questions concerning an issue in depth. The sperm bank has a capacity of 10,000 samples, with a stock of 4,200 samples at the end of 2008. Sperm donors may give up to five samples; this is accurately documented and communicated with other sperm bank centers. For an IVF treatment with donated sperm a double blind strategy is used – physicians in the IVF laboratory will know the patient´s name and the donations ID, physicians in the sperm bank know the ID and name of the donor but not the name of the couple treated. Couples who need a sperm donation will choose the donor from a list that has been made anonymous using the IDs.

All of the physicians I met talked about the details of their clinical work, which basically involves examination and monitoring of the patients before or during the treatment, respectively. None of the physicians perform the embryo transfer. This, they explained to me, only the professors are allowed to do. They talked about the great number of patients they have to deal with. Being asked for the reasons for the large number of couples having infertility problems they told me that, in most cases, there are some "tubal problems", which might be the result of an abortion performed in the past. One physician explained to me that there are many people in China, expecially in the countryside, who receive poor sex education. Therefore, there are many teen-aged or young women who unintentionally become pregnant. In many cases, as they do not want to marry or have no possibility to do so in the future, they have no other choice than to abort, since otherwise the baby would be born illegitimately and illegally. But abortion, one doctor told me, is also a social taboo so it will be carried out in secret and therefore mostly with a very low budget. In many cases, she told me that these abortions are badly done, often causing infections and constrictions of the Falopian tubes. Another doctor told me that there is also often a problem of low quality sperm; these two factors together result in a high number of couples who hope for a baby via IVF treatment. This hope is also nourished by the fact that being childless is socially stigmatised. All agreed to the statement that, in China, a woman ought to be married and have a baby before she is 26 years old. I should mention, however, that most of the physicians and also the other clinical staff were in their twenties and did not seem to share this opinion. But they explained to me that there is a severe social pressure to do so and that it is not easy to break with traditions – expecially if the couple is living in the countryside and has little education.

Compared with the results from the European studies (Haimes et al. 2008, Scully et al. 2008), the relation between the "need" to have a baby and the choice to undergo IVF treatment is interesting. Most of the couples, or at least the women, had a very strong desire to have a baby and were not able to become pregnant without IVF treatment, although physically they sometimes had a 50% chance. But after having the first child through IVF treatment, many of them got pregnant naturally. To discuss this relation is outside the focus of this project, but it might be an interesting issue for further studying the psycho-social influences on pregnancy.

Another topic we talked about was the decision-making of the patients concerning the question of embryo donation. The couples have to decide what should happen to the

"bad quality embryos" (see below 3.2: "good ones – bad ones"), as well as the frozen embryos after the paid period of stored freezing ends. This decision takes place while the couple waits for the embryo transfer and receives their first IVF or ICSI results (see below 3.1.4, where I will summarize my observations from the pre-embryotransfer interview). I was told that most of the patients chose to donate the embryos for research. Asked why this is the case, the physicians told me that, in their view, the patients wanted to contribute to medical research to help other couples with fertility problems. One of them told me that the only reason why patients refuse to donate their embryos for research is the fear that these could be used for other couples.

It would have been interesting to summarise the talks with the physicians about their attitudes towards the patients in a more detailed and systematic way, but from the availabe data this is not possible. What was obvious, however, is that there was a lack of time (about 4 to 10 minutes for each couple to receive the information about the results of the IVF or ICSI and to achieve informed consent) to conduct longer conversations with patients, and particularly a lack of time to explain embryonic stem cell research during informed consent. This brevity was dictated by circumstances.

The other visits and talks took place in the IVF laboratory, the genetics center and the sperm bank. Since I am no expert in the field of genetics and also these talks are barely related to the reported theme, I will not expand on them in detail.

The most structured interview that I could conduct was the one I had with the expert from the sperm bank. First he mentioned ethical principles: benefit, informed consent, protection of offspring, welfare, secrecy, and talked about commercial issues. I asked him how these principles are practiced and he explained each step to me using a handbook and patient information forms.

One comment, made by an expert working in the IVF laboratory, is still very present in my mind. In addition to other subjects, he explained to me how the eggs and sperm come to his laboratory, and what is the normal procedure of fertilization. Also, he shared with me what happens to the fertilized eggs, the "good and bad embryos", how they get to transfer, are frozen and how they (the IVF experts) handle the donated embryos: "once they are given to research, they are only a number". He was very enthusiastic telling me about his work in the IVF laboratory and I asked him: "What exactly are you doing there?". His answer was: "Creating life". I said to him that he seemed to be very enthusiastic about this and he said: "Creating life is amazing". I said that for me there is a conflict between "creating life" and "giving a number" of this created life (embryos) to research and he answered: "Yes, but research is necessary and otherwise there would be no use for it (the embryo)".

Personally, during these discussions with experts, I observed something identical to pride – to have so many patients, to be one of the best, to do this kind of research, to have ethical principles and so on. There was also a certain openness to talk with me, but there was also an uncertainty as to what I might be interested in or how to say things. People spoke more openly after they had met me several times. I did not conduct the expert interviews in a formal way, following any standardized questionnaire. I left it up to them what to tell me and when. With some of the experts, I went out to dinner more then once and on such occasions there was also a lot of

small talk. In the end, I performed participant observation without even recognising it. This is a non-scientific part of this study. It could perhaps have been utilized as data, if consequently protocolled and reflected upon. As it was, it greatly helped me adapt to the particular social context of the study.

Lectures

Every Monday, a 45-minute lecture is given to potential patients and their relatives. About 80 people attend each week. This lecture is not mandatory and most of the patients who already know the details of IVF treatment (for whatever reason) do not attend. It is held on the second floor of the clinic by a nurse, using a powerpoint presentation. It gives a short introduction to the concept of IVF treatment and it provides details on the work of Professor Lu. We are told that the research center and reproductive hospital has existed since 1980 and has been certificated by the Ministry of Public Health of P.R. China. We are shown the history of IVF babies (first birth, 1978, in the UK; first birth in China, 1988) and are provided with statistical data that in Xiangya hospital, as of 2006, 3,363 babies have been born thanks to IVF and ICSI. We are shown pictures of the professor together with a number of babies as well as with other famous clinicians working in the field of IVF. Reasons for infertility and the process of IVF treatment are visualized, using anatomical pictures. Also the circumstances of a natural pregnancy are explained. Pictures of embryos in the laboratory were also included in the show. Finally, the lecture ends by providing information on the timeline and the cost of IVF treatment, and on some statistical data about the increase in success rates of IVF treatment during the last years.

While this lecture is not mandatory, there is another lecture for patients who already have decided to undergo IVF treatment, which must be attended by each patient. It is given every day. After this lecture, the patients receive a questionnaire that will be used by the physicians for the informed consent interview. The IVF treatment procedure is explained in more detail, starting from the process of obtaining the eggs and sperm, and it is also explained how the eggs and sperm are joined in IVF or ICSI (intracytoplasmatic sperm injection). The couples are familiarized with the fact that they will have to stay in Changsha for at least 20 days for monitoring the outcome of the treatment. The next part of the lecture is about the medication used during the whole IVF process. After embryo transplantation, the patients will have to choose between taking the internationally used FSH (follicle-stimulating hormone) that will cost 400 RMB (Renminbi or Chinese Yuan, equalling about 40 €) per treatment and the Chinese derivative that will cost 40 RMB per treatment. The effects and also side effects of the hormones are explained. The patients are told what kind of examination will be performed during the treatment and what expenses they can expect depending on their decisions and the clinical outcome and progress of the pregnancy. This will amount to a sum of between 25,000 and 35,000 RMB per cycle. (The average monthly income in the region is about 3,000 RMB). The last two parts of the lecture are about possible complications in IVF treatment (such as extrauterine pregnancy) and the indications for an abortion (such as multiple pregnancy without a chance of a fetus reduction) and finally about frequently asked questions. These concern the patients' behaviour after the embryo transfer and deal with practical questions such as having sex, going to work, and using the shower or the toilet.

All in all, this lecture provides the patients with a whole lot of information. The questionnaire, which the patients have to fill out afterwards, asks for information

about their recent physical condition and medication, as well as what they understood or did not understand. The patients are told that the physician will later talk to them on the basis of this questionaire.

In addition to the lectures, more information for patients could be found on the hospital's web page (www.hn-ivf.cn), including an introduction to the hospital and to the medical staff, as well as practical tips concerning health, pregnancy and sterility.

Participant observation of physician-patient-interviews

After the introductory period of my study, there was an interruption in my research fieldwork due to the BIONET conference, which absorbed the time of He Jing[2], who had previously made all the contacts in the clinic for me, as well as myself, as I was presenting some of my findings to an international audience there. During more than two weeks, He Jing could not make any arrangements for me.

But in the last two weeks of my stay in Changsha I accompanied several physicians to their patient interviews whenever it was possible – six times in total. In these patient-doctor-meetings the results of the IVF or ICSI treatment were explained. They were held soon before the transfer of the embryos. There were two consulting rooms for this purpose, each with two tables and four chairs, and a waiting room for about 20 patients. Each day, there were about 30 couples who waited for the results and also for the last step of IVF to become possible: the transfer of the embryo. Most of the women were dressed down. Sometimes, there were two doctors in but most of the time only one was available. There was always a nurse and a doctor in the consulting room. The nurse prepared the patient's documentation and the physician talked to the couple. During my observations, the couple took seats in front of the physician, and I sat at one end of the table. It was interesting that the doctor, in the majority of cases, did not introduce me to the patient and the patients seemed not even to notice that I was there. In some of the observation sessions, the doctor asked the couples if they were interested in participating in my study. Then I was briefly introduced as a researcher and the doctor gave me their telephone number for later contact.

Several forms were given to the couple:

a) the results from the laboratory, including a consent form;
b) the contract on the freezing of "excess" embryos;
c) the informed consent form giving permission to discard the "bad quality" embryos or to give them to research;
d) the informed consent form giving permission to discard the frozen embryos or to give them to research, or to continue freezing them once the freezing contract expires.

The procedure took place in this sequence:

- The couple sits down.
- The physician explains a): x eggs have been extracted, y eggs could be fertilized, z of the fertilized eggs are good embryos, q of the fertilized eggs are bad quality embryos, r embryos will be transferred, s embryos are "spare".
- Most of the time, the couple looks at this sheet.

[2] Who worked at the administration of the hospital.

- The doctor asks them what to do with the "bad ones" and tells them where to mark it on the form to discard them or to donate them (see (c) above).
- The physician continues: The good ones, which the couple will not need now, could be frozen for later use. He gives them another form, explains it and shows where to sign (b).
- When the freezing contract expires, the doctor explains, they could either discard the frozen embryos, leave them frozen or donate them to research (d).
- The next step takes place in silence. The couple looks at the forms that are lying in triplicate in front of them.
- Sometimes they talk to each other or ask questions to the physician.
- Signing: the couple is asked to sign the documents. After signing, they have to give their fingerprints with red ink. There is an ink-pad and some toilet paper on the table. The doctor gives a piece of toilet paper to the patients after they have used the red ink.
- The couple then goes upstairs to the surgery.

During my observation of this setting most of the couples who had their first cycle were irritated about having their fingerprints taken. But nobody asked questions about this. They decided whether to donate or not without posing any further questions. The average duration of one interview was about five or six minutes.

Patient interviews

Sample

Due to the restricted time of my stay in Changsha, but also because of difficulties in establishing full contact with patients, it was only possible to talk to a small number of patients. Five women gave their consent to the study and were interviewed.

The first two interviews took place in an apartment close to the clinic which four women rented during the time of their treatment and shared together. In the living room, four beds were placed closely together. All the women were still lying in bed when the translator and I arrived at 9:30 in the morning. Both, Hui[3] with whom I talked first as well as Mai stayed in bed during the interview. The other women could overhear our conversation but they did not seem to be interested nor did the interviewees seem to feel uncomfortable with the situation.

Hui is a 24-year-old woman who has been together with her husband for six years, of which they have been married for three. In spite of their not using any contraception, she never became pregnant. They knew from friends that there is "some technology to solve fertility problems" and went to a hospital where they were diagnosed with some "tubal" problems" and "problems with sperm motivation". They started the first cycle with ICSI in autumn 2007, which was not successful. The day of our interview was the fourth day after the transfer of the two embryos that had been frozen from the first cycle. She had decided against donating spare "bad quality" embryos for research.

Mai is 28 years old and she had the embryos from her first cycle transferred three days ago. She had been together with her husband for eight years without becoming pregnant, although they never used contraceptives. They married two years ago and

[3] All patients' names have been changed.

after marriage they tried very hard to have a baby. She says that "in China, they think that if a woman cannot get pregnant, it must be the woman's problem", so she went to the hospital for an examination "but there was no problem and then [my] husband went to hospital and they found out that there is some problem with him". They knew from friends that there is something like IVF and started an internet search to find a hospital, using "test tube baby" as the keyword. She still had plenty of "good quality" embryos frozen and was willing to donate the spare embryos to research.

The third interview was with **Ling**, a 31-year-old woman who six weeks ago gave birth to her daughter whom she had from her first IVF cycle. She and He Jing, the translator, knew each other from earlier in their lives. Therefore, the visit had a semi-private character and took place in her parents' apartment. Two other friends joined us to visit her and there was some small talk before the interview began. Afterwards we went for dinner together. For the interview we separated from the others and went to the parents´ bedroom. Ling and her husband live in the countryside but during the week she and the baby live with her parents. They care for the baby while Ling is working. Ling and her husband had been married for several years before they started trying to have a baby. After an ectopic pregnancy in 2000, the doctors had to excise one of Ling's fallopian tubes, and told her that she still has a 50% chance of having a natural pregnancy. But from 2000 to 2007, her husband had to work far away, and they had no chance of being together very often. During this time, Ling already began to think about some form of treatment and went to the hospital, underwent some hormone treatment and gathered information about IVF. They were quite well informed about the whole process when they started IVF treatment. She decided against donating spare embryos to research.

The fourth and the fifth interviews took place at the inpatient ward of the hospital. Both women had become pregnant with triplets, and they had to stay in the hospital for observation after the IVF treatment.

Chen is 29 years old and in her eighth week of pregnancy after the second IVF cycle. She had been married for four years without becoming pregnant. She reported for a superficial examination, and it was found that she had an obstruction of the Fallopian tubes. She had several treatments in other hospitals, though she is not sure about what was exactly done there. Finally her sister in law, who herself had fertility problems, told her about IVF treatment and recommended that she go to the hospital for genetics and reproduction. She and her husband live in the countryside, her husband works as a taxi driver. Chen donated "bad quality" embryos to research.

The interview with **Xiaomei** was special because on the day of the interview she had just been admitted to the hospital for symptoms of miscarriage. The doctor told her that she was still pregnant, but it was still unclear if she could hold the triplets. The situation was more emotional than the others, and being asked about her story, Xiaomei started to cry softly. She had married 7 years ago but was unable to become pregnant because of tubal problems, which were diagnosed in 2002. After the diagnosis she went to many hospitals for treatment without any result and a friend finally told her about IVF treatment in "some kind of hospital". "When she went there, the doctors asked her to give extra money for the treatment and she didn't have much money, so she had to quit the treatment. Later, she met a woman who is working at our hospital and lives in the same street and so she finally received

treatment at our hospital" He Jing, the interpreter, explains. "She was already under much pressure from family members, from her parents and also from other friends, discussing about them and talking about this. So she feels a lot of pressure and she also says that, if she can´t get pregnant, she will obtain a divorce." In addition, for Xiaomei it was her second cycle with fresh embryos. She agreed to donate her spare embryos to scientific research.

Themes

There are evident limitations in what can be extracted from a small sample of five interviews. We decided to consider all interviews essentially as individual cases, which prove to be similar in some respects, different in others, and we thus abstain from drawing generalized conclusions. But since this investigation has the character of a pilot study, the experiences and concerns that these five women authentically and sincerely expressed might, however, be relevant (cf. Döring 2004). They can guide the preparation of more extensive studies, where the topics that came up here will be studied in greater depth and based on a larger sample.

There is another restriction: Not all the themes that emerged in the interviews can be described in sufficient detail. In order to do this, the sample would need to be larger, so that it would be possible to meaningfully contrast one experience with another. Some details that might be relevant were probably lost due to the bi-directional translation. The interpreter, He Jing, did the best one can do under these circumstances and both her language skills and her understanding of medical as well as ethical issues were invaluable. But summarizing all questions and answers in another language necessarily led to a certain loss of detail and accuracy.

Bearing this in mind as well as the purpose of the study, which was to learn about the patients' views on embryo donation, the views of the women themselves on the embryo will be described in the following section, which will also describe their considerations about the decision to donate embryos for research or not. The interviewees did not talk about their experiences in depth. It seemed to me that they just felt that it is "not a big thing", rather than feeling uncomfortable with the interview situation. In addition to the background of the women (outlined above) it should be stated that each woman was very conscious of how many eggs they had and in which cycle, how many had been fertilizied and how many were of good or bad quality. For all couples, it was clear that they wanted to have those embryos that were not transferred frozen for a later cycle. All of the women expressed a strong feeling of community with other patients, once they started treatment at the hospital. They exchanged experiences with other patients right from the beginning. After a successful treatment, the women I talked with had an attitude of wanting to help other women with fertility problems. Ling, for example, said (in the words of the translator): "like if they have friends, or [if] people in the same working place … have the same problem, they will also communicate and exchange their experiences. And then she suggests them to do this."

Before looking at the participants' views on embryos and embryo donation, I wish to summarize the experiences they shared with me concerning their desire to have a baby and the pressure involved during the period before our interview took place.

From the desire and the pressure to have a baby to IVF treatment
All of the women had a long-standing history of trying to become pregnant. In four cases, they never used contraceptives but, as soon as they married, they started examinations and treatments at several hospitals. Ultimately, each of the women was informed about IVF treatment by friends who had been in the same situation. In each case, IVF treatment seems to have been the last step on a ladder that each woman had to climb – sometimes more or less alone, sometimes with support from their husbands and parents. Hence, IVF treatment signifies their hope to finally have a baby. Xiaomei's statement was translated as: "even if she fails this time, she says she would do it again because she knows that for her, this is the only way to get pregnant." IVF is "the technology that can solve fertility problems" (Hui).

All the women started searching for the reason why they could not become pregnant on their own. Mai's statement was translated as "in China they think that, if a woman cannot get pregnant, it must be the woman's problem, so she goes to the hospital for examination." She was talking about "a lot of pressure during all the treatment and the waiting time." Being asked about this pressure, she made a more concete statement (summarized below) to the effect that she was not sure whether she could get pregnant or not because, although they were having premarital sex without contraception, no pregnancy had happened up to then; this meant that, once married, she was afraid of her husband discovering she was not fertile, resulting in arguments and possibly divorce. So, in her opinion, as they were still not married at the time, the pressure did not only come from her family or society but actually from herself as well.

> ("*…and she was afraid because they didn´t have any contraception and she was afraid that maybe after she'll get married and then her husband finds out that she can´t get pregnant and there will be some argument and some problem and they will get divorced or something like that so she thinks the pressure is not from the family or the society because at that time they were not married but from herself."*) – Interpreted by He Jing

But Xiaomeng on the other hand:

> "was already under a lot of pressure from her family members, from her parents, and also from other friends discussing about them and talking about this. So she feels a great deal of pressure, and she also says that if she can´t get pregnant she will be divorced." – Interpreted by He Jing

(I should mention that this indeed happens very often in China!)

Underneath this strongly emotional desire and/or the high social pressure to have a baby, for many couples, IVF treatment was a matter of money. Hui and her husband saved 100,000 RMB over a period of several years and they spent nearly everything on the treatment. If they are not successful this time, they will have to borrow money from their parents. Chen and her husband had to borrow money from relatives. In the first cycle, they were told that none of the embryos were good enough to be transferred, but Chen insisted on the transfer in hope it would work anyway. It did not, and they had to borrow more money for the second cycle and they decided to undergo ICSI in order to get more embryos so they could freeze some for later use.

They would not be able to afford a third cycle. Xiaomei was in a similar situation. Her statement was translated as: “her mother-in-law gave her 30,000 RMB for the treatment and if she succeeds it will be okay, but if she fails, it will not.” For her, the situation is even worse. Now she is pregnant with triplets, with a high risk of losing all the babies, and is worrying enormously about her family’s future. On the other hand, if she does have triplets, it will be difficult for her and her husband to earn a living. One exception to this difficult financial situation was Ling and her husband. Both were working, with her husband in a profitable business. They even both stayed at home for one year because “they decided to have a baby [...] they had saved enough money and they wanted to be successful in having a baby.”

But although IVF treatment is a financial problem for many couples, because there is no insurance to cover it, all participants in the interviews agree that it is worthwhile. Hui pointed out “that every woman also wants to be a mom and it is also very important for the family”.

None of the women talked much about the time after the examinations and IVF treatments started. Ling said that “they came to the hospital and also they had very good cooperation with the doctors, and then they just wanted to do this.” Xiaomei left it up to the hospital to do what was necessary: He Jing translates:

> “There is a lot of trust between her and the doctors, although maybe she doesn´t understand what is embryo and she says the only way for her to get pregnant is to cooperate with the doctors so she can get pregnant. And in the first cycle she doesn´t know all those things and procedures. The doctors have told her but she doesn´t understand everything in IVF treatment.”

There seemed to be no strikingly important step between the day they decided to undergo IVF until the day they obtained the results from fertilization, and had the embryos transferred. Mai was the only woman who had this experience for the first time and so it is still very present to her. “She says she feels fine and she is waiting”. Asked what she thought of the embryo in her womb, she replied: “yes, she thinks of it as a baby.” Hui also said she thought of the baby in her first cycle, but that her wish to become pregnant immediately after the first embryo transfer had ended in disappointment. Now, in the second cycle, she “tries to think about this in a common way and, no matter if she is successfull or if she fails, she just waits for the result.”

Ling told us that she stayed in bed right from the day of the transfer. “It was not that she felt uncomfortable or sick, but she felt that doing heavy work, running or being active in some way will, maybe, cause her to suffer a loss.” Actually she was talking about the embryo just transferred as if it was a baby that she could have. She did a pregnancy test every day because she wanted to have this confirmed, but for her, she was pregnant with a baby even 14 days before the test gave a positive result. This leads to the question of how the women imagined and defined the ‘embryo’.

The image and definition of the embryo

What is an embryo? When is an embryo a baby? These questions are descriptive in character but they also demand an ontological assessment. Therefore, it is important to ask the women involved if we want to discuss the ethical status of the embryo. (cf. Cong 2008, Nie 2005) The biological consideration of an embryo as being a

developing multicellular entity might be easier to explain. Results from interviews with couples undergoing IVF about their experiences in the UK and Switzerland (Haimes et al. 2008, Scully et al., 2008, Scully et al 2009) have demonstrated that the definition of what an embryo 'is' or 'means' depends on the situation in the course of the IVF process and therefore the question of what 'the' embryo is for patients, is not expected to have a simple or general answer. In the view of those persons involved, the ethical definition seems to be multiple and more dynamic than static.

In this small sample taken in Changsha, there were at least two distinctions that seem to have been important for the women and appeared in all the interviews. The first one is that between the "good ones" and the "bad ones" (embryos), the second is that between the tranferred and the frozen embryos.

"Good ones" – "bad ones"
To distinguish between embryos of good quality and embryos of bad quality is customary in the clinical praxis in the Changsha clinic. All the women I talked with told me how many "good ones" and "bad ones" they had. I asked them about the difference between both:

> "The doctors explained to them in a simple way about the good quality and the bad quality embryo. A so-called good one means that it develops in culture, but a bad one develops only very slowly or stops developing, hence their difference from the good ones. And, when talking about a four-cell-embryo and an eight-cell-embryo. [...] She thinks [that for] the bad ones there is no use" (Hui).

Mai only had "good ones" and "the doctors didn´t talk so much about the embryos, they only said the embryos are good." Chen thinks that "embryos are very important for her and the quality of the embryo has a very close relation to the success. [...] In her opinion, when a doctor talks about a good or a bad one, only a good one can be transferred." When Wang Xiaomei was given the results of her first cycle, which implied that there were no good embryos, she started to ask the doctor a lot of questions, i.e. why her embryos are not good, and what is a good one and what is a bad one? The doctor explained it to her with pictures: "the good embryo has eight circles around it and that is the good one which can make her pregnant."

From my observations I also had the impression that the couples did not pay attention to the distinction between "good" and "bad" *per se*. Instead, they had a rather pragmatic perspective and focussed on the embryos that can either be transferred or frozen. A bad quality embryo implies that it is an embryo that is less likely to be succeful in leading to a pregnancy.

Embryo - Baby
Most explicitly, the idea that the embryo was a baby was narrated by Ling and Xiaomei. Ling, as we have seen before, was pregnant immediately following her embryo transfer. She recounted – in the words of the interpreter – that "they were talking about embryos as babies and taking care of them" (Ling).

Xiaomei told us that:

> "she already sees the embryo as baby now, and right from the day they were transferred, she touched her tummy and said: Grow up and don´t leave me, and no matter if there are three of you, just stay! And from the day of the transfer, she also put up a (ultrasonic) picture, and talked to it every day. And she also gave names to the three embryos."

And Hui knew:

> "that they (the transferred embryos) have the possibility of failing in their development at every step [...] but still feels them to be similar to babies." Chen saw it more gradually. She said, "that if the embryo is in her body and then day by day it grows and becomes a baby. [...] From the day she had the pregnancy test – then, from that day it was not embryo it was baby."

Despite the fact that the women in the interviews talked of their transferred embryos as babies, they did not use the image of a child when they were talking about it. "Because the doctor already told them that the embryo is like one fourth of a drop of water, this meant that they could never imagine what it would look like in their bodies, and so they never connected with anything tangibly imaginable. It was not really material." (Hui) Xiaomei talked about the picture of the eight-cell-embryos but she petted her "babies" through her tummy.

Ling gave a very clear statement about when, in the course of IVF, the embryo becomes a baby. She saw the frozen embryos as the "possibility to become a baby", but "when it is transferred into the womb, then she thinks it is a baby." I summarized this in the interview: "So, in a more abstract way, an embryo is a baby when it has a mother? And an embryo in the fridge has no mother only somebody who gave eggs and sperms." Ling approved this summary: "Yes, it is like that."

Frozen Embryos

Being able to afford more embryos than will be transfered during one IVF cycle is a highly important factor for most couples, simply for cost reasons. Hui "is worried that if she does not get pregnant this time, she does not have any frozens left." And this would mean paying for another cycle. Although she knows that her chances of becoming pregnant with frozen embryos are statistically reduced, it is interesting that she thinks the "frozen ones are better, because the frozen ones stayed there for half a year and still survive. So being able to survive makes them stronger." The frozen embryo is "like a positive expectation for her and her husband, because they failed the first time and so they still have the frozen embryos, which gives them a greater hope for having a baby." Ling gives a similar account. Her husband told her "not to worry about whether they didn´t succeed, they still have six other embryos in hospital and they still can do this. They still can get pregnant." (Ling) Ling thinks that, "the frozen embryos have the possibility of becoming babies, but only the embryo inside her body is a baby." For Mai, the frozen embryos are like babies but "she does not think about the frozen ones, because she thinks the hospital will take good care of the babies and she will take care of these two (the transferred embryos) by herself."

Donating embryos for scientific research

All the women who participated in this study were asked to donate embryos for scientific research. Mai, Chen and Xiaomei decided to donate the "bad quality"

embryos to research, and to give away the frozen ones in case they became pregnant and no longer needed them. But none of the participants were really clear about the nature of the research they were asked to donate to. “She just thinks it`s medical research she doesn´t know about embryonic stem cell research” (Chen). Mai even intended to donate spare “good quality” embryos to scientific research. But she was not clear that it would be hESC research. Her idea of “scientific research” was that it would “maybe advance the technology and knowledge about IVF treatment.” This coincides with Chen’s view based on her ignorance about the nature of scientific research, as she thought, “it is just some medical research for the IVF treatment.”

Not knowing what kind of research might be performed with the donated embryos was the reason for Hui and Ling *not* to donate embryos, neither the bad quality embryos nor the frozen embryos. The interpreter summarizes Hui’s justification for her decision not to donate:

> “Because they don’t know the meaning or what purpose of that scientific research so they didn’t think about this. They just choose to destroy. There is no use for us, so destroy.” In the words of the interpreter, Ling explained that “it is because they don´t know much about scientific research, they are not clear about it. (...) She doesn´t really know what kind is scientific research and she thinks that it is maybe some kind of research using her embryo for other women. She doesn´t want to do this. And she didn´t choose. But if she knew about embryonic stem cell research and it was good for human health and implied solidarity with other women, then she definitely would do this.”

Two important issues emerge from this last statement: The first issue is the fear that donated embryos could be used for other women. This reason for not donating embryos was also often mentioned by the doctors I spoke with. They told me that sometimes, when the doctor in a particular case promises that the embryos will not be used for other women, the patients change their minds and give their informed consent without asking any more questions. “They are just afraid that the hospital is using these embryos for others.” (Ling) The second issue is the attitude of contribution to others. Right at the beginning of the interview, when I explained the purpose of my research, Xiaomei said, she would “donate eggs or embryos or anything for research because she wants to help others.” She does not really know what this research is about but she trusts the doctors and hopes it will help other women. “She says that she hopes that Prof. Lu could do more research so that the success ratio can be higher and then other patients can also have better treatment.” (Xiaomei)

Conclusions

The necessity for translation in both directions between Chinese and English brings several limitations to the interpretation of the interviews. Through the period of observation and getting in contact in the run-up phase to the interviews, a trustful relationship between He Chen, who translated, and myself was developed. This climate of confidence had a positive effect on the interview situation, as it appeared to me. Nevertheless it is important to keep in mind that He Chen is the secretary of the director of the clinic, Prof. Lu, and that most of the patients know this. It is unclear how much importance or meaning should be attached to this when interpreting sentences like “She feels good in our hospital because the doctors and nurses are good

to her and also everything goes smoothly, she is quite satisfied with the service." (Hui) Translation by a staff member is a factor to keep in mind when interpreting such statements, but there is also a factor of social desirability that could influence how patients talked about uncommon themes such as IVF treatment. The fact that no woman spoke about why she had medical problems might be related to this, particularly as no woman ever specified having had an abortion in the past; and this – as many experts in the clinic suggested to me – was a very frequent reason for their infertility.

But it was primarily the small number of women that I could talk with that made it difficult to draw conclusions from the results of the pilot study at this point in time. At best, it is possible to adumbrate the themes that came up in the individual interviews, as we have done, and perhaps to compare the results with some aspects from European studies. There are certainly a number of differences and similarities to be mentioned:

a) The relative number of couples affected by infertility might be different in Europe and China, and the reasons for infertility may also differ. A factor that certainly influences this type of study is the differing attitude to childlessness in European and Chinese societies.
b) Definitions and ontological determinations of the embryo of the Chinese women were very similar to those of the European studies (Haimes et al. 2008, Scully et al. in press): In both contexts they seem to change during the process of IVF and vary between the individuals. Similar categories have appeared. But one striking difference was that, in the Changsha interviews, after the establishment of a successful pregnancy, a frozen embryo loses its importance for the couple. We could hypothesize that, for Chinese couples, the embryo is more like a medicine that you consume when you are ill. The woman hopes to become healthy again, which is equivalent to becoming pregnant. The medication needs to be taken as long as necessary. When your condition is still pathological, the medication (both the pills you have just swallowed and those pills that still are in the pack) remain enormously important. Once you are healed (i.e. have a baby), the drug has no significance any longer.
c) The basic tendency in Chinese interviews was also that women considered their embryos to be "babies"; however, this less represents a doctrine that embryos are "persons" so frequently described in European contexts, as for example in Swiss interviews, where the term "Eskimo" was frequently used for frozen embryos. Perhaps it can be said that the women in Changsha saw all embryos together (!) as the baby, not each embryo individually as a potential baby.
d) The number of embryos that could potentially be donated to research differs due to the one-child policy in China. Basically, after pregnancy, a frozen embryo becomes useless.
e) Awareness as to the kind of scientific research donated embryos should be used for was slight. However, also in Swiss studies (Scully et al. in press), perhaps in contrast to those in the UK, the awareness of the kind of scientific research was correspondingly slight, and most women think that this research will benefit other couples in IVF. The decision to donate was made more or less without information. In part, this ignorance led to a rejection of the request to donate. For other women, this ignorance led to a motivation to contribute, by donating

embryos, to the improvement of IVF treatment for other couples affected by similar problems, and therefore to help these others through a gesture of solidarity.

f) Another factor that might differ (but was not studied here) is the effect of the public awareness of genetics and hESC research as ethically problematic in the European and American contexts (Streiffer 2008), but less so in the Chinese context.

g) Trust and informed consent has a different meaning in Changsha than in the UK and Switzerland, due to the different nature of the physician/patient relationship. Autonomy, in the sense of individualistic self-determination is a less determinant value in the decision-making process in the context of Chinese culture. This means that in the practice of IVF, the patient assumes the doctor to act in her interest. For her it is not necessary to know everything or to question anything. This however should not be judged morally. The responsibility of the doctor, in this relational setting, is not reduced but to the contrary perhaps even more intense than in Western countries: In Western settings, the doctor's responsibility is mainly (while not exclusively) based on the actual information and understanding of the patient, whereas in the Chinese context, responsibility is mainly (although not exclusively) based on the confidence, which the patient offers to her doctor. The process of decision-making and finally also the provision of informed consent to donating embryos needs to be seen within a relation of autonomy and care.

h) There was a strong wish to help other couples, to provide some helpful contribution. This was also seen in UK/CH interviews: there is a need to talk about the experiences and to help other couples who are in a similar situation. There was a strong sense of identification with the group of people with infertility problems that also made an impact on the patients' deliberations about embryo donation.

If the results prove to be reliable, they will help us to understand the processes of ethical decision-making about donation of embryos for hESC in both Chinese and European (or other) contexts from different participants' perspectives. A more comprehensive study could also be helpful for those working on physician/patient communication in Chinese and European centres. It would be significant for deepening our understanding of the bioethical questions around hESC research in general, particularly the clinical situations they involve or generate. It would be interesting to plan a larger study, based on these experiences in the Changsha pilot study. Such a study could contribute to the discussion about emerging structures of ethical governance.

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The Political Stabilization of Technology: The Case of Oocyte Contribution to Stem Cell Research in California, China and the UK

Megan Allyse

Introduction

This student project introduces the Political Stabilization of Technology (PST) model, a new theoretical framework, which seeks to offer predictive and explanatory insights into the policy process surrounding the normative State management of emerging scientific and technological developments, and applies it in three national contexts, including China and the UK. This model draws on and synthesizes theoretical and empirical work in the fields of Science and Technology Studies and Political Science, with the ultimate goal of facilitating communication and collaboration between these fields.

The questions at the center of the PST model involve the construction of systems of social control around normatively approved uses of technology, including the circumstances under which those systems become political. As such, the PST model sits within an emerging discourse on the co-production of science and society; in particular, it shares a '[rejection of] simplifications of both social determinism and scientific or technological determinism; it sees science neither as constituted by interests alone nor as an unmediated reflection of nature' (Jasanoff 2004: 274). Indeed, themes of emergence and stabilization will be recognizable to those familiar with past works in science and technology studies (see also Latour 1973, Jasanoff et al 1995, Foucault 1972, Hacking 2000, McLaughlin et al 2004). Even though, within this literature, stabilization is not universally defined, but I will claim that stabilization involves the successful management of a technology such that it is not perceived as an active threat to social values.

The PST model is also a Grounded theory in the postempiricist political science tradition (Fischer 2003) in as much as it strives to understand the policy development process as it is *in practice* with the ultimate goal of facilitating its development. Criticism of existing policies, especially those towards embryonic stem cell research, frequently centres on claims that they are internally and externally inconsistent. Rather than conduct a 'gap study', offering explanations for the failure to attain an idealized policy outcome, the PST model seeks to understand how the policy process behaves when it encounters controversial technologies. Policy outcomes are thus treated not as failures, but adaptations of the social and political environment to the normatively pluralist situations such technologies engender.

It is largely to facilitate this goal of future policy guidance that the choice of an internationally comparative study has been made. The ideal is to construct a model, which does not depend on the presence of a Western-style democratic system to function accurately. The inclusion of China as a research site serves this goal by providing a socially and politically sophisticated system that differs significantly from the more frequently-studied examples of the UK and the US. The overall goal of conducting fieldwork in China was therefore to gain an understanding, if possible, of

how one specific technology, oocyte extraction, came to be applied, contested and stabilized in the context of the Chinese system. Together with similar data from the UK and California, this information provides the empirical basis for the formation of the Political Stabilization of Technology model. It is hoped that the model will have future utility in a variety of national and international contexts, including China.
The aim of this chapter is to evaluate, specifically, the contribution of the BIONET consortium to the project and to offer some brief thoughts on the process of international collaboration and cross-cultural work, specifically between the UK and China. To begin, therefore, we offer a brief background to the technology of egg extraction and how it was selected for use in this study. A review of project methods, particularly as they apply to fieldwork, follows. Since China is the focus, we next present a summary of research activities pursued during the BIONET-funded fieldwork trip and a sketch of the results of the various interviews conducted. The following section offers some observations and preliminary analysis on the interview process, including some rudimentary contrasts between conducting such research in China versus the UK. Finally, we conclude with some suggestions for those wishing to follow in the BIONET tradition and pursue collaborative research in China.

Case study

In 1984, the first baby was born as the result of an exchange of oocytes between a fertile woman and an infertile one. Since then, the social construction of ex-vivo human oocytes in a range of cultural contexts has been unusually uneven. In Israel and Denmark, for example, the extraction of oocytes from those who are not assisted fertility patients is not permitted. In the UK, it is permitted but non-patients may not receive money in exchange for oocytes. However, women wishing to undergo assisted fertility treatment may trade oocytes for fertility services. In the US, oocytes are openly traded, with young women receiving significantly higher financial compensation if they can demonstrate that their genetic material is desirable. And in Spain, oocyte donation is done anonymously, in exchange for financial compensation, but without the accompanying premium on physical and mental exceptionalism.
This diversity of approaches vacillates between conceiving of oocytes as personal commodities and regarding them as the incommensurable carriers of cultural ancestry. But although none of these frameworks, in the context of fertility treatment, is free from criticism, neither have they occasioned sustained international controversy. Contrast this relative passivity with the events of 2005, when media reports of the rise and fall of South Korean Hwang Woo Suk gave the impression that a significant portion of the world was involved in debating the contribution of oocytes to stem cell research projects.[1] Further investigation reveals that the events of South Korea were only the most dramatic manifestation of contestation surrounding the exchange of ex-vivo oocytes, not the first. Two years earlier, the US state of California had undergone a heated campaign featuring ex-vivo oocytes, culminating in a state of regulatory affairs whereby the practice of exchanging money for oocytes is acceptable in the context of fertility services but not if the oocytes are destined for a research laboratory. And although they had already permitted uncompensated, non-patient

[1] Coverage was prompted by the revelation that South Korean Professor Hwang Woo Suk, previously known for his work on somatic cell nuclear transfer in both animals and humans, had not only used thousands more human eggs in his research attempts than previously reported but that some of them had been extracted from postdoctoral workers in his own laboratory (Cyranoski and Check 2005).

oocyte contribution to fertility treatments in 1998, the UK's Human Fertilisation and Embryology Authority still hesitated for more than a year over the issue of allowing oocyte contributions to research in 2006.

It is apparent, in reviewing these contradictions, that the social acceptability of oocyte extraction must be a factor of something other than the technology itself. Oocyte extraction does pose an unknown risk to the health of women, but it is the same unknown risk regardless of her motivation in undergoing it. Once extracted, ex-vivo oocytes remain within a woman's social control, but society increasingly proscribes how she may dispose of them. In certain circumstances, oocyte extraction is a component in an economic transaction and in others it is prohibited from involvement in fiduciary matters. But the circumstances under which such conditions hold are not consistent across or even within political and cultural systems, begging the question of where such conditions derive. Why is oocyte contribution so heavily politically stabilized and how did this stabilization come about?

Methods

To answer this question, we have attempted to trace as precisely as possible the regulatory process surrounding the contribution of oocytes to research projects using the somatic cell nuclear transfer (SCNT) technique. Because this technique sometimes goes by its more inflammatory (although technically correct) name 'human cloning', its conduct, and the contribution of oocytes thereto, has occasioned sustained controversy in several, although not all, national contexts. As previously mentioned, three such contexts have been selected for inclusion in this study: the US state of California, the United Kingdom and Mainland China. To understand the cause, and effect, that controversy or lack thereof can have on the social integration of technologies, this study seeks to evaluate the technology of egg extraction in each context during each of the three stages posited by the PST model: application, contestation and stabilization (see Allyse, submitted). Qualitative methods were chosen throughout the study for their greater ability to capture the normative beliefs and motivations, which underscore a complex policy process and the cultural context that shapes it.

Field methods include in-depth, semi-structured interviews with scientists, activists, policy-makers, journalists and academics. Document review of relevant legislation and media reports and participant observation at scientific gatherings, public meetings and government proceedings were also employed where available. Two separate trips to China were undertaken in the spring of 2008, for three months, and 2009, for one month. The primary base for research efforts was Beijing, but visits were also made to Changsha and Shenzhen, under the aegis of the BIONET conferences, as well as Shanghai. Contact with proposed study participants was initially conducted by email until it was discovered that telephone was a much more efficient method of obtaining responses. Some interviews took place at the offices of participants, others, at the request of the participant, in public venues such as restaurants or cafes. Where permitted, interviews were recorded digitally but it was noted that more participants seemed uncomfortable with this procedure in China than in other national contexts. Where digital recording was expressly refused, or appeared to make participants uncomfortable, handwritten notes followed by detailed interview summaries were employed.

It should be noted that the researcher does not speak Mandarin. A majority of interviews were conducted in English, by grace of the participants' knowledge, and a few required the services of a translator. Relevant legislation, including the 2001/2003 *Regulation on Assisted Reproductive Technologies*, the 2003 *Ethical Guiding Principles for Research on Human Embryonic Stem Cells* and the 2007 *Regulations on Ethical Reviews of Biomedical Research Involving Humans* were also read and interpreted in English. Efforts were made to obtain 'official' translations, which had been sanctioned by the promulgating authority but it is acknowledged that the act of translation is a linguistically sophisticated process in which shifts of meaning and intent can occur. In general, document and public discourse analysis formed a much smaller portion of available data in the Chinese context, when compared with the UK; in part, this is due to the language barrier and the comparatively thin mass media communications sector.

That said, the experience of living in Beijing for a reasonably extended period of time offered its own advantages in trying to assimilate a rough understanding of Chinese culture and society. Choosing residence situations located in the heart of the *hutongs*, or traditional residences, and almost exclusively populated by Chinese working families allowed for daily immersion in local life. Although it is difficult to interact effectively with many residents unless one has a knowledge of Mandarin, the mere act of shopping for food, bicycling through traffic or even walking down the street occasions levels of interaction which, when taken cumulatively, do offer insight into the Chinese experience. Such insight is inevitably colored by personal experience and cultural biases but has nevertheless offered some alternative interpretations or angles when interpreting and analyzing empirical data. Despite its acknowledged weaknesses, this insight gives the impression of being one of the most valuable aspects of being able to work 'on the ground' in China.

Results

As previously mentioned, research took place during two extended visits to China. The primary focus here is on the second, BIONET-funded trip in 2009, which commenced in Shenzhen, although the majority of applicable research took place during a three-week residency in Beijing. Although this visit was shorter in duration than the 2008 trip, it benefited from a follow-up effect. Several key contacts had already been made and a certain level of trust established with some local academics and scientists. A second advantage of this trip was the retention of a freelance translator who was invaluable in arranging meetings and conducting simultaneous translation during interviews. Although financially significant, this is a strategy, which, in retrospect, should have been employed at the beginning of the project.

As before, individual members of the BIONET consortium proved an invaluable resource, particularly those who were directly involved in the practice or regulation of assisted reproductive technologies. Professor Cong Yali was endlessly helpful and patient, offering both extensive personal time and valuable introductions to key participants in the Ministry of Health. Professor Lu Guangxiu was generous in granting a second interview, covering procedures for the extraction and exchange of oocytes as well as reactions to the 2003 regulations from the perspective of a practitioner. Dr. Li Rong, of the Beijing 3rd Hospital fertility center, discussed her own experiences with women making decisions about whether or not to exchange oocytes and some reflections on the motivations which may underlie such decisions,

particularly in light of the intended destination of contributed oocytes. Professor Qui Renzong also consented to a second interview to continue discussions on the past and future functionality of the Ministry of Health Ethics Group and the process of research and technology regulation more generally. Finally, Professor Wolfgang Hennig offered a European perspective on working within the Chinese scientific establishment and some of the differences, both material and cultural, between the structures of scientific research in the two regions.

Much of the scientific community was both open and generous with their time. Dr. Jiang Hujun, of the National Natural Science Foundation, discussed the evolution of funding for scientific research in China and the ways in which ethical governance interacts with funding decisions. Professor Li Linsong, at Peking University stem cell centre, discussed his work and the obstacles to commercialization of medical research in the current regulatory environment. Both Dr. Li and Professor Zhou Qi, of the Chinese Academy of Sciences, have conducted SCNT research and recounted their experience of designing research procedures to address the process of contribution while navigating the stabilization system already in place around oocyte contribution. Professor Qi, who continues to conduct SCNT research, talked further of potential difficulties with the system and the potential for clarification and development. Professor Pei Xuetoa of Beijing Institute of Transfusion Medicine is also active in the Ministry of Science and Technology (MOST) grant review process and helped to lay out the process whereby certain strands of research are selected for government support. He also offered valuable insights into the process of regulation from the perspective of the MOST and the ways in which it is evolving.

From a regulatory perspective, Dr. Qi Guoming, formerly of the Ministry of Health and now of the Chinese Medical Association (CMA), offered both concrete aid in the form of the English translations of several relevant pieces of regulation and recollections and reflections of his time as the head of the Ministry of Health Ethics Committee. His description and discussion of the growth of civil society, as partially embodied by organizations like the CMA, was also invaluable. Dr. Yu Xiucheng, of the Ministry of Health, was personally responsible for much of the 2003 regulations regarding assisted reproductive technologies. Over the course of two generously long interviews he explored many of the implications, both actual and potential, of such assisted reproductive technologies on the Chinese culture and the efforts, on both his part and the Ministry more generally, to mitigate and manage those effects. Given the centrality of cultural perceptions and reactions to the predictive component of the PST model, Dr. Yu’s input cannot be overstated.

Discussion

Unsurprisingly, a full account of the findings and conclusions derived from the China case study is beyond the scope of this chapter. Here, we offer instead some reflections on the research process and how it differed from similar research conducted in the UK and California. In doing so, it is impossible to avoid some preliminary observations regarding the policy process in China and the UK.

The highly contextual nature of Chinese social interaction is one of the most commonly cited sociological differences between ‘East’ and ‘West’. In particular, commentators have stressed the role of social context in forming personal identity within traditional Chinese society and the corollative importance of social institutions,

most notably the family, in establishing and sustaining personal and social stability (Tao 2004, Hui 2004, Dallmayr 2002, Fan 1997). Although the 'communitarian' nature of Chinese society is, by this time, something of a cliché it is nonetheless observable and experiential. From a methodological standpoint, its most frequent manifestation is the necessity of *guanxi*, or social connections, in navigating Chinese society. Although it is possible to make some preliminary contacts and arrangements as an unrelated stranger located outside of China it is difficult to make much progress in this manner. Indeed, trying to contact potential participants without the benefit of some mutual acquaintance or the intercession of a social mediator can be a frustrating, and largely ineffective, process. In this respect, research 'consortiums' like BIONET are immeasurably valuable in as much as they provide a known core of persons with insider knowledge of the relevant field and, if one is lucky, the willingness to extend their social capital on behalf of new, especially foreign, researchers with no *guanxi* of their own.

From a theoretical standpoint, it can be difficult for Western-raised researchers to encompass the mental shift necessary to place the institution of family at the core of sociological research, a space more familiarly occupied by the individual. In this study, for instance, certain policy decisions surrounding the use of egg extraction technologies were puzzling until they were reviewed in light of State prioritization of the support and maintenance of traditional constructions of the family.

Another interesting observation about the Chinese case concerns the issue of participant anonymity. All participants were given the option of remaining anonymous but among the Chinese cohort almost none elected to do so. This contrasts interestingly with the trend in the UK where several participants agreed to speak only on condition of anonymity. It is speculated, although not asserted, that participants in China may have viewed the act of speaking with a foreign researcher as a public act in of itself, and thus inappropriate for anonymity. By contrast, participants in Europe and the US may in some cases view the interview process as revealing their personal opinions as separate from their public roles. Anonymity would thus be required in order to maintain separation between the public and the private.

This concept of 'public speaking' amplifies existing concerns about the nature of the interview process and its relationship with 'truth' (Dingwall). Although Chinese participants were gracious, often openly enthusiastic, about participating, in keeping with the 'public' implications of speaking to foreign, particularly Western, researchers there was a sense in which some meetings resembled a diplomatic encounter as much as an interview. In as much as participants in China felt that they were acting, in some sense, as ambassadors of China by participating in the interview process, it would be unsurprising to find a lack of criticism, or even vaguely promotional, content within the interview discourse. By contrast, in the UK, where the researcher was considered less foreign, the opinions expressed varied more widely; participants frequently offered active criticism of government policies and actions.

This finding must be contextualized by wider observations about the nature of public discourse in the two countries. Where public discussion and criticism of government policies in the UK is considered a sign of healthy democracy, traditional Chinese culture seems to regard such disrespect as more indicative of a dangerous social disorder. On a more theoretical level, this dichotomy has larger implications for the

study as a whole. According to the PST model, contestation, specifically the contention that current State action is incorrect or incomplete, is a critical step in the normative policy process. But given a cultural norm exerting pressure away from an open or antagonistic expression of such contentions, contestation may have to be understood in a different way. The *process* whereby alternative policy proposals are presented and defended is still in effect, but its operations may be harder to identify for those who are more accustomed to the more theatrical public discourse of many Western democracies.

The 'diplomatic' aspect of encounters also has a second component in as much as the interview process, in this context, takes on a more discursive element of the exchange of information, rather than a one-way transfer from participant to researcher. Once the participant becomes an ambassador for China, so does the researcher become an ambassador for the West.[2] Participants frequently asked for information about British or American (these two more than any other) policies or regulations on certain issues and seemed to expect that the goal of the interview process was not only to generate data for a specific study, but to contribute actively to the development and growth of local governance or scholarship. Such an exchange is, after all, at the core of the BIONET agenda. But it must be acknowledged that undertaking policy research from within the aegis of BIONET transforms the process into something closer to participant observation. By agreeing to provide legislative documentation or giving presentations on the relevant governance structures in other countries, the researcher contributes to the very process of policy development and change she is there to study. This reflexivity, while not uncommon in fieldwork, requires some acknowledgement, not least in the time parameters employed in data analysis.

Finally, it must be stressed that none of these observations is meant to imply that the data collected in China are in any way less valid than those collected in California or the UK. Merely, caution must be exercised when interpreting data in order to walk the line between acknowledging the limitations of the interview process and overcompensating by indulging in extrapolation as to what participants 'meant' to say.

Conclusion

Notwithstanding the acknowledged vagaries of the process, the choice of interviews for this project remains easily supportable. Although language, and the complexities of translation, can be a formidable complication, the process of communication, especially in the long interview format proved both fascinating and informative. It has the added value of providing a rich source of additional ethnographic and sociological research for future research. Also of value was the decision to remain immersed on site for a reasonably extended time. The experience of participant observation, while methodologically complex, offered a great deal of context to subsequent formal methodological encounters and is highly recommended. On an only slightly contradictory note, researchers who do not speak the local language are encouraged to recruit a fluent translator early in the process in order to allow for the growing sophistication of translation that comes from increasing familiarity with the subject matter at hand.

[2] The precise nationality of the researcher was rarely requested.

Given the above, it seems relatively uncontroversial to assert that this same study, if conducted by a Chinese researcher, would potentially yield very different results. But here again is one of the positive aspects of participating in a project such as BIONET where it is possible to talk and compare notes with other young researchers who are also conducting internationally comparative work in the same field. In particular, conversations with young Chinese researchers about their own experiences of conducting research in China are illuminating. In many instances, their experiences support the observations here; native Chinese researchers are not seen as ambassadors, and so the dynamics of gaining access and negotiating interview content play out differently. This may mean that the interview process plays out in a more linear fashion, rather than the reciprocity expected between participants and Western researchers. It may also, although this is more speculative, effect the element of 'public' and 'private' inherent in the interview process if speaking to a fellow Chinese is perceived as closer to a private interview than speaking to a foreigner, this may have an effect on the contents of the interview. Certainly, if future projects could be designed to explore these potential effects, on both Chinese and Western participants, the results might be very interesting. On a more pragmatic level, the recruitment of both Chinese and Western researchers is recommended for any large-scale collaborative project.

Of course, all research is dependent on its researcher, but this may be especially true in projects such as this one, which seeks not only to understand the social and cultural discourse of widely divergent national contexts, but to synthesize them, as much as possible, into an inclusive theoretical framework. If the PST model is to offer insight into the development of normative technology regulation in all arenas it must be founded on a reasonably rich sociological understanding. In particular, the distinction between the multiple social and scientific contexts within which oocyte extraction has come to be employed is central to assimilating how it became contested in three such widely divergent social and cultural contexts. Achieving this understanding in culturally alien surroundings can feel, at times, more like anthropology than political science. But the results, for both the researcher and the project, have more than rewarded the effort.

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The Regulation of China's Stem Cell Research in the Context of Cosmopolitanization

Joy Yueyue ZHANG

Field of interest and guiding questions

As in many other countries, China's burgeoning life science industry emerges both out of its long scientific traditions and its ongoing engagement with current trends in international development. Accordingly, China's role in stem cell research is shaped both by national factors and debates in the global scientific and bioethical communities. My research takes the debates on China's stem cell regulation as a case study to understand national policy-making processes in relation to international influences. It employs Ulrich Beck's cosmopolitanism theory (Beck, 2004[2006]), FEI Xiaotong's theory on Chinese social institution and Chinese philosophy (Fei, 1947[1998]) to investigate how social values are being reiterated and how through such reiteration, social values are adjusted with new interpretations.

Stem cell research presents a good case for studying the development of scientific governance in China, for it is one of the most recent examples of China's passion for modern science and technology. In 2006, the State Council (the highest executive organ of the Chinese Central Government) issued '*The National Mid-term and Long-term Science and Technology Development Plan* (2006-2020)', in which stem cell research was identified as one of the priority development subjects. As international investment, natural resources and academic exchange are becoming the norm, scientists and regulators' roles in stem cell research are shaped as much by national factors as they are by debates in the global scientific and bioethical communities. One such example is that on visiting a regional headquarters of the China Hematopoietic Stem Cell Data Bank, the director told me in the original planning of their office space, people coming in were first welcomed by a whole wall of glass panel covered shelves, with hundreds of huge binders holding donor data. 'It wasn't considered an *ethical* issue. It was an *aesthetic* issue. Plus, it is difficult to persuade people donating blood stem cells in China (because traditionally blood is considered as the essence of life). I thought a whole wall display of the data books behind the glass panel is a magnificent display of our hard work. It would boost up morale. It would also help to build trust with visitors, as they can see at a glance that we have so many prior experiences.' However, during my visit, there was no documentation storage in sight. The director explained, 'I saw no data collection shelves during my visit to stem cell donor data banks in the US, I asked them why. They told me data books are stored in limited-access rooms to protect patients' privacy. Then I realized: Ah! The display of shelves is a matter of *ethical* concern. Now, all the hardcopies of donor data are stored in non-transparent lockers in the back room. We are more professionalized.'

As illustrated by the above cases, the internationalization of research rewrites the criteria for good practice through the process of ethicisation: former non-ethical issues are being recognized as ethical concerns. It calls for attentiveness to different values held by potential collaborators, and through such processes, it redefines new duties, responsibilities, and concerns. The focus of this study is to examine how the

globalization of the scientific community has influenced the regulatory developments and shifts in scientific practices *within* China. Thus, it is *not* a comparative study. Comparison of the Chinese situation with that of other countries, although inevitable, is not of a primary concern to this research. It is aimed at investigating how Chinese stakeholders (such as researchers, clinicians, patients and regulators), through the process of international communication, compare, reflect and accommodate diversity in research practices. This is what I define as the cosmopolitanization of science.

Expectations

By analysing data from media and news coverage, visiting hospitals, stem cell laboratories and biobanks, and by interviewing medical researchers and policy makers, this project is mainly focused on the following questions:

a) From the administrative framework-building aspect, how are new 'issues' emerging from stem cell research being acknowledged, assessed and described as ethically 'problematic' by Chinese scientists and bioethicists?

b) From the actual implementation aspect, how do Chinese research teams evaluate and develop research collaborations with others?

c) How are 'Chineseness' and 'international norms' being accommodated within current Chinese bio-regulations in the context of the cosmopolitanization of science?

Description of study method

This research employs a grounded theory approach, in which both data and analysis are placed with equal importance in producing theory. Successive levels of investigation through comparison among literature, media reportage and fieldwork findings constitute the core of my analysis.

With the support of a BIONET exchange studentship and a WellcomeTrust Studentship, I was able to take part in three of BIONET's major events and conducted in total 40 days of fieldwork in six cities (Beijing, Tianjin, Shanghai, Hangzhou, Changsha and Guangzhou) in China, in Spring 2008. I have conducted forty-eight interviews, including two MOH officials, one former popular science editor, seven bioethicists, and thirty-eight stem cell researchers. The bioethicists interviewed, four based in Beijing and three in Shanghai, were the core group who took part in the first draft of the Chinese stem cell guidelines and have been the most influential in China's policy making in this field. Although most of the interviewees were very generous in providing information and consented to my using their real name in publications, a few interviewees have expressed reluctance in revealing their real identity. As the topics in the interviews cover mostly opinions on regulatory issues and personal incentives, after much thought, I have decided to give anonymity to all my interviewees to ensure their confidentiality, except in circumstances where the linkage between the name and the specific research under discussion is public knowledge.

Interviews in this research are all semi-structured in-depth interviews with a mixture of general and specific questions. General questions are mostly on topics concerned with life science in general, such as interviewees' experiences with funding application processes. Meanwhile specific questions concern interviewee's individual research circumstances, such as progress or difficulties in their own research. Mostly interviews took place in sites familiar to the interviewees, usually their lab or office,

with no other person present. Interviews lasted on average one hour each and, with the exception of three, were all recorded on a digital recorder and transcribed. When recording was refused, interview notes were taken. In total 21 questions were prepared, but not all were asked for every interview. The interviews were designed to be flexible. Prior to the interview, emails or messages were sent to interviewees, informing them that questions may vary depending on the circumstances, but will focus on four general aspects: a) their personal engagement with stem cell research; b) their evaluation on China's societal regulations of bioscience; c) their evaluation of Western societal regulations, and d) other related issues interviewees would like to discuss. This not only ensured respondents of a range of questions that would not exceed their scope but also gave them time to reflect.

Many social scientists' works have suggested that interviewees' concerns often extend beyond participation in social research. They are equally interested in ensuring what they say matters (Miller and Glassner, 1997; Charmaz, 2006). Therefore I deliberately left room in my interview plan for 'other related issues interviewees would like to discuss'.

Taking into account the case in China, where the communication among government, scientists and public is poor, some interviewees saw this as a chance to voice their concerns. One clinician in Beijing told me how the 'rotation-system' of staff members going to conferences (meaning attending conferences is not based on individual merits or interests, but everyone takes turns) has created a politics within the research group itself. Another junior scientist was perplexed as to why a medical appliance company refused doing business with Chinese labs (for investment or political reasons), making it necessary to go through a third-country for the needed equipment. There are always circumstances that are beyond social scientists' ability to predict and neatly incorporate into questions before hand. These unplanned anecdotes have greatly helped me to expand my research in ways that I would have overlooked.

It is useful to keep in mind that the purpose of this research is to examine the case of Chinese stakeholders' participation in the global development of stem cell research, and to further contribute to the characterization of cosmopolitan science in-the-making. Therefore, my research method was tailored to better serve this particular purpose: *'how'* my interviewees construct their narratives and *'how'* they reflected on others is as important as detecting the 'truth'. In fact, conflicting interview data sometimes do arise in fieldwork. One typical example at hand is that during my fieldwork in southern China, on issues of the first hybrid-embryo, one scientist in Shanghai and one scientist in Guangzhou told me two different versions of the same affair, which result in conflicting attitudes and contradictory verdicts on Chinese stem cell societal regulation. These two interviewees, one a family friend, the other a respectable scientist, both have provided me with genuine help, and there is no sound reason for them to *intentionally* distort the 'facts' in interviews. Although the accounts given by both interviewees are too contradictory to assemble a consistent piece of 'truth' of what happened, their different interpretations of the circumstance accurately reflect, and is coherent with, their different views. The primary issue is not to convey and argue for an absolute 'fact' but to 'give an authentic insight into people's experience' (Silverman, 2001: 87). Of course, most interviews are not as dramatic as the example mentioned above. Differences in perceptions and minor disagreement on issues are common, but when comprehended with specific circumstances, they have

exhibited the 'capacity to access self-reflexivity among interview subjects, leading to the greater likelihood of the telling of collective stories' (Miller and Classner, 1997: 130). In other words, I see my interviews as dynamic occasions where the focus is as much on the process of *how* Chinese scientists construct their versions of reality and the circumstances of such construction, as on an accurate depiction of 'what' the social world is actually like.

How did my study develop?

Although my focus was on what is happening in the stem cell labs in China, my research started in London. As a member of the secretariat of the Chinese Life Scientists Society, before beginning fieldwork in China, I first visited senior Chinese stem cell scientists in London. These scientists, who once worked in China, are currently based in Imperial College, University College London and Kings College London. Not only are these Chinese scientists well-experienced with both the Chinese and British research framework, but many of them still play important roles in China-UK collaborations and China national funding decisions, such as being the overseas-reviewers for the National Natural Science Foundation. Dialogues with Chinese stem cell scientists abroad significantly supplemented my preparation for fieldwork in China and later enriched my analysis of the data.

Preliminary fieldwork in China was done in early spring of 2007, during my assistance to Professor CONG Yali in Peking University in organizing the first BIONET workshop in Beijing. Through the coordination of workshop programs among Chinese BIONET partners, I visited the Institute of Reproduction & Stem Cell Engineering at South China University, the Medical Ethics Department at Peking University, the Medical Ethics Department at the Chinese Academy of Medical Sciences and the Centre of Applied Ethics, Institute of Philosophy, Chinese Academy of Social Sciences.

At South China University, with the help of BIONET partner Professor LU Guangxiu, I was able to observe treatment procedures and patient-doctor interactions in the IVF clinic. Despite the diverse educational, financial and social backgrounds of the patients, I found that for most patients with serious infertility disease, the attitude toward surrogacy treatment was regularly ambivalent. On the one hand, most of such patients saw surrogacy as culturally acceptable, as it was their 'last hope' in having genetically-related children. Yet such treatment was banned in China because of previous social dispute it created due to inefficient legislation and law enforcement in protecting parties involved, such as the wellbeing of the surrogate mother, the legal rights of the infertile couple, etc. As surrogacy is banned in China, many infertile families felt they were deprived of the only chance for them to have their own child. On the other hand, equal understanding was also shown among patients on the actual difficulty of developing and implementing adequate legislation in China to regulate such treatment across regions. Therefore, at the first workshop, I presented comparative research findings on social and legal aspects of surrogacy in China and in the UK. By demonstrating how potential surrogate mothers could easily be found on on the internet in China, and such practice can be done in underground clinics, I argued, a simple ban does not suffice in protecting infertile couples and potential surrogate mothers (usually from the countryside) from the potential harm of surrogacy. The question remains open whether China will eventually follow, e.g. the UK's route in making legislative proposals on surrogacy.

On-site observations during preliminary fieldwork also gave vivid demonstrations of the value system at work. One case in my visit to Xuanwu hospital involved a university student who changed his mind several times before donating his blood stem cells to a leukaemia patient. When informed that a matching recipient had been found, his first response was shock. Although he had originally agreed to donate two years earlier, during a routine blood test, this student had never seriously considered the realistic possibility of an actual donation when he ticked the box that read 'agree to blood sample being stored in stem cell bank'. After consulting his parents, he withdrew his consent; however, he then did his own research on stem cell donation, got his dad's support, and re-consented. By the time I interviewed him in the ward, he was still worried about his mom's reaction. This student's hesitation and change of mind were not due just to individual concerns, but also reflected embedded social values and ethical traditions, such as the importance of having a *family* consent to blood stem cell donation. To better understand the complexity and ambivalence of reality in medical settings in China, I sought guidance from existing research on China's medical sociology.

Through visits to medical ethics centres in Beijing, I learnt that the social study of biomedicine is a relatively new discipline in Mainland China. In an oversimplified way, three 'Chinese' features in bioethics were repeatedly referred to by different bioethicists: the first one was the relative absence of religion in Chinese society, which led to the divergence of Chinese definitions of 'personhood' from the West. The second feature was the family-oriented nature of social ethics. And the third one was the traditional cultural belief, which holds an optimist attitude towards scientific advancement. Yet, despite branches of ethical investigations focusing on different aspects of medical research and intervention, many ethicists in Mainland China have taken up a 'practical wisdom' (Doering, 2002) approach, in which questions such as finding practical guidelines and strategies to promote efficiency were prioritized over developing theoretical frameworks. To gain a better understanding of Chinese values at work, I decided to draw linkages between Chinese ancient philosophy and contemporary schools of thought and seek wider reflection on Chinese development and political shifts. In the BIONET Shanghai Workshop, which took place in October 2007, I presented theoretical findings on Chinese traditional social perceptions of scientific advancement. Drawn on comparative philosophical works such as that by Julia Annas (1993), the Aristotelian school and Stoic philosophy was compared with Chinese Confucian thoughts on three themes: how virtue was defined; how self interest and others' interests are balanced; and how 'happiness' was interpreted. It was argued that science has long been celebrated in China, for it is not viewed as a mundane fast-track to improve living standards, but rather a way to *relieve* life *from* mundane worries. In Chinese tradition, scientific research has not only been perceived as sufficing curiosity, but also as a means of achieving moral objectives.

The BIONET Shanghai workshop put me into contact with a range of key stem cell centres and bioethics institutions in China. By visiting labs and talking to researchers of different rank, the aim was to understand the norms in establishing international collaborations within China's stem cell field. Reflexiveness on China's scientific development was shown by most senior researchers. On the one hand, with the frequent contact with foreign research groups, scientists in China were quite aware that for further development in science, China still has an 'image' problem to deal with, such as China being a well-equipped and well-financed 'Wild East' or China

being utilitarian and ignorant of 'blue sky' research. They also acknowledged an existing brain-drain, social scepticism on unproved therapies, and inefficient coordination among administrative agencies as disadvantages for life science in China. On the other hand, the recognition of supportive national or local authorities, ample financial and biological resources, and industrious young researchers also enables life scientists to improve local research cultures, conducting high-level research and establishing international collaborations on the basis of mutual benefits. In general, Chinese life scientists were optimistic on China's potential contribution to global stem cell research.

By way of analysing the development of laboratory conduct and research norms in China, I was able to trace out a trend of 'cosmopolitanization of science' exemplified by stem cell research in China. It was argued that the fast development of China's stem cell research was achieved not solely by a governmental top-down approach, but was initiated, supported and promoted by a variety of social and professional/scientific actors across institutional, regional and national borders. In April 2009, I was invited by Professor Ulrich Beck to present my findings at the 'Varieties of Second Modernity' workshop in Munich. Insights from theorists specialized in American, Asian and European modernization processes, together have significantly expanded the vision of my research.

Have expectations been met or was the approach significantly changed during the study?

Fieldwork and participation in BIONET programs have enabled me to collect data regarding questions set out at the beginning of this research. The analysis and categorization of data is still ongoing and some have been sent off for peer-review, on topics such as 'the organization of scientists and its effect on research efficiency' and 'the cosmopolitanization of science'. For the limited space, I choose only to state core findings.

The first research question was, 'how are new "issues" emerging from stem cell research being acknowledged as ethically 'problematic' by Chinese scientists and bioethicists?' With the intensification of cross-border communications, ethics is no longer a segmented social aspect that roots solely and directly out of cultural specification. Local practice is not isolated from but is an extension of international experience. The pressure to publish in Western journals, the necessity to establish cross-border collaborations so as to strengthen one's long-term competitiveness, and also the *fact* of global bio-exchange (such as stem cell tourism, transnational stem cell donation; more importantly, exchange of bio-materials and cross-national research collaborations) together exerted professional, financial and political pressure upon scientists and regulators in addressing the concerns originating both at home and abroad.

Some of the research limits and codes of conduct were drawn due to initial concern from within China, but more in response to discussions in the wider life science profession. One such example is the usage of surplus embryos from IVF treatment. With China's one child policy, using surplus embryos from IVF patients who have successfully given birth, was never discussed as ethically 'problematic' for there is a rare chance of surplus embryos ever being used. Thus, during the late 1990s, informed consent procedures for using surplus embryos for research differed in form (such as oral or written) and varied in procedure (such as who should talk to patients and

when). Yet, increasing international communication has also promoted the awareness and the enforcement of bioethical scrutiny among Chinese stakeholders. By experience sharing and assimilating international norms, the practice of using surplus embryos from IVF patients is currently more standardised in China.

For the second research question: in actual implementation, how do Chinese research teams evaluate and develop research collaborations with others? For many Chinese researchers, collaborating with others is not an option but rather an 'imperative'. One main reason for this is that as the range of scientific research expands, the growing diversity of research topics has encouraged an increasing division of expertise. The proliferation of specialization has consequently decentralized research assets: both material resources and intellectual proficiency are dispersed among respective sub-divisions of a profession. Even the most well-equipped research centres may hesitate to call themselves 'self-sufficient'. One immediate example is material resource sharing. China's rich biological resources have always been deemed as one big advantage of its life science industry, however, during my fieldwork, I found that most research labs would rather import their key research material from abroad than culture it themselves. Many research teams interviewed pointed out that taking into consideration the scale and competitiveness of contemporary research, it is in vain to struggle for achieving expertise in every single aspect of research.

Scientific research is not just about how much one group knows or is competent to achieve, but is about how best one can yield results utilizing international resources and sharing others' expertise. Consequently, other groups' material resources are brought on board with mutual agreement on terms of use, or to acquire 'permission' with reference of one's research agenda. In establishing and negotiating international collaborations, Chinese researchers have indicated a changed perception on the value of communication. One example is from Zheijiang University, School of Basic Medicine. One senior scientist recalled that at the beginning of China's reform and opening-up policy in the 1980s, Chinese universities reckoned that the best insurance for research advancement was to be connected with the outside world. In a striking contrast with the decades of isolation and anti-intellectual ideology that prevailed during the Cultural Revolution, in the 1980s, the symbolism of 'international experience' was once deemed as something 'higher' than national experience. In other words, communication was more or less one-way learning experience of the Chinese scientists. Importing international standards and the acknowledgement from foreign researchers alone had great intrinsic value. However, as scientific research and governance evolved, such one-way communication became no longer effective or necessary. In fact, as scientific development progresses, Chinese scientists have become more aware of local particularities, advantages and limits in scientific research. There is a growing attentiveness in giving voice to local situations in seeking potential collaborators. In other words, currently attention has shifted from communication itself to the consequence of such communication: how Chinese scientists could synthesize international experience into progress at home.

In terms of the third question, 'how are 'Chineseness' and 'international norms' being accommodated within current Chinese bio-regulations in the context of the cosmopolitanization of science', endeavours can be seen from both scientists and bioethicists. With strengthened transnational exchange in recent years, Chinese researchers at home and abroad have become aware of the fact that without sound

reasoning of China's own circumstances, Chinese research endeavours cannot be fully appreciated and supported by the world society. It dawned on Chinese stake holders that the cosmopolitanization of science is not about how well one assimilates foreign practice nor about how one should be left undisturbed in one's own ways, but about how well one is being accommodated by others on the basis of mutual understanding. One such example is that in March 2006, Jim Giles (2006: 9) noted in *Nature* that 'China lacks clear national policies, with different institutes following different rules'. Immediately, in the April issue, by providing information on China's existing guidelines and regulations on stem cell research, CHENG et al. (2006: 992) argued that 'It is true that national policies on human stem-cell research in China are not laws. With some further improvement, however, we think they are adequate, as nearly all scientific research in China relies on government funding.' That is in effect, only limited research could proceed 'without required government approvals or appropriate clinical trials.' Many researchers interviewed have also taken active part in explaining the Chinese situation to the West. In addition to introducing international debates, social scientists' approaches in seeking good governance in Chinese life science have also shifted its orientation towards finding 'common ground with non-Asian counterparts on important issues' (Qiu R-Z, 2004). The cosmopolitanization of science did not show an erosion or disavowal of diversity. On the contrary, it manifested the fact that there are values that are, and should be, universal, just as there are lots of values that are, and must be local.

Lesson learned

The process of the cosmopolitanization of bio-regulation reflects two distinct characters in today's scientific world: how to govern international research collaborations whilst respecting cross-cultural differences. In the past decade, China has shown commitment in joining international endeavours[1], however the difference in existing institutional infrastructure and social conventions requires a different emphasis in terms of policy-making. Two lessons can be drawn from the development of stem cell research in Chinese institutions.

Firstly, as indicated by the development trajectory of stem cell research, the advancement of contemporary life sciences cannot be promoted solely with a top-down approach. Rather, it involves multi social agencies and includes initiatives generated from different levels. As explained above, research cultures are formed by both, national directives and permissive regulations, and by local scientists and bioethicists. In addition, the response to foreign (and domestic) criticism and enhancing mutual understanding with Western institutions, are no longer considered an exclusive diplomatic responsibility that is assigned only to governmental agencies. Individual researchers, local labs and social scientists have increasingly taken up a

[1] In relation to stem cell research, China's participation in global regulatory initiatives in the past decade include, the Guidelines on Ethics in Medical Genetics (WHO, 1998); the Universal Declaration on the Human Genome and Human Rights (UNESCO, 1997), the Helsinki Declaration on Ethical Principles for Medical Research Involving Human Subjects (WMA, 2000), the Human Embryo Research and International Solidarity and Cooperation (UNESCO IBC, 2001) and the Universal Declaration on Bioethics and Human Rights (UNESCO, 2005). China also supported the United Nation's ban on human cloning for reproductive purposes.

more active role in transnational communications and demonstrated more initiative in facilitating data exchange.

Secondly, harmonization in stem cell research regulation is the key to promoting local research progress. By harmonization I mean the inclusion or incorporation of global concerns into China's own regulatory agenda, such as the stand on banning reproductive cloning in the Ethical Guidelines for Research on Human Embryonic Stem Cells (MOH and MOST, 2003), and authorization procedure for stem cell treatment (MOH, 2009). Yet, harmonization does not mean unification. Chinese medical professionals and administrators have shown increasing awareness in accommodating stem cell research with local resources and contextual particularities. In other words, it was the awareness of dependency that promoted the globalization of research, and it is the acknowledgement of interdependence that enables cosmopolitanisation.

What are the remaining questions, additional research that should be done along these lines?

Apart from evident endeavours from related professions, such as bioethics and life sciences, in China in facilitating the development of stem cell research, there are also some social gaps that need collaborative efforts from a diversity of social actors. One such issue is public education on stem cell research. It is true that many major hospitals, such as Peking University's Third Affiliated Hospital and the Reproductive & Genetic Hospital of Citic-Xiangya, have organized routine patient seminars and public lectures regarding clinical and social implications of specific stem cell techniques. Yet, such dissemination of related knowledge is still oriented at limited audiences with a narrow focus. Currently, public education on stem cells is still quite weak in most parts of China, including major cities like Beijing and Shanghai. The situation is worse with regards to the fact that most of the public circulation of information depends on journalists and other forms of lay media, with few stem cell researchers and medical professionals engaged. Consequently, there is a greater opportunity for misunderstood, misinterpreted and misleading information on stem cells to be circulated among the public. Misconceptions of stem cell research and partial knowledge of stem cell donation have generated avoidable hesitation and scepticism towards medical conduct. They have also built up higher barriers for stem cell scientists in China to promote public participation and gaining public support. The difficulty for blood stem cell banks in China to recruit and enlist donors, enlarging the sample database is one such example. On the other hand, many stem cell researchers have acknowledged the imperatives in promoting public understanding of this research. Yet most of them have limited knowledge and means on how to approach the public. Although in trying to better embrace regional differences, the Ministry of Health has appointed prominent life scientist WANG Yifei in early 2008 to conduct a survey on the diversity of ethical concerns on stem cell research, I learnt from professor WANG in the BIONET Changsha workshop that such studies currently are still mainly limited to opinions from professional institutions. There is still a lack of research on current public opinion towards stem cell research in China. So far, in the globalization of science, the comprehension of 'Chinese' limits and needs lack empirical data from the lay public. To further promote stem cell research in China, organized public dialogues, with the involvement of bioethicists and scientists, are thus necessary. The 'Reporting Bioethics' satellite workshop BIONET held in Changsha (March 31-April 1, 2008), which directly involved public media in related

bioscience discussions, set one example of much needed efforts to bridge the distance between the scientific and public domains.

Conclusion

The cosmopolitanization of science has brought with it the dissemination of values, ideas, and customs. It unavoidably challenges local norms, questions existing frameworks, and contests traditional conventions. However, the function of the international community has shifted from assimilation-seeking to awareness-raising. On occasions, the cosmopolitanization of science does transform local non-ethical issues into ethical concerns, or convert formerly acceptable conduct into inappropriate practice. But such local transition is not completed by receiving an 'all-embracing, one-size-fits-all global solution' (OECD, 2007). It is carried out through negotiations with respect to the different political systems, social structures and cultural traditions of each side.

Of course, as pointed out at the beginning of this paper, China, like many developing countries, is far from exerting the same influence over issues as their Western counterparts. In the development of stem cell research, China has imported and contributed actively to the making of many international standards, such as ethical guidelines, funding policies, and professional assessment systems. It would, of course, be naive to assume that the cosmopolitanization of science, when extending seats at the negotiation table to all, would automatically grant each participant an equal status. Yet, it would be equally wrong to turn a blind eye to the emerging possibilities of negotiation for the less advantaged participants.

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Ethical and Social Aspects in Neuroscience: Focus on Medical Interventions of the Brain

Wang Chunshui

Introduction

Neuroscience, arising from the interdisciplinary collaborations of anatomy, physiology, pharmacology, and psychology, has been challenging previously maintained notions about the structure and function of nerves and the nervous system, the nature of the brain-mind-self relationship, and the intersection of neuroscience, ethics, and society. Recent advances in neuroscience have not only raised hopes of new insights into the human brain, cognitive processing, human memory, learning, performance, and judgment, but also treatments for some previously intractable conditions. However, it has also raised social, ethical, legal, governance, and political issues of current and near-term priority that have been stressed increasingly by some philosophers, sociologists, scientists, and ethicists.

Broadly speaking, neuroethics is a new field concerned with the ethical, legal, and social policy implications of neuroscience, and with aspects of neuroscience research itself. However, term ‘neuroethics’ refers to two projects, one of which refers to ethical reflection on new technologies and techniques produced by neuroscience so as to answer questions about the applications of neuroscientific knowledge. The other project refers to the ways in which the new knowledge emerging from the sciences of the mind explores traditional philosophical topics, which show that neuroethics is somewhat different from the enterprise of bioethics.

It was my great fortune to have the opportunity to spend one month focusing on studying the ethical and social aspects in neuroscience, especially medical interventions of the brain, at the LSE’s BIOS center, which is an amazing academic environment for social, political, and ethical studies of the life sciences and biomedicine, thanks to being generously funded by the BIONET project. For me, it was one of the most exciting and challenging experiences of my life.

The main purpose of my study at BIOS

As a nascent field, neuroscience generally encompasses all scientific studies involving the nervous system. Psychology, as the scientific study of mental processes, may be considered a sub-field of neuroscience. Medical interventions of the brain, a specialized field of neuroscience that includes pharmacological treatment of depression, attention or memory deficit disorder, as well as the enhancement of cognition, mood and vegetative state, brain/psychosurgery for treating mental diseases or drug addictions and brain-reading (fMRI) for detecting dysfunction, have already been applied in clinical practice in some countries including China. For example, in one hospital, in 2001, brain surgery was performed on more than 200 people with drug addictions, according to the rationale that there is a self-rewarding system for drug use in the brain. If this system can be successfully destroyed, the addiction, especially psychological addiction, will be removed. The institution that performed these surgeries claimed that the efficacy rate was at least 85% as compared to the high repeat addiction rate observed in recovering drug addicts. However, after finding

many problems in this project, such as scientifically invalid evidence, therapeutic misconception among patients, disproportional risks/benefits, and so on, the Chinese Ministry of Health announced a ban on this surgery as a routine practice. Brain operations were also performed to treat people with psychosis. Additionally, some antidepressant drugs, such as Prozac, have been used in the treatment for depressed teenagers in order to reduce levels of depression. However, these fields are raising some social and ethical issues, many of which are faced by all countries. These involve safety, long-term or delayed side effects, informed consent, privacy, freedom or coercion, equal opportunity, medicalization of inner life, etc. for individuals; fair distribution, differences in capacity, the possibility of widening the gap between rich and poor, raising our standard of normalcy, worsening the situation of the disadvantaged etc. They even raise issues about whether we should be able to improve ourselves with medical interventions beyond the limit of human nature? To date there has not been much attention to such social and ethical issues in China. Therefore, the aim of my study was to learn how to identify these new issues and learn the methodology of social studies and other relevant methods, and try to learn how to address these issues, especially in the context of China.

Study at the LSE

As sociology was a new field for me, I began my study by exploring the meaning of 'social issues' and 'ethical issues' related to neuroscience, and also trying to find out what is the difference between these two kinds of issues. I benefited a lot from sociologist Professor Nikolas Rose, the Director of the LSE's BIOS Centre, for introducing me to helpful literature on social and ethical aspects of neuroscience. He helped me understand what we mean by social issues of neuroscience, namely the social conditions and social consequences of developments in the neurosciences. For example, what is driving the agenda of research and development? Moreover, what will be the consequences: will they lead us to the use of more psychoactive drugs for children? Alternatively, what implications might there be of using brain imaging for screening? On the other hand, what would be the implications of screening elderly people for markers of future development of dementia, even when they have no current symptoms? Sociologists can describe the social consequences objectively, using empirical research, observing, interviewing and so forth. Neuroethics is a way of developing a normative evaluation of these developments – judging if and how they are desirable or undesirable.

Moreover, I learned that social issues also include economic issues. Economic incentives can push neuroscience in particular directions. For example, the wish to develop drugs to delay the onset of dementia is seen as a very big market opportunity for pharmaceutical companies, and hence some companies are investing heavily in them. Sociologists have already seen the ways in which 'depression' has expanded as a diagnostic category, and some argue that the drug companies 'market' the disease label as well as marketing the drugs. On the other hand, governments are concerned about the 'burden', including the economic costs, of 'mental disorders' – such as days lost from work, low productivity, as well as direct health care costs.

I also understood that social and economic issues cannot be 'solved' without empirical research, using sociological research methods, in order to identify what has happened, what is happening, and what is likely to happen, and help us understand the costs and benefits of different developments. I kept on reading (some of them are

illustrated in the attached 'References'), and then I developed an interest in further studies on the social and ethical issues that arise in connection with neuroscience. This topic not only is related to traditional issues including the safety of technology, long-term or delayed side effects, informed consent, privacy, freedom or coercion, equal opportunity, medicalization of inner life, fair distribution of the technologies, capacity divide, widening gaps between rich and poor, etc., but also include some novel issues such as free will that deserves careful study. Neuroethics, which is one area of bioethics, is a new field that examines what is right and wrong, good and bad about the treatment of, perfection of, or unwelcome invasion of and worrisome manipulation of the human brain in medical practice and biological research.

Participating in activities at BIOS

With the kind help of Dr. Ayo Wahlberg, I had the opportunity to attend some courses, such as 'Key Issues in Bioscience, Biomedicine, and Society' and 'Key Methods in the Social Study of Bioscience and Biomedicine', which were of great benefit to me in terms of learning about social theories and social analytical approaches. They not only provided me with an opportunity to learn social methodology and concepts related to the study of biomedicine, bioscience, and biotechnology, but also offered me a chance to explore problems arising from the development of technology from a social, ethical, and political perspective.

We should consider the relationship between scientific research and social, political, and economic contexts. Just as Merton's norms, 'the ethos of science is that affectively toned complex of values and norms which is held to be binding on the man of science. The norms are expressed in the form of prescriptions, proscriptions, preferences, and permissions. They are legitimized in terms of institutional values'. The course also helped me develop an awareness of contemporary research, bringing together perspectives from across the social sciences to explore the social, political, economic, and ethical implications of developments in biomedical technologies and pharmacology. I learned some key themes in biomedicine, bioscience, and biotechnology, and also learned some key concepts and approaches in biosocial studies, such as biocapital, biopolitics, biopower, biological citizenship, biomedicalization, biosocialities, biobanking, etc.[1]

BIOS is a place that provides an academic platform for students. What made a deep impression on me was the conversational academic atmosphere at LSE, especially at BIOS. This included a number of reading groups, seminars and roundtables held by scholars who helped me learn about not only social theoretical knowledge, but also approaches to thinking about and solving social issues. For example, a scholar from Brazil gave a presentation on "Color, race and genomic ancestry in Brazil: Dialogues between anthropology and genetics" that presented the results of an interdisciplinary research project, incorporating approaches from genetics and anthropology. He addressed topics such as the complex terminology of color/race classification in Brazil, perceptions about ancestry in the context of ideologies of Brazilian national identity, and the relationship between genetic information about the Brazilian population and a socio-political agenda that turns on questions of race and racism. I also had a chance to attend the reading group on "The New Spirit of Capitalism" held by Professor Kathrin Braun, which discussed the book, "The New Spirit of

[1] Avaible at: http://www.lse.ac.uk

Capitalism" written by Luc Boltanski and Eve Chiapello, that analyzes the transformation and re-organization of capitalist political economy and ideology over the last 30 years, which resulted in the emergence of a new neo-management system and talks about the core question of why such a change seemed to transpire without encountering any pronounced hostility.

BIOS is also a place filled with hard-working colleagues and students who are busy in writing and reading books everyday, and also willing to take time to communicate to each other. Thanks to Prof. Nikolas Rose and Dr. Ayo Wahlberg's help, I had an opportunity to conduct interviews with several colleagues, such as Joelle Abi Rached, Giovanni Frazzetto, and Caitlin Connors. We discussed questions concerning the meaning of 'social issues' and 'ethical issues' related to neuroscience, what is the difference between these two kinds of issues, and how to study and solve these issues. This helped me to rethink the issues that confused me most.

The proposal for my future study

Based on the experiences described above, I am now planning my future study as follows.

Provisional title

Social and Ethical Aspects in drug treatment for Children with ADHD: A Comparative Case Study of China and the UK

Background & rationale

Attention-Deficit/Hyperactivity Disorder (ADHD), which is most commonly diagnosed in children, is a disorder characterized by a persistent pattern of inattention and/or hyperactivity-impulsivity initially appearing in childhood, which manifests itself with symptoms such as hyperactivity, forgetfulness, poor impulse control, and distractibility. Evidence has shown that stimulant medication is the most effective way to treat the disorder. However, Ritalin, which is a drug intended for children with ADHD, is also effective in enhancing the abilities of normal children. Therefore, this development in pharmacology has been considered as a way of enhancing the cognitive abilities of children without pathology in some countries including the United States, the United Kingdom, and China. There have been some social, ethical, and governance problems faced by all countries in this area.

Questions

Within the context of a comparative case-study involving China and the UK, my future study project pursues the following questions:

1. What is the situation concerning the use of Ritalin both in China and in the UK, such as the procurement and allocation of the drug? Does the drug work?
2. How do health practitioners, parents, and children understand the disorder? What do they think the medication does? How do they understand the moral dimensions of their self? etc.
3. What is the definition of equality and normal functioning?
4. Should normal children be encouraged to enhance their cognitive abilities by this means? How do health practitioners, parents, and children think about the medication for the purpose of enhancement?
5. What regulation exists, such as laws, regulations, and guidelines? Are there any provisions that outline general social values?

6. What principles can be said to formulate the laws as they currently exist?
7. What are the potential effects of national culture on the outcomes?
8. What are the political, social, cultural, ethical, and legal implications related to the use of Ritalin?

Methodology

This project would be extended to include fieldwork comprised of qualitative interviews with health practitioners, teenagers, their parents, and other stakeholders (including pharmaceutical companies, parental groups, etc.) to explore some of the social and ethical challenges surrounding ADHD and Ritalin, for instance, how they understand this disorder, what they think the medication does, and how they feel about their child now that he/she is undergoing treatment. Moreover, it will also comprise desktop research involving content analysis of social values, cultural contexts, governance instruments, formal policy statements, and scholarship around these issues.

Outputs

Apart from fieldwork, this could result in a paper publishable in English and in Chinese in the UK and China.

I would like to acknowledge that studying at the BIOS Centre and enjoying the different cultures, customs and lifestyles in London opened up a new horizon for me and also broadened my academic perspective.

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Informed consent in the clinical work of ART and the research of stem cells

Li Rong

Field of interest and guiding question

1. *Informed consent in the clinical work of Assisted Reproductive Technology (ART).*
In our center, the Reproductive Medical Centre of Peking University's Third Hospital, I face 40-60 female patients per day and I feel that I do not have enough time to explain all the relevant details to the patients and their husbands. A practical problem is that there are many patients who come from all over the country and who do not make an appointment before hand. We hope to give everyone five minutes to discuss the procedures and another five minutes to do the examinations. So I wondered how doctors in Germany and the UK organize the informed consent process (namely, so that it is a procedure, not just getting a signature) among their other duties, such as examinations and treatments.
2. *The management of some ethics problems in clinical work related to the doctors' clinical job on informed consent and the role of the clinical ethics committee.*
There are many ethical problems in reproductive clinical work, such as the status of the parents and children, or the relationship between surrogacy and egg donor. Proper recording and filing of personal data has turned out to be crucial and sensitive work. I wondered about the management of these ethics problems in the EU and the UK and how an ethics committee could be set up to work properly.
3. *Management in clinical work, especially on surrogate motherhood.*
Surrogacy is forbidden in China and it is very difficult to find egg donors due to difficulties in dealing with a number of ethical problems, such as the parental relationship: who should be the true mother and whose child is someone who is born from a "surrogate mother"? However the use of eggs donated after IVF treatment can help treat some female infertility problems, such as endometrial damage and premature ovarian failure. I wondered how these infertility problems were dealt with in the UK. (As egg donation is illegal in Germany, I could not study such practices in Germany.)
4. *The management and practice in stem cell banking and research.*
Since surrogacy is forbidden in China, and adoption is impractical, it was difficult to deal with infertility caused by endometrial damage. My PhD research focused on endometrial stem cells as a resource to help cure this kind of damage. It was very important to deal with the ethical problems in this research, considering endometrial stem cells are a human tissue resource, which raises questions, such as informed consent, embryos' rights, etc.

Expectations

In this project, I started with these expectations:
1. To learn more about the clinical work of assisted reproductive technology, ART, informed consent and how to manage ethics problems in clinical work, especially through observing doctors' work in the first Beijing workshop and through personal visits in EU and the UK.

2. To discuss some informed consent problems we encounter in clinical practice and research, such as the relationship between egg donor and recipient, and to find methods to deal with these problems during personal visits in the EU and the UK.
3. To learn more about the role of clinical ethics committees during visits to ethics committees in the EU and the UK.
4. To learn more about the management of clinical work during clinical visits in the EU and the UK.
5. To learn more about management and practice in stem cell banking and research during the BIONET's Changsha conference and through my personal visits in the EU and the UK.

Description of study method

Method
Presentations of my own work to experts, discussions and personal visits

Time
20-30 minutes per presentation and 1-2 hours per visit

***Presentations**
1. "Research Findings on Regulations and Practices in Europe and China", at the first Beijing workshop of the BIONET: Mainly introducing Chinese regulations on Artificial Reproductive Technology (ART) treatment.
2. "Clinical prospects of Endometrial stem cells", at the Institute for Science and Ethics, Bonn University: Discussion of the ethical problems addressed in my PhD research on endometrial stem cells.
3. "Endometrial stem cells and informed consent on surrogacy", at the BIOS Centre (LSE): Discuss the ethical problems from my PhD research on endometrial stem cells and surrogacy in UK.

***Places visited and visited experts**
1. Clinical Visit to Fertility Center 1 in Hamburg.
2. Center for Kinderwunschbehandlung in Osnabrueck.
3. Institute for Science and Ethics, Bonn University.
4. Clinical Visit in Fertility Center 2 in Hamburg.
5. UK Stem Cell Bank, National Institute for Biological Standards and Control, in London.
6. Genevra Richardson, King's College London, ART law expert.
7. Emily Jackson, member of HFEA License Committee, ART management expert.
8. Participation in the License Committee meeting of the Human Fertilization and Embryology Agency (HFEA), in London. Visit Deputy Chief Executive/Director of Regulation, HFEA and Policy Development & Co-ordination Manager, Veronica English and Deputy Head of Medical Ethics, British Medical Association.
9. Dr. Cristina Navarette, National Blood Service, expert consultant on ART.
10. Mr John Parsons, Lead Consultant on Surrogacy Assisted Conception Unit, expert consultant on surrogacy.
11. Visit to the Institute for Wissenschaft and Ethics, Bonn University.

Details / Observations

Different work mode between EU and China

As required by law and professional ethics, German doctors always request informed consent, regarding it as a procedure, not just a signature during their examinations and treatments. The procedure often takes the doctors 1 hour for the first visit and 20 minutes for the following visit. Doctors need to receive informed consent from both the wife and her husband. Compared with my institution, most German couples do not let other family members and friends attend the procedure, since they do not want other people to know about their fertility problems. In our center, I see 40-60 patients per day, so I do not have enough time to explain details to the patients and their husbands, except for information about the success rate, fees, risks and possible complications. We have a special nurse who is in charge of explaining the concrete procedure. She also checks their ID, marriage certificate and pregnancy certificate, which are papers that are legally required in China. We would like to have the opportunity to pay more attention to informed consent in the treatment procedure and give them more encouragement, not just information on complications.

In Germany, the doctors spend half an hour on informed consent during the first visit, mainly introducing information about the couple's infertility problem and the methods of treating their condition. After the first visit to a specialist, the patients need to visit another doctor to do informed consent to make sure that they have received sufficient information about their condition and the options for treatment. And then they spend one hour explaining the IVF procedure and the possible complications within IVF treatment. At last, the couple signs an informed consent form and chooses a treatment schedule.

In China, the patients have to pay for all infertility treatment fees by themselves, whether they have health insurance or not. Some patients want Assisted Insemination from Donor (AID) treatment even when they can receive a genetic offspring through Intracytoplasmatic Sperm Injection (ICSI) treatment, since the AID treatment fee is cheaper than ICSI. According to regulations set out by the Health Ministry in China, The Code of Practice for Assisted Reproductive Technology of 2003, doctors can proceed according to the patients' choice. However, we do not do AID treatment for these kinds of patients in our center, because economic problems are only temporary. Once the couples have enough money, they may want a genetic offspring through ICSI treatment. We think it is unfair to the child to be conceived through AID.

There are no similar problems in Germany. The insurance companies do not cover the fee for AID-related treatment. After the insurance companies began to only cover 50% of the fee for IVF treatment in 2004, IVF treatment cycles have been reduced by one third. The insurance companies cover the IVF treatment fee for the first three cycles and cover the fee as it relates to other factors, such as age (older people pay less). The insurance policy has a large affect on the IVF treatment decision.

Because the patients need to pay half of the treatment fee, which is more than the percentage they needed to pay before 2004, today they choose to receive half the previous number of IVF cycles. Doctors must pay more attention to informed consent, because the patients pay more money than ever. In German centers, the doctors give the related information to the couples, and then they will make their own decision.

In China, the information we provide is similar to the information provided by the German doctors. However, Chinese patients rather prefer the doctors to make the treatment decisions for them, since they think the doctors have the necessary medical knowledge. Chinese female patients like to discuss their problems with other family members, such as their mother, their mother in law and their friends. Sometimes, other family members have a decisive effect on the patients' choice.

The reproduction doctors must receive 5 years of training as a gynecologist and 1 year as an endocrinologist and some additional special training, such as how to explain the IVF procedure in more detail.

Different opinions of parents in Germany and China

In Germany, children have recently been granted the right to be informed about their genetic father at a certain age and the sperm donor cannot refuse. When they become a donor, they must agree to this. In China, there are almost no sperm donors who want their offspring to know their identify. In other words, the child has no right to know his/her biological father and the donor has no duty to be responsible for his biological child. Clearly, there are some different customs between the two countries.

Different opinions on Pre-implantation Genetic Diagnosis (PGD) in Germany and China

Embryo selection is prohibited in Germany, so doctors need to decide how to deal with the fertilized eggs that cannot be implanted into the uterus. All the embryos must either be stored or implanted. Pre-implantation genetic diagnosis (PGD), is also prohibited in Germany. Doctors are permitted to test the polar body, but this method cannot be used deal with genetic abnormalities coming from the male side. Some doctors may think this is not good practice. Chinese embryologists, like many embryologists in other countries, are permitted to choose which embryos are to be stored or given up on Day 3. In my professional opinion, it is more reliable to judge the growth potential of embryos on Day 3.

Governance of reproductive medicine

There are some laws, regulations and rules to manage clinical treatments in Germany, just like in China. Doctors in China do all the treatments according to these laws, the most important being: The Code of Practice for Assisted Reproductive Technology. (http://www.moh.gov.cn/publicfiles/business/htmlfiles/mohyzs/s3576/200804/29614.htm) In special cases, doctors will consult an ethics committee. Clinical practice is governed by the Ministry of Health, insurance companies and other departments. For example, clinics send their clinical data to the Ministry of Health which governed their management, At the same time, insurance companies review "dealing indications", whether the couples need the treatment or not.

In the United Kingdom, provisions for surrogacy are included in the Human Fertilization and Embryology Act (HFEA) of 1991 and these regulations are used to guarantee and avoid problems associated with surrogacy. Surrogate mothers must be in good health and be able to undergo a pregnancy with a minimum amount of risk to their own health. The legal mother is always the carrying mother, so the couple seeking her services must either apply to adopt the child or apply for a parental order in order to become the legal parents of the child(ren). In this way, the UK government

seeks to govern surrogacy, rather than forbid it. Before a new and effective method is used in the clinic, we should find ways to deal with and govern surrogacy.

Advice received for my PhD endometrial stem cell research

I met some specialists at the Institute for Science and Ethics, Bonn University. I made a presentation to introduce our university, hospital and my research and discussed 2 clinical cases. They also gave me some advice based on their experience,.
In China, like Germany, researchers must gain the permission of a research ethics committee before the research can begin. All the research that is conducted in my hospital requires such approval. My research also requires that I get informed consent from my patients. This procedure is similar in China and Germany, too.

For my research, the audience suggested that I collect endometrial stem cells from endometrial tissue. This method might raise fewer ethical problems and might make it easier to get informed consent. However, the endometrial stem cells are too few to do this research on endometrial tissue. I will try my best to test this method.

Remaining questions

1. How to look upon surrogacy, why should it be forbidden or permitted? Some infertility couples need this treatment to obtain their own hereditary children, but the treatment may injure the women themselves and raises issues regarding their childrens' rights.
2. How to handle informed consent in research? The clinicians should spend enough time on informed consent, and not just think of it as a formality.

Conclusions

Informed consent to treatment is a procedure that accompanies the treatment. The purpose of obtaining informed consent is to ensure that patients know what doctors propose to do and freely grant their permission. German doctors spend more time on informed consent than Chinese doctors.

Surrogacy and donated eggs are both prohibited in Germany, surrogacy is prohibited in China, but they are both permitted in the UK. The UK government has developed some rules to handle the procedure, such as identifying parent-ship and children-ship. In the future, these rules / regulations may serve as a model for China, if the government changes its current regulations.

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Key observations

1. Informed consent to treatment is an ethical requirement. The purpose of obtaining informed consent is to ensure that patients know what doctors propose to do and freely grant their permission.

2. Informed consent is a procedure accompanying treatment, not just a signature.
3. German doctors spend more time on informed consent. Chinese doctors pay more attention to the examination.
4. It is prohibited to conduct embryo research including pre-implantation genetic diagnosis in Germany. German doctors can test the polar body to exclude certain genetic disorders coming from the mother.
5. Surrogacy and egg donation are both prohibited in Germany. If patients need these kinds of treatment, they can go abroad.

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Comparing the Practice of Genetic Counselling in the UK and China[1]

Suli Sui

Objective of research

The BIONET's research student exchange programme provides a platform for Chinese research students to develop comparative research projects on ethical governance related to advancements in biological and biomedical research in China and Europe. As part of this exchange programme, I carried out fieldwork and literature collection for the above-titled research project from November 2008 to January 2009 in hospitals, research institutes, and patient organizations in the UK. I had earlier carried out fieldwork on the application of genetic counselling in China. The main research methods I used were interview and literature research. Clinical observation was also carried out during fieldwork in China. The rapid development and application of genetic testing technologies make the provision of genetic counselling increasingly important. In practice, genetic counselling concerns some ethical issues, such as non-directiveness, informed choice and decision-making, and it reflects the administrative, political and socioeconomic environments of a certain society. I hope this empirical research can offer a way to show the differences in the qualifications required for genetic counselling providers, the model of genetic clinical services, and its governance and supervision in these two countries.

Main activities during the fieldwork in the UK

During my stay at the LSE, I visited four regional genetic centres: South Thames (West) Regional Genetics Centre of London, South Thames (East) Regional Genetics Centre of London, North East Thames Regional Genetics Centre of London and All Wales Medical Genetics Service, Cardiff. I visited two patient social institutions: the United Kingdom Thalassaemia Society, a national registered charity for people with Thalassemia, and Action Duchenne, a national registered charity for people with Duchenne Muscular Dystrophy. I interviewed 7 professional genetic counsellors working in the different genetics centres and the executive coordinator of the UK Thalassaemia Society and a board member of Action Duchenne. I conducted phone interviews with 2 Chinese geneticists, which helped me to better understand the practical side of genetic counselling in China. I contacted the chair of AGNC (Association of Genetic Nurses and Counsellors), who is a senior genetic counsellor for Royal Devon, and Exeter Hospital to consult about my queries about AGNC. Additionally, I attended, *Key Issues in Biomedicine, Bioscience and Society*, a master's seminar at the BIOS Centre (LSE) convened by Professor Kathrin Braun, which helped me to better understand the social and ethical implications and issues surrounding recent advancements in genetics.

[1] Based on the interviews, personal experiences during fieldwork and the literature archive study in China and the UK, I wrote one paper titled *Genetic Counselling – Comparing the governance and practice of genetic counselling in China and the United Kingdom,* and submitted it to an international peer reviewed journal, *Biosocieties.*

Main fieldwork findings

The professional genetic counsellor in the United Kingdom

The Association of Genetic Nurses and Counsellors (AGNC), founded in 1980, is the professional organization which represents genetic counsellors and genetic nurses in the United Kingdom. The AGNC is not a government institution but a self-financed and self-governed professional body. AGNC membership is open to professionals whose work involves contact with families or individuals affected by or at risk of a genetic disorder. Membership to AGNC is not spontaneously awarded; rather, a practitioner achieves registration by submission of a portfolio of evidence to the Genetic Counsellor Registration Board (GCRB), which is assessed to ensure the required level of knowledge and practice-based competence has been attained. The academic standards applied to the portfolio are at a Master's level (GCRB 2009). Currently, there are around 300 AGNC members within the UK, of which around one-third to one-half are registered genetic counsellors. The AGNC is currently applying for statutory regulation, with the Genetic Counsellor Statutory Regulation Steering Group, a working group within the AGNC. As the current chairman of AGNC, Gilly Bromilow, explains:

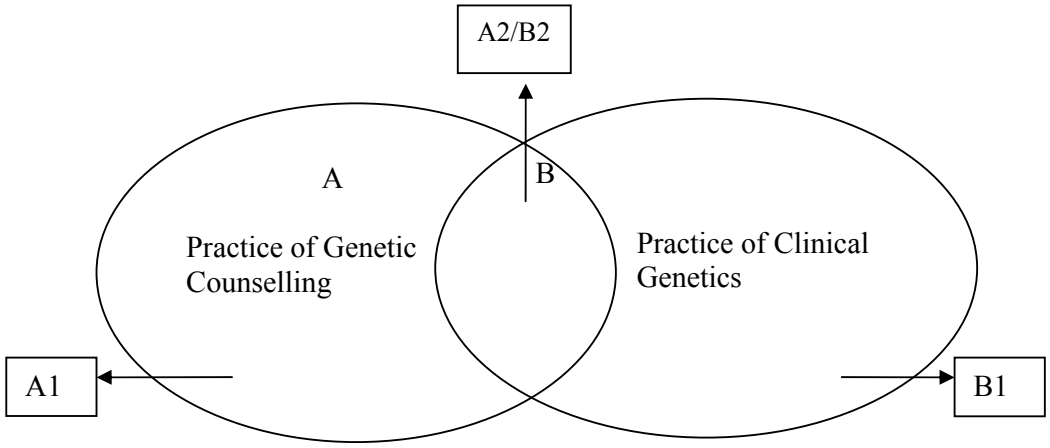
> We are currently a voluntary organization. At present, our professional registration is voluntary but we are in the process of applying for statutory regulation by the Health Professions Council. This is a long process that has to be ratified by an Act of Parliament. But this will mean that we will then be recognized as a separate profession with our own regulation and registration.

The practice of genetic counselling in the United Kingdom

In the UK, genetic counselling is provided by professional teams operating out of regional genetic centres within the medical care system, the National Health Service (NHS). These genetic centres include: North East Thames Regional Genetics Centre and South West Thames Regional Genetics Centre in London, West of Scotland Regional Genetics Service in Scotland, and All Wales Medical Genetics Service in Wales. Genetic counselling sessions are regularly provided in different clinical settings within their area by counsellors or clinical geneticists from a regional centre. This is more convenient for patients and obviates the necessity to travel long distances to receive genetic counselling. The counselling services and allied medical treatments are free for patients within the NHS.

The clinical genetic counselling teams consist of medical geneticists and genetic counsellors. In practice, genetic counsellors and clinical geneticists work in close partnership, and part of the counselling services they offer are joint or combined. As is shown in the figure below, *ellipse A* represents the practice of genetic counselling and *ellipse B* the practice of clinical genetics. Generally, genetic diagnosis and the determination of hereditary characteristics are done by the clinical geneticist, as shown in *B1*; the clinical procedure of genetic testing, the explanation of the implications of the diagnosis and the help/support for the patient in terms of decision-making, are done by the genetic counsellor, as shown in *A1*. Prenatal diagnostic counselling and pre-test and post-test counselling for predictive/carrier genetic testing, the estimation of recurrence risk, and the explanation of genetic testing results could be done by the genetic counsellor or the clinical geneticist, as shown in

A2/B2. Increasingly, a proportion of counselling work is counsellor-led.



Referral system in the UK

Within the National Health Service in the UK, patients do not visit genetic counselling clinics directly, but must be referred by medical professionals in a certain hospital or local healthcare provider. The referral document for a patient is sent to the local Regional Genetics Service when the doctor/family doctor considers the patient needs to attend genetic counselling. The referral procedure takes 6 to 8 weeks, but less than 2 weeks for urgent cases, such as pregnant women with a family history of a genetic disorder and fetal anomalies. During the waiting time, the counsellor will read the referral document and may contact the patient or referring physician to gain a better understanding of the condition and the issues for the patient.

The current practice of genetic counselling in China

In China, there are no professional genetic counsellors and, in practice, genetic counselling services are offered by clinicians. The government has been trying to regulate the clinical application of genetic counselling. The Chinese Ministry of Health (MOH) promulgated *Guidelines for Genetic Counselling* in 2003. The guidelines are official government rules that regulate the application of genetic counselling, particularly when related to prenatal diagnosis. According to the Guidelines, genetic counselling should be offered by clinicians who have a background in genetics, have a certificate of qualification in maternal and infant healthcare, and have a concerned interest prenatal diagnosis. The guidelines also state the common procedures and requirements for genetic counselling. For example, it states that in the genetic counselling session, the clinician working as the genetic counsellor should: collect information and draw a family pedigree, provide information on prenatal genetic diagnosis, diagnose genetic disorders and confirm the mode of inheritance, estimate recurrence risk and offer advice to patients. Currently, only hospitals or healthcare providers with authorization from the Provincial Health Department to practise prenatal genetic diagnosis can develop a genetic counselling service. At present, only well-known hospitals get such permission. For example, in Beijing, only five hospitals have permission to offer prenatal genetic diagnosis: Xiehe

Hospital, Beida Hospital, Beiyi No.1 Hospital, Beiyi No.3 Hospital and Beijing Maternity Hospital (Liu 2007). Usually, these hospitals have the genetic counselling clinic in the paediatric department and/or in the gynaecology department, which have regular sessions one or two times a week.

There is no national medical health coverage system *(guojia gongfei yiliao tixi*) in China that covers genetic counselling. Patients pay the costs for medical care.[2] There is no organized referral system among the hospitals, and every hospital charges its own medical care fee. The hospitals establish a new patient record during the first visit to the clinic, and only take responsibility for what they do for patients in their own hospital. The patient can choose to visit clinics in the city and hospital of their choosing, depending on their own preferences and their financial means, including the possibility of incidental expenses such as the costs of transportation and accommodation. However, in practice, the choices here are very limited because of the limited availability of genetic counselling clinics across the whole of the country.

Qualifications for providers of genetic counselling

The education of counselling providers plays an important role in genetic counselling. The understanding of the significance of genetic counselling, the required standards of genetic counselling, the professional skills and codes needed, can only be well appreciated after relevant education and training. Suitable qualifications, education and training are prerequisites for practicing genetic counselling.

In the UK, currently, clinical genetic counsellors have either a background in nursing with appropriate training, or have completed a master's degree in genetic counselling. Two master's programmes in genetic counselling were developed in Manchester in 1992 and in Cardiff in 2000, which are designed to educate students in clinical genetic counselling. Applicants for the MSc in Genetic Counselling program at The Institute of Medical Genetics of Cardiff University, for example, are requested to be either professionals already working in the field of genetic counselling or related areas, or graduates from an approved university with at least a second-class honours degree in nursing, genetics, biology, psychology, social sciences or education. The students in such programmes are educated to be clinical genetic counsellors. In the UK, there are two routes to enter into the genetic counselling profession: a minimum of six years of usual training and work experience prior to entry to the profession, for the professional route, or five years for the MSc in genetic counselling route. Registration to be a professional genetic counsellor can only be undertaken after a training period of two years following entry into the profession by either of the routes. The requirement is the submission of a master's-level portfolio of evidence of professional competencies. By registration, therefore, all prospective genetic counsellors will have completed seven to eight years of training, with many having considerably more training. Also, the AGNC attempts to clarify and guide the conduct of genetic counsellors practising as Registered Genetic Counsellors. All genetic counsellors must be aware of the ethical implications of their professional role, and adhere to the principles and guidelines in the code developed by the AGNC (AGNC 2008).

[2] Government officials and employees in state-owned units can get a proportion of their medical care expenditure reimbursed from the units they work for. The healthcare insurance system is underdeveloped and inherited diseases are excluded from insurance. In fact, the majority of the population pay medical costs themselves.

In China, *the Guidelines for Genetic Counselling* regulate the requirements for counsellors. Firstly, a counsellor must be a clinician with a licence. In addition, they must also have either: (1) a bachelor's degree of medical education, at least five years of clinical experience working in an obstetrics department as an obstetrician or other interrelated clinical departments, and have specific training in clinical genetics; or (2) at least ten years of work experience in prenatal diagnosis with special knowledge of clinical genetics and technology skills. They are also required to be well educated in genetics, have ample genetics knowledge and the ability to accurately diagnose conditions, accurately analyze test results, and appropriately estimate the inherited risk and recurrence risk of genetic disorders. At present, there is no official degree programme in genetic counselling. In practice, genetic counselling providers are clinicians trained as paediatricians or obstetricians. Training programmes for prenatal diagnosis are sometimes available, for example at the national prenatal diagnosis training programme hosted six times by Hunan Xiangya Hospital prenatal diagnosis centre. Usually these training sessions have a lecture on genetic counselling given by a senior geneticist (Xiangya Hospital 2008).

Non-directiveness and decision-making in practical genetic counselling

In the UK, non-directiveness is treated seriously in counselling concerned with reproductive decision-making. In my fieldwork, all the genetic counsellors I interviewed in the UK strongly insisted that genetic counselling should be non-directive, and they considered their genetic counselling clinical practice to be non-directive. Such opinions are shown in their own words:

> During the counselling session, we tell the clients their genetic condition. As for the decision-making, especially for the reproductive decision-making, we do not tell the patient what they should do. We offer options to patients but no suggestions. We help and support any decision the patient makes without our judgement. Certainly, I have my own opinion. But, I try to avoid my opinion influencing my patient's decision-making. We do not lead or hint to our patients to make their decision. Actually, I think it is patients who 'lead' us. During our counselling, from what the patients told us, we can feel their worries then help their relief. Sometimes we can feel they have already made their decision but they are hesitant because they need support psychologically, then we support them.
>
> I think we are always trying to help our patients reach the 'good' decision from their personal view. We let the patients understand there is no right or wrong, only a suitable decision. The important thing is they understand well their choice and what will happen if they take this choice. We do not guide them to any decision, as to test or not to test, to terminate a pregnancy or to keep it. We never say 'maybe it is better to do …'
>
> If a patient asks me what I would do if I were him/her, I will tell him/her everyone is different. We are different and something I think is good for me may not be good for you. I do not regard non-directive counselling as irresponsible. I will do my best to help a patient to make their personal decision, but not lead or direct.

In China, offering advice is one of the duties of a clinician working as a genetic counsellor. According to the *Guidelines for Genetic Counselling,* clinicians working as genetic counsellors should offer advice on marriage, reproduction, or some general consultation. It regulates that clinicians should try their best to avoid expressing their own opinion during counselling. A medical expert I interviewed pointed out that currently few clinicians pay more attention to psychological aspects when they offer genetic counselling. In fact, for most patients, the feasible options are limited because of their economic situation, the healthcare system and family-planning policy. One genetic counsellor's words demonstrate this:

> In most conditions, I need not say more and the patients know clearly what they can choose. They resort to the genetic counselling clinic with the clear wish to have a healthy, unaffected baby. I think I need not or cannot say keeping an affected fetus is an option. The patients already thought this is not an option for them. Imagine, when I say she also had the option to keep the affected fetus, that the patients asked me where they can get money to treat their baby. I would be dumbfounded [*sha yan*] and could not say anything. [Trans: SSui]

One clinical geneticist also expressed a personal opinion on non-directiveness:

> I think nowadays we are trying to be non-directive in counselling. We require the patients to sign an informed consent form before they take a genetic test, which we already have installed as a necessary procedure. We cannot promise that the test results are always 100 per cent accurate. We need to make sure that the patients voluntarily take the test and voluntarily take the risk. This is also a way to avoid potential dissension. We do not write 'clinician suggestion' on the test report and we do not advise patients to terminate or continue with a pregnancy. We explain the test result to patients. Usually the patients have already thought over their choices, which depend on the test result. In fact, when the patients understand the test result, they know what they will do. [Trans: SSui]

One genetic counsellor shared her experience and her opinion about non-directiveness and informed decision:

> Usually, if the pregnant woman already knows the fetus is affected, they will terminate the pregnancy. For this, they hardly need any advice. They regard the test as a way to avoid having an affected baby and understand well it is so hard to have an affected child. Actually, I have only come across one case that a pregnant mother still kept her pregnancy when she knew the test result was 'bad', which was years ago. She already had one affected child and I explained to her that her fetus would have the same condition as the affected one. She did not believe it, because she resorted to the fortune teller, and the fortune teller

> told her this fetus was perfect and would bring amazing good luck to her family. I think I had told her what I should have. After the fetus was born with a disorder, she came to the clinic again for diagnosis with great regret. But it was too late for regret [*houhui moji*]. Judging on the basis of this case, I think sometimes we still need to 'direct' the patient. [Trans: SSui]

Discussion about non-directiveness and non-judgement

The counsellors I interviewed insist that genetically at-risk individuals must govern themselves and their lives, and the counsellors regard what they are doing in practice as non-directive, but non-directive counselling is difficult to attain. For non-directiveness, it is essential that the counsellor/clinician be non-judgmental. In practice, the counsellor's motives, conscious or unaware, are relevant during counselling, and it is the counsellors who decide what kind of information should be given to the patients, which involves a value judgement. In fact, it is not easy for counsellors to avoid their personal value judgements. It has been suggested that 'non-directive' counselling is an abdication of professional responsibility and that it is impossible to maintain a sincerely non-directive approach to counselling about a genetic disorder while simultaneously aiming to prevent that disorder (Clarke 1991).

The counsellors I interviewed consider that there is still scope for improvement for the ideal of non-directiveness, even though some of them regard their current mode of counselling as very good or perfect. However, most of them do not agree that non-directiveness is irresponsible. At the same time, they do not deny that sometimes, to a certain extent, directive counselling is supportive and understanding for the patient. In China, one of the main aims of current genetic counselling is prevention of genetic disorders, and the guidelines/regulations require clinicians to offer advice to patients. Also, from the aforementioned Chinese interviewee's words, current genetic counselling in China can be said to differ from non-directive counselling, although the clinical geneticists consider it to be non-directive. Nowadays, with the development of medical ethics in China, the recognized principle of non-directiveness is becoming well known. It is understandable that counsellors wish their work to be in accordance with ethical principles. Also, in practice, claims that counselling is non-directive, and that no directive advice is offered to aid patients' decision-making, perhaps helps the counsellors avoid potential dispute or litigation.

Frankly, in practice, ideal non-directiveness and non-judgement in genetic counselling is hard to achieve. This is a general observation, which applies more or less to all societies, owing to the intrinsic character of medical practice. Although non-directiveness connects with free autonomy of decision-making, in fact, more understanding and psychological support for patients are needed. Sometimes, under certain conditions, even for a very personal decision such as reproductive decision-making, directive and feasible advice from experienced clinicians/counsellors is also very helpful.

In fact, the practice of genetic counselling should be seen within the social contexts of different countries, including knowledge of the prevailing economic conditions, distribution of health resources, the medical care system, professional governance, population policy, and cultures. It is evident that much more research and experience

from co-operations is needed in order to generate the data and develop models for a system of genetic counselling involving different cultures.

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Engaging the Interactions between Scientist and the Public: Understanding the New Partnerships in Today's Biological and Biomedical Research

Su Yeyang

Abstract
This research focuses on understanding and analyzing contemporary scientist-public engagement, which is initiated and led by life scientists. Interviews are employed to get in-depth perspectives from different stakeholders during public engagement activities. The research finds that, first of all, although scientist-led-reach-out strategies have their shortcomings, such as potential conflicts of interests, and limited participation, as a first step towards bridging scientific knowledge gaps, such initiatives should be encouraged. Secondly, science communication is a process, and proper training and education should be provided to scientists and students, who are interested in interacting with the public. In addition, the call for investing more into basic science is commonly heard throughout this research. Research on how to assess recently proposed public-private partnerships in biomedical research, and how to understand the evolutionary role of research participants is required.

Introduction

Recent breakthroughs in human genetics, namely in personal genomics, have unveiled a new medical era. In this new era, large-scale biomedical research requires not only collaboration between scientists, but also contributions from the general public. The scientific community increasingly realizes the importance of science communication. On the one hand, public engagement / consultation has been widely used during policy development in developed countries; and the Chinese government has started calling for public input into revising proposed policies and regulations. On the other hand, unlike other topics, science, especially basic science, does not have tight connections with the public. How to reach the public, and effectively conduct public consultation is a challenging task for leaders in the scientific community.

I started my BIONET research in March, 2009, with the desire to understand how different stakeholders perceive public engagement in biomedical research, and to identify different needs and expectations that different groups have towards such consultation. This research is ongoing.

Methods

Interviews are employed throughout this research. In March, and July, 2009, I visited and interviewed scientists, science communicators, researchers in science communication and intellectual property, members of ethics councils, and representatives from patient groups. The UK Biobank and PRRI (Public Research & Regulation Initiative) were chosen as two cases.

Considering the socio-economic impacts of the life sciences and their ongoing public engagement activities, I first interviewed scientists in the field of genetics / genomics, including Dr. John E. Sulston from the UK, Dr. Marc Van Montagu from Belgium, Dr. Kurt Zatloukal from Austria, and Dr. Yang Huangming and Dr. Chu Jiayou from

China. Then I visited the UK Biobank Head of Communications, Mr. Andrew Trehearne, and the Secretary of the UK Biobank Ethics and Governance Council, Ms. Adrienne Hunt. Thirdly, I talked with people from patient groups (Ms. Christiane Lohkamp, Deutsche Huntington Hilfe, Germany), industry (Dr. Detlef Niese, Novatis, Switzerland), and researchers who untangle challenges in good clinical practice (Dr. Francis P. Crawley, Good Clinical Practice Alliance – Europe, Belgium), science communication (Dr. Patricia Osseweijer, the Delft University of Technology, Holland) and patent laws (Dr. Li Xuan, the South Centre, Switzerland).

In addition, participating in the first BBMRI (Biobanking and Bimolecular Resources Research Infrastructure) Stakeholder's meeting this September provided me with deep insight into the interactions between scientists and representatives from industry and patient groups.

Preliminary findings

Scientists: the need to reach out

Most life scientists have relazied that their work are undergoing a crisis of losing public trust. During the past decades, cloning, genetic modified technology and stem cell research have raised continuous bioethics debates, and various international and national regulations been developed to ban or restrict such studies (UN, 2005). When the malpractice of South Korean stem cell researcher Hwang Woo Suk was uncovered and explored in 2005, integrity in scientific research became an issue of global concern (Gottweis, 2006).

In previous debates, scientists once played a rather passive role, but when international / national regulations were announced, scientists could no longer take a backseat in the wider debate on science and technology. During the campaign to win support from the public for the International Human Genome Project (HGP), the leaders of HGP actively reached out to the public, to explain 'what, why, how, and by whom' questions to citizens in the US and the UK, the two major investors in this international project. Their candor won genuine understanding and sustainable support from the public, and ensured the success of HGP, and later, the International HapMap Project.

When I interviewed Dr. John E. Sulston, a leader in the HGP, he gave me some background. In the 1990s, when the international genomic community focused on their laboratory work, Dr. John Craig Venter announced the launch of a private human genome project. Dr. Venter claimed that the public joint research took too much time and cost too much money, and he had a better idea to do the same job. Meanwhile he co-founded a biocompany named Celera Genomics. What is more startling is that Celera Genomics was going to charge future researchers for downloading / analyzing the sequence of the human genome decoded by its research team. This broke the consensus within the genomic community that sequences longer than 1,000 base pairs should be released on the public domain within 24 hours (HUGO, 1996). The leaders of the International Human Genome Project sensed that if they could not make it clear to the public why tax payers should pay huge amount of money for this 'public' research, and why the public needed to back the public research instead of the private one, the benefit of launching this majestic project would never be fulfilled for humanity. This crisis sparked genuine communication between scientists and the

public, which in turn guaranteed the success of the HGP, and the solid establishment of the 'Done by all, Shared by all, and Owned by all' HGP spirit.

However, this was a rare victory in the life sciences. Research on genetically modified organisms, for example, met furious resistance from environmental groups from the very beginning, though leaders in that field aimed at developing this technology for relieving hunger. Concepts like 'gene-flow' and 'mess with nature' are widely used by enviromental groups for warning the public. What is worse, politicians joined the game, teaming up 'against-GM (genetically modified)' in their campaign strategies; developing policies and regulations to restrict basic research in this field. Dr. Marc Van Montagu, the discoverer of 'the gene transfer mechanism between Agrobacterium and plants', conveyed his concerns on, what he perceived to be, an irrational battle: "The basic research needs support, anyway. What the public have been talked to [about] is not science, but misleading information. The danger of 'polluting nature' is emotionally horrifying, but is not true. The first step of science communication is to let people know about real science, about what we are doing, and why we, as scientists, find our work meaningful and important." When I asked him about the trigger-effect emotion can play in the debate, Dr. Van Montagu told me that it was sadly true that people are reluctant to listen to what scientists say about GMOs, after receiving too much biased information from certain groups. But he believed that even if people would not accept scientific truth immediately, they will later acknowledge that most reasons they use to take a stand against GMs are emotional, not rational. And that makes people start thinking on their own.

The need for science to go beyond the laboratory leads to inspiring initiatives. In 2004, the Public Research & Regulation Initiative (PRRI) was established, to encourage and actively involve public researchers in international meetings which discuss and draft biotechnology regulation (http://www.pubresreg.org/). Another example is: at its preliminary feasibility phase, the UK Biobank began conducting public consultation in 2000, and later an independent UK Biobank Ethics and Governance Council took an active role in gaging public opinions and then appropriately advising this national project (UK Biobank, 2009). Similarly, on Stepember 16th, 2009, the pan-EU Biobanking and Bimolecular Resources Research Infrastructure (BBMRI) program held its first Stakeholder's meeting in Brussels, Belgium, to broadly introduce the project to, and seek feedback from various stakeholders, including patients / patient groups, industry, funding agencies, and the general public (IPPOSI, 2009).

Nevertheless, hype-science also catches scientists' attention. Some bio-companies have over-advertised or even misused genomic knowledge, and this has generated heated debates in this field (Hogarth, 2008). Dr. Yang Huanming, for example, has declared his concerns on rapid application of immature genomic knowledge.

Therefore, how to transfer accurate scientific knowledge to the public is the main challenge, and most scientists have acknowledged the importance of transparency in their work, including sharing their motives, passion, and social and ethical concerns.

Ethical council: 'a foundation for trust'

To ensure high ethical standards in the operation of the UK Biobank, the main funders of the UK Biobank established an independent Ethics and Governance Council

(EGC), to monitor and advise this large-scale, long-term, scientific project. As Ms. Adrienne Hunt emphasized, this special independent council was launched to 'monitor and report publicly on the conformity of UK Biobank's activities with the Ethics and Governance Framework under which the project operates'. In the annual report Ms. Hunt gave me, which can be accessed from EGC's website, EGC indicates that "at the heart of that Framework is the protection of participants and the public". (EGC, 2008)

Although the council is neither the UK Biobank's ethics committee, nor an entity that has any 'formal power' with respect to the UK Biobank, it plays a monitoring role over the UK Biobank. The annual report concludes that the EGC continuously checks on the UK Biobank's operation, makes recommendations on particular procedures, and responds to questions and concerns from the public. (EGC, 2008)

Besides using members' expertise, the EGC also directly seeks advice from the public. Since its establishment in 2004, the EGC has held five public meetings, including meetings in London, Manchester, Oxford, Edinburgh, and Cardiff. Ms. Hunt told me that during this process, the Council improved their communication skills. For example, they added a 'round table discussion' session after EGC presentations, and a general Questions & Answers session, to motivate participants to voice their concerns and questions. After formal meetings, participants are invited to a reception to continue their discussions and to provide a networking opportunity. The feedback from these public meetings are then adapted to the EGC's recommendations to the UK Biobank. All meeting reports are put on the EGC's website. Their open and transparent work lives up to their slogan – 'building a foundation for trust'. The EGC offers a place where people can meet, and thereby strengthens relationships and build trust between the UK Biobank's participants and the public in general.

The success of the EGC provides a new model for ethical governance in biological and biomedical research. Recently, at its first public meeting, the leaders of the pan-EU Biobank initiative, Biobanking and Biomolecular Resources Research Infrastructure (BBMRI), proposed to develop a similar council to provide advice, and monitor its future operations.

Science communication: skills and training

The UK Biobank has also developed its own public communication strategy. During my meeting with the UK Biobank Head of Communications, Mr. Andrew Trehearne, I was introduced to various methods the project employs to enhance communication with, and promote participation from UK citizens. After using mass media to advertise at both national and local level, UK Biobank's invitation letters are sent to individuals' homes. Inside the letter a detailed introduction about this project and a general Questions & Answers document are contained. Individuals are welcomed to directly contact the UK Biobank via a toll-free number, regular mail (stamps are provided), and email. They can also visit local assessment centres and communicate face-to-face with researchers there. The communication department not only answers people's questions, but also adopts the public's concerns and suggestions into their work. Mr. Trehearne gave me an example: once they received an upset phone call from a lady who had just been diagnosed with cancer, she was emotionally hurt by receiving an invitation letter from the UK Biobank, which is designed to promote the health of UK citizens. Soon after, the UK Biobank added one sentence into their

invitation letters: “unfortunately, (these invitation letters) may arrive at difficult times in people’s lives: if this is the case for you, please accept our sincere apologies.” (UK Biobank, 2008) Again, it is through the process of interacting with the public, that the UK Biobank’s science communication improves, and in turn, maintains trust between the UK Biobank and their participants.

Before joining the UK Biobank, Mr. Trehearne was a senior journalist, and now helps UK Biobank translate science into easily understandable language. The role of mass media in communicating with the public is increasingly appreciated by the scientific community. Although incomprehensive or even biased reports once devastated basic research like therapeutic stem cell research, some scientists still have confidence in mass media. This April, at the BIONET Shenzhen Workshop, Dr. Yang Huanming compared the relationship between science and mass media with that of water and a ship, which he illustrated with Chinese idioms: “PM (press media), like water, can carry a boat, or sink a boat”, or “A boat can’t become a real boat without water.” He then proclaimed that: “The only way to let PM become mature is to ‘use’ them, and make friends with them… We (scientists) have to pay the cost! It will be more expensive if we don’t!” (Yang, 2009). In my visit with Dr. John E. Sulston in Manchester, the UK, he also expressed his positive opinions on working with mass media, though “it is understandable that some scientists doubt about ‘could we trust them (mass media) to correctly quote what we say, or understand what the knowledge is’, and ‘can the journalists be neutral?’”.

Therefore, how to help mass media understand science progress and acknowledge bioethics discussions is a new task for scientists and bioethicists. That is highly appreciated by partners in the China-EU BIONET (Ethical Governance of Biological and Biomedical Research: Chinese-European Co-operation) project: from the beginning, BIONET values the role mass media playing in introducing research progress to the public in both China and European countries. For example, the BIONET partners hold a satellite meeting: the “Reporting Bioethics” workshop, with journalists on March 31st, 2008, during the BIONET Changsha Conference. With this platform, for the first time, Chinese journalists had an opportunity to get in-depth information about bioethics discussions. This workshop was highly appreciated by the attendees, who expressed strong requests for researchers holding similar workshops and training programs (BIONET, 2008). In countries like China, where biomedical research advances quickly and raises new ethical, legal, social and cultural issues, while at the same time whose public just start showing interests in participating in such discussions, the function of mess media should be properly considered.

The good news is that communication skills are something that everyone, not only science journalists, can learn and should continuously improve. Even though until now, most ‘public figures’ in the scientific community are those seniors (who have won their reputation within their community), like Drs. John E. Sulston, Marc Van Montagu, and Yang Huanming, junior scientists, and science / medical students are becoming interested in science communication, as Dr. Patricia Osseweijer pointed out. For example, the executive manager of BBMRI Stakeholder’s Forum, Dr. Derick Mitchell, has extended his career from molecular medicine to science communication. During a discussion with Dr. Osseweijer about ‘emotion talk’ during science communication, she illustrated that emotion does play a role in the public’s perception of science and technology. She argued that, instead of being frustrated, scientists and

people involved in science communication should recognise this and try harder to motivate the public to think about science and technology, and address those ethical, legal and social challenges together with professionals. In addition, scientists, health professionals, and current science / medicine students can benefit from professional training in communicating with the public.

Concerns on privacy and benefit-sharing

Among the feedback the UK Biobank has received, the greatest concerns relate to 'privacy'. Even though the UK Biobank only sends out invitation letters after weeks of local promotion in local media and on public transportation, people who received invitation letters raised questions like "how could you get my contact information". Some of them even felt offended. Notwithstanding, once their concerns are genuinely addressed, people become interested in the project and want to learn more.

When discussing the issue of 'benefit sharing', Mr. Trehearne told me that most participants joining UK Biobank want to improve the health of the next generation, and they fully understand that they themselves might not receive any direct benefits. A small piece of evidence is that most participants who travelled to the assessment centres to participate in the project, and spared ninety minutes for their participation, did not claim travel expenses, even though they had been told so. "That is a kind of altruism", Mr. Trehearne concluded.

However, researchers have other concerns. During my visit with Dr. Li Xuan at the South Centre, she conveyed her concerns of some stakeholders of developing countries about uneven benefit sharing under the current intellectual property system. Dr. Li is a senior researcher and the Coordinator of the Innovation and Access to Knowledge Programme, at the South Centre, an intergovernmental organization for developing countries based in Geneva, Switzerland. Dr. Li remarked, " It could be a source of contention if a business group gets access to traditional knowledge and associated science findings for free, while the indigenous groups, and in many cases the scientists who are involved in preserving or generating the knowledge, are kept from the commercial or non-commercial benefits."At the international norm-setting level, all these kind of factors should be taken into consideration for a balanced multilateral regulatory regime so as to create a fair and equitable environment for sustainable development.

Discussion

The limitation of scientist-public engagement

In this preliminary study, I focused on scientist-lead public engagement. Some may argue it is more like 'public education', rather than 'public engagement'. To some extent, this kind of public consultation does not directly change the scientific goal or design of research. However, the reaching-out strategy used by chief investigators in large-scale / pioneering / controversial research is a starting point to actively facilitate direct dialogues between the scientific community and laymen. In the past, the public only heard certain groups, like journalists, industry, and politicians, talking about science and science regulation, but did not hear from the scientists. A new communication 'high-way' can bridge the knowledge gap between scientists and the public. The experience of the HGP has evidenced that transmitting true knowledge into the public domain is the first and necessary step for involving public in further

ethical, legal, social and cultural discussions concerning scientific developments. Therefore, transparency and respect for people are two principles scientists / researchers must appreciate during public engagement.

This strategy, however, does have limitations. First of all, since it is initiated by scientists, the practical goal is to let the scientists' voices be heard by the public. It remains a challenge how to eliminate conflicts of interests and to motivate people to think about science and related issues on their own. The UK Biobank's EGC public meetings may have set a good example by letting an independent committee organize public consultations, in which both the scientists and the public can speak for themselves.

Another challenge of scientist-public engagement is that the participants / audience are limited, for only certain groups of people are interested in interacting with scientists and researchers. Neither those who attended the UK Biobank EGC's public meetings, nor those who participated in the BBMRI Stakeholder's meeting, can fully represent the whole public. In the first case, most participants are students or researchers who are eager to know more about the UK Biobank, and in the second case, attendees are representatives from patient groups, funding agencies, and industry. Even patient groups have particular interests in biomedical research; therefore they cannot speak for the public in general.

The obstacles of misconception, presumption and emotion

Alongside my research, the misconceptions or presumptions the public hold towards science and related issues caught my attention.

On the one hand, "controversial" research, like stem cell research and genetically modified technology, undergo a lot of misinterpretation and misunderstanding during bioethics debates. Dr. Yang Huangming vividly illustrated this point at the BIONET Shenzhen workshop this April. He first gave participants an example about the misuse of terminology in life science. On March 8th, 2005, the UN General Assembly adopted the United Nations Declaration on Human Cloning, which prohibited both reproductive and therapeutic cloning (UN, 2005). At that meeting, the representative from China argued that scientifically speaking, therapeutic cloning has nothing to do with 'human cloning', and should not be treated the same as reproductive cloning. However, this point was ignored, which had a negative impact on stem cell research, and fuelled years of bioethics debates all around the world. Early this year, the US finally removed the ban on stem cell federal funding and started promoting embryonic stem cell research (Obama, 2009). Considering the ups and downs of stem cell research during the past years, Dr. Yang questioned: "A innocent victims (stem cell research) is delayed by many years. But, by what, and by whom?" GM research was similarly delayed. After being accused of 'polluting nature' for many years, GM scientists and researchers started explaining their work to policy makers and the public as a whole, and they renamed 'GM-Food' as 'Bio-Food', to lower emotional resistance. Ironically, the most-astonishing-till-now biotechnology, 'man-made life', escaped media and public attention by picking up a neutral name: "synthetic biology". (Yang, 2009)

On the other hand, the pharmaceutical industry is accused of pursing profits by sacrificing public interests. I met Dr. Detlef Niese, the head of Global Affairs at

Novartis, at the BIONET's Xi'an Conference. During the debates at that meeting, I sensed a strong mistrust against science, and wondered how much stronger it would be towards pharmaceutical companies. After a short discussion in Xi'an, I visited Dr. Niese at Novartis' Campus this June. Before joining the Sandoz AG (later Novartis AG), Dr. Niese was a clinical researcher, and he is still a professor of medicine at the University of Bonn, Germany, and teaching at the University of Basel, Switzerland. We first discussed the non-trust of industry. Dr. Niese pointed out that, compared with gaining profit, a stronger motive behind investing biomedical research and clinical trails of pharmaceutical companies is to produce medicine, which are needed by patients and advance medicine. (Big) Pharmaceutical companies clearly work in a responsible way and do not sacrifice public interest for their profits, for misconducts will certainly ruin their reputations and public relations, which in turn reduce the market sharing. "People may do stupid things but it is our responsibility to prevent that from happening. Together with health-care professions and bioethicists, our department designs / modifies right policies for Novartis in issues related to ethical, legal and social issues", Dr. Niese elucidated. Of course, such a strong ethical position on behalf of one pharmaceutical company does not alleviate people's concerns about the sponsors of clinical trials. At the same time, as Dr. Francis P. Crawley, Executive Director of the Good Clinical Practice Alliance – Europe, stated: " Not only implementing, but also developing, best practices for clinical research requires that we engage all parties involved. Pharmaceutical companies have wide experience and in-depth knowledge regarding what works and what does not work in clinical trials. We exclude pharmaceutical companies from the discussion, not only risking less improvement in good clinical practice and ethics standards, but also at a potentially high cost to health science and patients."

It is true that bad things happened in scientific research, and that is why international / national laws, regulations, guidelines, and best practice are drafted and implemented, to prevent bad things from happening again. However, scandals are not sufficient evidence to halt scientific development; neither are one-sided stories spread by certain groups, which hold strong opinions against scientific research. In consideration of that, before rushing into a quick judgment, why not listen to the scientists, who are working to build a better life for humanity; some of whom are misjudged as crazy? The same is true for pharmaceutical companies. Sometimes, we need a little faith in the conscience of others.

However, trust cannot be built, unless scientists, health-care professionals, and industry work transparently, and under careful scrutiny of the public. When emotion talks, more efforts are needed to let reason work.

The evolutionary role of science and the public

The concept and principle of protection of human rights in biomedical research were established after the Second World War. During the dark period, human beings were cruelly treated as experimental subjects by Nazi doctors. This lesson is too heavy for any human being to burden. With joint effort, human dignity and human rights have come to be increasingly respected and generally guaranteed in biomedical research, by laws, regulations, guidelines, and ethical review procedures.

Noticeably, during the past decades, contemporary society has seen impressive growth of patient groups. Unlike health-care professionals, patient groups are "experts

in caring (not for medication)", according to Ms. Christiane Lohkamp, a wife and mother of three Huntington patients, and former chairperson of Deutsche Huntington Hilfe, Germany. In addition, more and more non-profit-foundations are founded to support patients and patient groups, and directly invest in biomedical research. Recently, patient groups became an increasingly loud voice in biomedical public consultation, and even in policy lobbies. The impact of patients / patient groups in biomedical research needs more careful analysis.

Furthermore, in 2008, a heated debate on direct-to-consumer genetic testing was raised in the US. In this case, Internet users became consumers and supporters of novel biotechnology. Even though scientists all around the world have warned the public that this application of genomic knowledge is not mature enough to give customers any precise information about their health or help them design their lifestyles, bio-companies like 23andMe advertises that "so when you send in that spit sample, you're not only learning about yourself, you're joining a community of motivated individuals who can collectively impact research and basic human understanding." (23andMe, 2009) This time, the bubbles are produced by certain bio-companies and customers. While the scientific community worries about the real future for personal genomics.

With rapid progress in human genetics / genomics, life science is no longer only an intellectual activity, which asks for individual dedication, nor a purely social activity, which requires collaboration among scientists and researchers at local, national and international levels; it is now opening an unpredictable market related to health and understanding of humans. As the line between basic research and science application blurs, the question of how to define the role of and protect the rights of participants, in situations like direct-to-consumer genetic testing, becomes increasingly important for today's biomedical scientists and bioethicists.

Conflicts of interests vs. private-public collaboration

The 'natural' suspicion of industry leads the public to distinguish between scientists working in industry from those working in academia (Bubela, 2009). But is it really true that public scientists have no personal interests? Obviously the answer is no. Most scientists work with a passion for science. But today's pressure for publication and funding is enormous. Dr. Herbert Gottweis has analyzed the Hwang Woo-Suk's case from a governance perspective, and illustrated that it is the 'poor national mechanisms for accountability, competition, transparency and ethical oversight' that 'allowed Hwang Woo-Suk's descent into ethical, and ultimately scientific, misconduct.' (Gottweis, 2006) In that case, the pressures of nationalism and national pride played a part in increasing pressures on scientific work. The simple truth is, it is impossible to rule out all personal interests in today's scientific work. While the bottom line is, those personal interests must be in line with the public's interests.

After all, basic science is a human activity that deserves support, emotionally, politically, and financially. The demand for investing in basic science is heard over and over again during my research, not only from scientists, but also from patient groups. Considering the need for sustainable funding in basic science, industry has been called to co-invest in public research. Initiatives, like establishing international public-private partnership to generate 'chemical probes' for biomedical research(Wellcome Trust, 2008), have been launched during the past years. Another

example is BBMRI's newly proposed 'expert centre' model. BBMRI will avoid directly delivering samples or raw data to industry, but will provide expertise in analyzing samples and data for industry. In this model, those expert centres will protect the confidentiality for pharmaceutical companies; hence in return, industry will invest in BBMRI's basic research. Neither the expert centres nor BBMRI will make profit from working with industry, but the service fees will contribute to sustaining BBMRI's management and development. (Zatloukal, 2009)

Undoubtedly, issues of intellectual property and benefit sharing now enter into the discussion on these 'public-private partnerships'. Co-investing, putting fundamental knowledge into the public domain, and co-patenting discoveries, are proposed as one solution. Therefore, the HGP spirit: "Done by all, Shared by all, and Owned by all" should be highlighted in this new era.

Conclusion

Once upon a time, science set out in pursuit of understanding ourselves and the world around us, and technologies were developed to improve the quality of human lives. However, in industrialized societies, science is not only driven by personal intellectual interest, and public trust in science and technology is becoming fragile, leading to increasingly anti-science activities. It is under such circumstances that life-scientists actively reach out to the public, and invite the public into science communication and research consultation.

For various reasons, the public holds several misperceptions or hyper-expectations towards science and its applications. The practical goal of scientist-public engagement is to let science's voice be heard, or in another words, to transmit scientific knowledge to the public. It is also intended to better protect the public from misunderstanding and misjudging science, its progress and future. Although the public's interest in knowing scientific research (not technology) is low but increasing, and although such initiatives have limitations, they are the first step towards bridging communication gaps between the scientific community and outsiders, and therefore are laudable.

Science communication is a process, during which scientists and participants get to know each other, and enhance their relationships. Science communication is also something that can be learned and should be polished. Proper training and education should be provided to those scientists, science / medical professionals, and students who are interested in interacting with the public.

Rapid advancements towards personalized genomics and the new biomedical era, on the one hand, may transform bioscience's potential into bioeconomy, but on the other hand, turn the public into consumers, who can be misled by advertisements and become victims of immature scientific applications. Studies are needed in this field to analyze the dynamic relationships between bioeconomy and the public (consumers).

Last but not least, the new partnership between public and private research is established at the beginning of this biomedical era. Research on the assessment of such partnership and on issues like intellectual property rights and benefit sharing is required.

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PART 3: KEY RESOURCES

Contents

1. Chinese Institutions: Who is Who?

Further details and background information on the following government bodies in China.

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2. Chinese Academy of Sciences (CAS)
3. The National Natural Science Foundation of China (NSFC)
4. Ministry of Health (MOH) and MOH ethics committee
5. Chinese Academy of Medical Sciences (CAMS) / Peking Union Medical College (PUMC).
6. State Food and Drug Administration (SFDA) / (NICPBP)
7. China Centre for Disease Control and Prevention (CDC)
. National Institute for the Control of Pharmaceutical and Biological Products (NICPBP)

1. Ministry of Science and Technology (MOST) / China National Centre for Biotechnology Development (CNCBD)

The Ministry of Science and Technology (MOST) makes, manages and administers national policy for all aspects of science and technology, with a strong emphasis on commercialisation and the industrial application of new technologies. It was created in 1998, reflecting the importance placed on science and technology by the administration of the then Premier, Zhu Rongji. MOST is primarily concerned with the development of high technology and economic returns: its major concerns in the area of research governance are the targeting of funds and scientific integrity.

MOST controls a number of important science programmes, including the 973 programme, which is the major source of funding for basic science in China. Although focused on basic research, the programme still emphasizes applications and "strategic research". Another funding programme is the 863 programme, which funds research in high technology. The 863 programme is the source of funding for many of China's stem cell projects.[1] Bioscience and biotechnology funding under the 863 programme are managed by the *China National Centre for Biotechnology Development* (CNCBD) - an affiliated agency of MOST. CNCBD comprises eleven divisions including four dealing with medical biotechnology: Biomedical, Chemical, Public health and Traditional Chinese Medicine (TCM)**.** Other departments that also deal with related matters include: International cooperation, Industry and Biomedical resources.

The Project Administration infrastructure at MOST includes Offices for Internationalisation of TCM, a National Office for new drug development

1 Du, Jiansheng et al (2004). "Stem cell mission to China, Singapore and South Korea" *Report of a DTI Global Watch Mission*, September 2004.

(these areas are both national priority projects) and an Office for Commercialisation of Biotechnology. It also deals with Bioresources and Safety and the latter includes ethics.

On the website for CNCBD[2] its mission is summarized as:

- To develop biotechnology, cultivate new bio-industry, promote bio-economy;
- To study biotechnology and bio-industry strategies, policies and measures home and broad.
- To take the responsibility and participate in the revision and formulation of biotechnology and bio-industry development laws, policies, projects and plans.
- To assume the management of biotechnology programs.
- To assume the management of bio-safety and bio-resource issues
- To involve in consultation on the policies and technologies related to bio-industry
- To take responsibility the issues related to bio-association
- To promote international exchanges on biotechnology;

2. Chinese Academy of Sciences (CAS)

The Chinese Academy of Sciences (CAS), founded in 1949 by the State Council, is a highly respected and powerful organisation within Chinese science. Election to membership is very prestigious and academicians are selected by nomination and ballot. The mission of CAS is to conduct research in basic and technological sciences (including the provision of scientific data and advice for governmental decision-making). Acting as a research agency, CAS runs over a hundred institutes. CAS and its institutes continue to receive the lion's share of government research funding.[3] One of the six divisions of CAS is life sciences and medicine. CAS funds 3 stem cell institutes: CURE delegates visited the Key Laboratory for Stem Cell Research at the IHS / SIBS in Shanghai.

CAS is also involved in training, running a university and a graduate school, as well as various information and publishing services.[4] Last but not least, CAS has a remit to promote high-technology enterprise.[5]

3. NSFC The National Natural Science Foundation of China

The National Natural Science Foundation of China (NSFC) directs, coordinates and funds basic research and applied basic research. It is also charged with identifying and fostering scientific talent and promotes science and technology.[6] The NSFC was set up in 1986, but only became

2 http://www.cncbd.org.cn/INTROE/INTRO/index1.html
3 Huang et al (2004), p.369.
4 http://english.cas.cn/eng2003/page/about_03.htm
5 http://english.cas.cn/eng2003/page/T46.asp and http://www.casholdings.com.cn/english/
6 http://nsfc.gov.cn/e_nsfc/2006/01au/01mr.htm

fully independent from MOST in 2000. A few years later, in 2005, the NSFC adopted a new constitution, drawing on principles adopted by science foundations in developed countries. The new constitution includes a number of provisions designed to encourage good research practices and discourage corrupt or biased funding allocations. These include external peer review, transparency and a term limit of four years for members of the evaluation committee.[7] (The NSFC has posted an English translation of its constitution on its website.[8]) The NSFC has been held up as a model of good governance by a number of commentators.[9]

However, the amount of funds allocated by the NSFC remains relatively small, albeit rising even more rapidly than the general increase in government spending on R&D. In 2006, the NSFC budget was 3.4 billion yuan, which is only about 5% of annual government spending on science and technology.[10] Nature commented that the impact of the NSFC's constitution "depends on how well it can inspire other organizations… to take steps to improve the fair and effective deployment of their money".[11]

4. Ministry of Health (MOH) and MOH ethics committee

The mandate of the Ministry of Health (MOH), also sometimes translated as the Ministry for Public Health, is to promote health: as well as formulating and implementing policies to promote health development, the MOH's tasks include the supervision of medical institutions, medical education, the oversight of clinicians and other health professionals. Although the MOH's roles also include the development and organisation of medical science, technology and health research, this is not its primary focus. The MOH is also tasked to "guide the dissemination and application of medical achievements".[12]

The MOH also administers the State Administration of Traditional Chinese Medicine.[13] Other institutions affiliated to the MOH include CAMS, PUMC and China CDC (for further details on these bodies, please see below).

The MOH has had a central role in initiating bioethical regulation in China. The MOH receives advice from its own Ethics Committee. This Committee was originally formed to deal with issues arising from international collaborations but now deals with a broad range of bioethics issues. In

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7 Heping, Jia (2005). "Chinese funding agency lays out its rules". Available from http://www.scidev.net/news/index.cfm?fuseaction=printarticle&itemid=2027&language=1

8 http://www.nsfc.gov.cn/e_nsfc/2006/07con/index.htm

9 See, for example "New Accountability in China", *Nature*, 434, p.1053.

10 http://www.nsfc.gov.cn/e_nsfc/desktop/dtxw.aspx@infoid=8859.htm

11 Nature editorial (2005). "New Accountability in China", *Nature*, 434, p.1053.

12 http://english.gov.cn/2005-10/09/content_75326.htm

13 http://english.gov.cn/2005-10/09/content_75326.htm

addition to this national committee, the MOH also requires each of its research institutions to have its own ethics committee

The commitment of the MOH to bioethical regulation appears to have been reinforced by the appointment of the new Minister of Health, Chen Zhu. The new Minister is an internationally recognised research scientist with overseas training and experience. His former positions include Director of the Chinese National Human Genome Centre and as a vice president of CAS.

5. Chinese Academy of Medical Sciences (CAMS) / Peking Union Medical College (PUMC).

The Chinese Academy of Medical Sciences (CAMS) is a large multidisciplinary institution for biomedical research.[14] The membership of CAMS consist of experts and professors with high levels of experience and academic expertise who have made outstanding contributions in the medical science field. (Membership of CAMS overlaps with CAS and the Chinese Academy of Engineering.) CAMS also works with "young outstanding experts with national or ministerial certification" and a small number of "Cheung Kong Scholars" who have returned from overseas. CAMS is directly funded by the State Council and funding has recently been increased.

Peking Union Medical College (PUMC) is one of the most prestigious medical schools in China. It was founded in 1906 with the joint support from the then-Chinese government and several British and American religious groups (thus the term "Union"). In 1917, it was re-organized with the support of the Rockefeller Foundation. PUMC was described to us as having a similar model to Johns Hopkins Medical School. One hundred students per annum undertake an eight year course with a medical PhD. The College recently began collaboration with Tsinghua University which is a large Beijing based university with a strong humanities and law base.

PUMC is affiliated with CAMS and both CAMS and PUMC function under the leadership of the MOH. A large group of institutions are funded by CAMS and jointly managed with PUMC. These include at least 18 research institutes, 5 academies, 6 or 7 clinical hospitals (including the PUMC hospital) and five specialist hospitals in areas including: Cardiovascular, Oncology, Haematology – each is the largest in China for its specialty.

CAMS also runs the Pathogen Biology Institute, a new national scientific research unit responsible for important national programs on pathogen biology. Its research priority is basic prevention and treatment technology for emerging epidemics and AIDS. It is engaged in consultation and academic exchanges on emerging infectious diseases with businesses and institutions both in China and abroad.

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14 The CAMS / PUMC website (Chinese language only) may be found here: http://www.cams.ac.cn/allnew/index.htm

6. China Centre for Disease Control and Prevention (CDC)

The first Centre for Disease Control and Prevention was created in 1998 by the Shanghai government. This Shanghai Centre consolidated many institutions into a single new agency, modelled provided by the US Centers for Disease Control and Prevention (US CDC). It served as a model for the national level China Centre for Disease Control and Prevention (CDC), which was created in 2002 as "a policy response to the shifting of disease patterns, perception of disease, and governmental changes in China".[15]

China now has a system of regional and local CDC centres which conduct surveillance, collect health data and provide training and health care services. CDC has research centres and also collection / data collection outposts throughout regions. There are a total of approx 2600 CDC surveillance centres throughout China. These have 40 000 computer terminals to collect the surveillance data, which is linked to hospitals. Central CDC has scientific / professional contact with these surveillance centres but they 'belong' to the local governments. Some of the surveillance data is available on MOH website, full data is internally accessed through the CDC website.

China CDC has a key role to play in coordinating and managing China's response to emerging infections:

- organizes and implements control and prevention plans for different kinds of diseases;
- acts as national working group for diseases prevention, emergency relief, and construction of public health information systems.

In addition, China CDC conducts applied scientific research and aims to strengthen research on strategies and measures for disease control and prevention.[16] Medical research performed by China CDC can include involvement in clinical trials. CDC has 18 different sub centres for research with laboratories. Five of these research labs are for infectious disease. Others are for public health, hygiene etc. Those relating to infectious disease are:

- Institute for viral disease control and prevention
- National institute for parasitic disease
- National Centre for AIDS / STD control and prevention
- National centre for tuberculosis control and prevention
- National centre for chronic and noncommunicable disease control

CDC has a strong interest in vaccine development and also infectious disease treatment eg antiviral treatments such as cytokines, interferons. Some clinical trials for related products are performed in CDC clinics. CDC does not design the trial protocols – these come from the research and

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15 Jing Peng et al, 2003. "Public Health in China: The Shanghai CDC Perspective" *American Journal of Public Health*; 93(12): 1991–1993. http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1448136

16 http://www.chinacdc.cn/n272562/n275958/index.html

development of the companies who have developed the product. These protocols are reviewed by SFDA and local ethics committees.

7. State Food and Drug Administration (SFDA)

We were informed that there are about 180 staff working at their headquarters in Beijing and over 40,000 staff working for the various provincial FDA offices. The SFDA licenses all new medicines including vaccines, biological products and devices. All such medicines and products developed in China have to undergo phase I, II and III testing under licence before approval for marketing.

The SFDA also requires every new drug introduced into China to be subject to further analysis in clinical trials, even if the drug already has FDA / MHRA approved. The rationale for this is that due to variation in metabolism there are potential differences in drug safety and efficacy in the Chinese population as compared with the previous trial population. The only exception to this is generic HIV treatments due to the 'Green Way' process. All other medicines and products have to be further tested by clinical trial before approval can be given. Generic drugs can proceed straight into phase II studies. Generic HIV treatments manufactured in China have to submit biosafety information but do not require further full clinical trial in China before being licensed for marketing

Medicines are categorised into 4 groups:

1. New drugs
2. Generic drugs
3. Changes of use
4. Also changes of use

8. National Institute for the Control of Pharmaceutical and Biological Products (NICPBP)

The National Institute for the Control of Pharmaceutical and Biological Products (NICPBP) is an agency of the SFDA. Their responsibilities include quality standards and technical services for drugs and biological products and medical equipment, including evaluating efficacy and safety for new drugs and biological products evaluation.[17] Within the NICPBP, the responsibilities of the "Biological Products Inspection Agency" include the inspection of imported biological products and national standards for biological products. material research, calibration, verification, and responsibility for the biological products standards material management.

17 http://www.nicpbp.org.cn/cmsweb/ (in Chinese only)

2. Ethical Guiding Principles for Research on Human Embryonic Stem Cells (2003-460)

(Promulgated by the Ministry of Science and Technology and the Ministry of Health, People's Republic of China on December 24, 2003)

1. The "Ethical Guiding Principles for Research on Human Embryonic Stem Cell" (hereinafter referred to as the "Guiding Principles") are formulated for the purpose of bringing human embryonic stem cell research in biomedical domains conducted in the People's Republic of China to accord with bioethical norms. They are aimed at enabling human embryonic stem cell research in Chinese biological and medical domains to accord with life ethical standard, to ensuring internationally recognized bioethical guidelines life ethical criterion and related regulations in China to be respected and complied with, and to promoting a healthy development of human embryonic stem cell research.

2. The human embryonic stem cells described in the Guiding Principles include stem cells derived from donated human embryos, those stem cells originated from germ reproductive cells and those stem cells obtained from somatic cell nuclear transfer.

3. Any research activity related to human embryonic stem cells conducted by investigators from any institution or in any sector, in the territory of the People's Republic of China shall abide by the "Guiding Principles".

4. Any research aiming at human reproductive cloning – cloning a human being genetically identical to another, either live or dead – is prohibited in the People's Republic of China in China.

5. Human embryonic stem cells used for research purpose can only be derived from the following means with voluntary agreement:
1) Spare gametes or embryos from IVF (in -vitro fertilization);
2) Foetal cell tissues from accidental or spontaneous or voluntary abortions;
3) Embryos obtained by somatic cell nuclear transfer technology or parthenogenetically split embryos; and
4) Reproductive germ cells voluntarily donated.

6. All research activities related to human embryonic stem cells shall comply with the following norms regulations:
1) The in vitro culture period for embryos obtained from IVF, human somatic cell nuclear transfer, parthenogenesis or genetic modification techniques, must not exceed 14 days starting from the day when fertilization or nuclear transfer is performed.
2) It is prohibited to implant embryos created by means described above into the genital organ of human beings or any other species.
3) It is prohibited to combine human gametes with the gametes of any other species.

7. It is prohibited to buy or sell human gametes, fertilized eggs, embryos and foetal tissues.

8. The principle of informed consent and informed choice shall be complied with. All research activities involving human embryonic stem cells must comply with the principle of informed consent, the form of informed consent shall be signed, and the subject's privacy shall be protected. Embryonic tissue donors must sign a "Letter of Informed Consent" so as to protect the privacy of the tissue donors in all research activities related to human embryonic stem cells.

The informed consent and informed choice mentioned above refers to the fact that the researchers shall use accurate, clear and understandable language to inform tissue donors of the expected aim of the experiment as well as the potential consequences and risks and to obtain their consent agreement by signing on a form of informed consent – "Letter of Informed Consent".

9. Research institutions engaged in human embryonic stem cell shall establish an ethical committee which consists of research and administrative experts from multidisciplinary backgrounds in biology, medicine, law and sociology with the responsibilities for providing scientific and ethical review of research as well as consultation and supervision of the ethics and science of the research activities related to human embryonic stem cells.

10. Research institutions engaged in research related to human embryonic stem cells shall formulate corresponding detailed measures and regulatory rules in compliance with the "Guiding Principles".

11. The Ministry of Science and Technology and the Ministry of Health of China are responsible for the interpretation of the "Guiding Principles".

12. The "Guiding Principles" enter into effect as of the date of its promulgation.

Descriptors: biology; medical research; ethical principle; circular

3. Ethical Guidelines for Human Embryonic Stem Cell Research

Ethics Committee of the Chinese National Human Genome Center, Shanghai

Adopted on 16 October 2001 / Revised on 20 August 2002

Human embryonic stem cell (ES) research is a great project in the frontier of biomedical science for the twenty-first century. Because the research involves the use of human embryos, it triggers serious debate on ethical issues. Opponents consider the embryo to be an early form of human life that should be respected and not destroyed. However, the majority of scientists support embryonic stem cell research, believing that it offers good prospects for the treatment of diseases that have remained incurable until now and so will benefit humankind. The Ethics Committee of the Department of Ethical, Legal, and Social Implications of the Chinese National Human Genome Center at Shanghai seriously discussed the ethical debate initiated by embryonic stem cell research. We concluded that we should support the scientists of our country in actively carrying out human embryonic stem cell research for the noble cause of "medicine being a beneficent art." For the healthy and orderly development of human embryonic stem cell research in our country, we put forward the following recommended Ethical Guidelines for Human Embryonic Stem Cell Research as a reference for leaders, administrative departments, and related scientists.

PREFACE

Article 1. Human embryonic stem cells are the primitive cells that play the main role in the growth and development of a human body. These primitive cells have the potential for infinite proliferation, self-renewal, and multi-directional differentiation. If scientists can discover the mechanism of differentiation of human embryonic stem cells, it will be possible to induce differentiation of human embryonic stem cells to form various types of human cells for clinical cell therapy. If human embryonic stem cell research can be integrated with modern biomedical engineering techniques, it also will be possible to make repair and replacement of human tissues and organs a reality.

Article 2. There are two ways to classify human embryonic stem cells. One way is to classify them according to their potential for differentiation. There could be three kinds of stem cells: totipotent stem cells, pluripotent stem cells, and unipotent stem cells.

- A totipotent stem cell has the potential to develop into a whole individual. It can differentiate into the more than 200 cell types in the whole body, construct any tissue or organ of the body, and finally develop into a whole individual. The fertilized egg and the cleavage cells at the very early stage of embryonic development are totipotent stem cells.
- A pluripotent stem cell has the potential to differentiate into many cell types derived from the three embryonic layers. However, it has lost the capacity to develop into a complete organism.
- A unipotent stem cell is derived from the further differentiation of the pluripotent stem cell. It can differentiate only into one cell type such as a hematopoietic stem cell, neural stem cell, and others.

The other way is to classify human stem cells according to their source. There could be two kinds of human stem cells: embryonic stem cells and tissue stem cells (also called adult stem cells). The former involves experimentation with embryos, which

has serious ethical implications. Ethical issues associated with the latter are mainly expressed in the various opinions regarding the allocation of health resources.

Article 3. Human embryonic stem cells are the group of cells called the blastocyst inner cell mass during the early stage of embryonic development. They are the main source of totipotent stem cells, and hence the focal and hot point in stem cell research. Studies on the clinical application of embryonic stem cells probably will involve use of the somatic cell nucleus transfer (SCNT) technique, which destroys the early human embryo.

At present, the ethical and moral debate is very serious in human embryonic stem cell research regarding whether the research will develop into reproductive cloning or not, whether it blasphemes human dignity or not, whether it infringes upon human rights or not, and other questions, which should draw the highest attention of our government and scientific
researchers.

Article 4. Human embryonic stem cell research is a bright cause in the history of human civilization development, and hence we should support scientists of our country in actively carrying out research in this field. In order to guarantee that the research work is carried out smoothly, we should establish a set of ethical guidelines for the research and use of embryonic stem cells, which should both accord with international bioethical principles and accommodate the national situation of our country as well, and should handle carefully and skillfully the dilemmas which will be met in the ethical, legal, and social fields of embryonic stem cell research in our country under the supervision and guidance of the Expert Committee and the Bioethics Committee. This is the purpose of these Guidelines.

ETHICAL PRINCIPLES OF EMBRYONIC STEM CELL RESEARCH

Article 5. Beneficence and saving life.
Human embryonic stem cell research aims at curing diseases and saving life so as to make persons healthy and long-lived. Researchers and medical workers should embody the moral integrity of kindheartedness, beneficence, and saving life, and resist consciously any unethical and immoral action.

Article 6. Respect and autonomy.
Human embryonic stem cells can be collected from early human embryos. Even though the human embryo within 14 days of development is only biologically cellular tissue and not a “human being” in the moral sense, it still should be respected. In 1996, the HUGO Ethical, Legal, and Social Issues Committee pointed out in its Statement on the Principled Conduct of Genetic Research: “1. Recognition that the human genome is part of the common heritage of humanity; 2. Adherence to international norms of human rights; 3. Respect for the values, traditions, culture, and integrity of participants; and 4. Acceptance and upholding of human dignity and freedom.” These principles should be observed in human embryonic stem cell research.

Both the donors and the recipients of the embryonic stem cells should be informed truthfully of the expected aim as well as the probable consequences and risks, so that the responsible person or his/her relatives can freely act and choose.

Article 7. Harmlessness and benefit.
When a conflict between benefit and harm appears in the research and future clinical applications of human embryonic stems, one ought to adopt, in weighing the benefits and harms, the principle of "taking the lesser of two evils," and all possible measures should be taken to avoid the harm.

With respect to the plans and actions of the researcher and clinical practitioner, scientific judgment should be used. The research or clinical procedure should be stopped immediately if a potential for harm to the human body emerges.

Article 8. Being informed and consent.
All donors of embryos, aborted fetuses, and oocytes should be treated the same as tissue and organ donors, and the principle of informed consent should be applied conscientiously. The researcher should explain to the donors the aim and significance of the procedures as well as any possible problems and preventive measures using scientific, popular, and easily understandable language, and the procedures can only be implemented after the signing of an informed consent document.

Article 9. Prudence and confidentiality.
Human embryonic stem cell research is a new kind of study using advanced science and technology, and hence there remain many issues to be explored at the technical, ethical, and legal levels. In addition, factors such as economy, culture, religious belief, ethnicity, people's morals and customs, and other aspects of society may lead to different understandings about human embryonic stem cell research. Therefore human embryonic stem cell research must be carried out prudently under the guidance and supervision of the Expert Committee and Bioethics Committee, and with timely release of the scientific information to the public.

Researchers should keep confidential the collection, culture, and use of human embryonic stem cells. Although human embryonic stem cell research is part of the common heritage of mankind, the research techniques should be kept confidential for a certain period of time so as to prevent them from being used for profiteering or other illegitimate aim.

Article 10. Forbid reproductive cloning.
There is possibility that human embryonic stem cell research might involve use of the somatic cell nucleus transfer technique, and hence there should be strict administration of the cloning technique, opposition to abuse of the somatic cell cloning technique, and rigorous forbidding of its use for any research with the aim of reproducing the human body. This is because all such studies to date have violated ethical norms.

Article 11. Support therapeutic cloning research.
If the technique of culturing embryonic stem cells in vitro can be integrated with the somatic cell nucleus transfer technique in order to produce specific cells and tissues to be used for clinical therapy, it will be possible both to provide enough material for patient tissue repair and to overcome patients' rejection response as well. Such therapeutic cloning, which could bring benefit to patients, accords well with the ethical norms, and hence should be supported.

Article 12. Treat embryonic experimentation with care.
At present there are three sources of different forms of human embryonic stem cells, i.e., embryonic stem cells collected from spare embryos following in vitro fertilization, embryonic germ cells (EG) collected from aborted fetuses, and embryonic stem cells collected from embryos created with the somatic cell nucleus transfer technique. These three sources of stem cells all involve issues of embryo experimentation and hence must be treated with care.
1) Separation and culture of the embryonic stem cells from spare and voluntarily donated embryos following in vitro fertilization attempts of an infertile couple conform with the ethical norms.
2) Separation and culture of embryonic stem cells from an artificially aborted embryo which is voluntarily donated to establish a pluripotent stem cell line to be used for clinical therapy could be viewed the same as use of a donated organ for organ transplantation, and hence conform with the ethical norms.
3) Separation and culture of embryonic stem cells could be done using a human blastula created by the somatic cell nucleus transfer technique, i.e., the nucleus of the oocyte was removed and replaced by a somatic cell nucleus from the patient. This kind of stem cell is then genetically identical to the patient, and hence can avoid the rejection response when used for clinical therapy. This procedure definitely will bring benefit to the patient, and conforms with the ethical norms as well.

Article 13. Research to establish embryonic stem cell lines using donated embryos leftover from assisted reproduction procedures must abide by the following action norms:
1) Only the use of voluntarily donated, spare embryos following assisted reproduction is permitted, and the researcher should explain to the donor that the embryos will be destroyed in the process of the research;
2) In vitro development of the embryo cannot exceed 14 days;
3) Reimplantation of the donated embryo into the woman's uterus is not permitted;
4) Use of embryonic stem cells produced from the donated human embryos for nontherapeutic purposes is not permitted. However, it is permissible to use them in basic research;
5) Joining a human gamete with an animal gamete is not permitted;
6) The person who harvests the donated embryos and the researcher who uses them in embryonic stem cell research should be strictly separated from each other; they are not permitted to be the same person;
7) The identities and various kinds of information pertaining to the donors and recipients of the embryonic stem cells must be protected, and hence the researcher should strictly abide by the principles of privacy and confidentiality;
8) When a health institution provides embryonic tissues, it must provide at the same time written evidence of the absence of pathogenic bacteria. Otherwise, the embryonic tissue should not be used.

Article 14. Embryonic stem cell research using embryos produced by the somatic cell nucleus transfer technique must abide by the following action norms:
1) The oocyte must be leftover from assisted reproduction procedures and voluntarily donated by the infertile couple;
2) The embryo produced by the somatic cell nucleus transfer technique can only be cultured in vitro, and the culture cannot exceed 14 days;

3) Implantation of an embryo formed through somatic cell nucleus transfer into a woman's uterus or the uterus of any other species is forbidden;
4) Use of the "human-animal" cell fusion technique is permissible in basic research with non-clinical application if the requirements expressed in the first three points of the present Article 14 are satisfied. However, use of the product formed by combining a human somatic cell nucleus with the oocyte cytoplasm of an animal using the "human-animal" cell fusion technique is strictly forbidden in therapeutic cloning research for clinical application in the treatment of human diseases.

Article 15. Encourage scientists to carry out basic biological research on human embryonic stem cells, such as to explore in depth the directed differentiation of stem cells as well as the mechanism by which the oocyte cytoplasm reprogrammes the adult somatic cell nucleus so as to bypass the embryonic stage and establish pluripotent stem cell lines directly from the patient's somatic cells. In this way, it will be possible both to avoid too high a cost and also to reduce the ethical debate.

Article 16. Establishment of embryonic stem cell lines is beneficial to expand resources for treating diseases with stem cells. However, strict and close supervision of their use should be in place. Reasonable distribution of the resources taking into account safety, benefit, fairness, and justice is the major ethical guideline, and their use should be verified and evaluated by the Bioethics Committee.

Article 17. Researchers involved in the study of embryonic stem cells for clinical therapy must be medical professionals who should have had special training, technical proficiency, and licensed qualification. "Avoid harm and benefit the patient" is the action guideline that must be observed in the use of embryonic stem cells.

Article 18. Studies on embryonic stem cells to be used for therapy in the treatment of difficult and complicated human diseases probably will produce great commercial value once accepted by ethics and law. Therefore patent protection and related legislation for the products of human embryonic stem cell research should be fully established. Commercial operation and profiteering in the research and application of embryonic stem cells should be opposed as these activities will run counter to the aim of embryonic stem cell research, which is seeking benefit for humankind.

Article 19. The mechanism for examination, supervision, and evaluation by the Bioethics Committee should be established and improved. The Bioethics Committee and the Expert Committee should strictly examine the plan for the human embryonic stem cell research and evaluate the progress and results of the research, in order to make the human embryonic stem cell research accord with the related international rules, declarations, or guidelines and with the related policies and regulations of our country so as to be beneficial to human health services.

Article 20. As life science and technology develop, and in conjunction with the advancement of international cultural exchange and cooperation, these Ethical Guidelines will be continually enriched and perfected, with the hope that human embryonic stem cell research can further contribute to a happy life with health and longevity for humankind.

4. Regulation on Assisted Reproductive Technology

Issued in 2001, and revised by Ministry of Health, P.R. China, July, 2003

Assisted Reproductive Technology (ART) includes both In Vitro Fertilization and Embryo Transfer (IVF-ET) and Artificial Insemination (AIĎtogether with its deriving technology. All organizations having ART clinics or family-planning clinics should follow this code.

1. The regulation on In Vitro Fertilization and Embryo Transfer and relevant techniques.

Currently, in vitro fertilization and embryo transfer and related technology include IVF-ET, gametes or zygote intra- fallopian transfer (GIFT or ZIFT), intracytoplasmic sperm injection (ICSI), frozen embryos, pre-implanted genetic diagnosis (PGD), et al.

A. General Standard

1) Organization and facility criteria

a. Specialized or general hospital holding the "License of Medical Institute", or family-planning services stations operate by provincial above (including provincial) authorities with "License of Family-Planning Service Station"

b. Chinese People's Liberation Army medical organizations should follow the two "Measures"; before operating IVF-ET and related technology, all organizations should undergo following procedures: experts discussion, inspection, and apply to Ministry of Health for approval. All procedures are under the directorship of medical administrative authorities from the province, autonomous region, municipality or Hygienic Department of the General Logistics Department.

c. The joint venture or international cooperative organizations must hold both the Ministry of Health Approval Certificate and the Certificate of Approval of Foreign-funded Enterprise from former Ministry of Foreign Trade (now Ministry of Commerce)

d. Organization must have gynecology and andrology department with technical ability and facilities for inpatient open-abdomen operation.

e. Reproductive medical organization is made up of reproductive medical clinics (Clinic) and IVF labs (Lab).

f. Organization must have the ability to do selective embryo reduction of multifetal pregnancies.

g. Organization must have technical ability and facility to freeze, preserve and thaw embryos.

h. Sperm bank is not allowed to be set up within the same department in one organization; it must be administered separately from reproductive medical organization.

i. All organization planning to establish ART organizations should be first reviewed by the medical administrative authority of relevant province, region or city according to local program and medical treatment needs. Then it should apply to Ministry of Health for approval on its experimental run. Experts from Ministry of Health will have a pre-approval inspection after the initial setting up of the ART organization. Inspection for final official approval will be held one year of after the experimental run.

j. All applications of IVF-ET and related technologies must seek for Ministry of Health's approval.

2). Staff member criteria

There should be General Person Responsible, Clinical Person Responsible (CPR) and Laboratory Person Responsible (LPR). CPR and LPR must not be the same person. Reproductive medical organizations should have no less than 12 specialized professionals; among those, no less than 6 clinic practitioners (including 1 andrology practitioner), no less than 3 laboratory specialized professionals, and no less than 3 nurses. All such staff must have had professional training from pointed medical organizations by Ministry of Health. Professionals with foreign nationality or from China Taiwan region, Hongkong and Macao

Special Administrative Region must follow relevant national regulations in conducting ART treatment.

a. Clinical practitioner
a. Specialized clinical practitioner must have obtained medical bachelor degree and have achieved middle or above clinical practice level, or lincenced gynecology, andrology, urology practitioners with master degree on reproductive medicine.
b. CPR must be a lincenced gynecology practitioner with high clinical practice level specialized in reproductive medicine.
c. Clinical practitioners must have following knowledge and clinical abilities: To grasp female reproductive endocrinological expertise, especially the use of ovulation induction and menstrual control. To master how to do vaginal ultrasound examination and use ultrasound to do follicle monitoring and egg harvesting. To have the ability of operation and deal with the ART complications.
d. Organization should have specialized andrology clinical practitioner with the knowledge of basic theories and clinical technologies of male reproductive medicine

b. Laboratory professionals
a. Embryo-cultivation laboratory professionals must have bachelor degree of medicine or biology, or graduated from vocational college but have achieved middle technical level.
b. LPR must be a person who have achieved high technical level on medicine or biology, the person should also have had training from cell-biology, embryology and genetics; have the cell cultivation and ART laboratory ability, and capable of laboratory administration.
c. At least one person should be able to make semen analysis according to the WHO standard procedure.
d. At least one person should have been trained in one of Ministry of Health pointed organizations with a systematic understanding of frozen-thaw semen and embryo techniques.
e. In the ICSI carried out organizations there should be at least one person has been trained in such field in one of Ministry of Health pointed organizations and provided micromanipulation with IVF-ET related laboratory ability.
f. In the PGD carried out organizations there should be some person has been trained in such field in polar body and blastomere biopsy, medical genetic theory and single cell genetic diagnosis. The organization can carry out genetic counseling and prenatal diagnosis.

c. Nurse All nurses must have Nurse Qualification License, have received reproductive medicine nursing training. The Person Responsible for nursing must have achieved middle professional level.

3). Facility criteria
a. ART site including waiting room, diagnosis and treat room, examination room, sperm-taking room, sperm dealing room, data archives, cleaning cell, buffer area, ultrasound room, embryo culture room, egg harvesting room, IVF Lab, embryo transfer room and other assisted area.
b. Total space for reproductive medicine treatment should be no less than 260 square meters.
c. The space arrangement must be reasonable. ART site should meet hygienic standard; construction and fitment materials should use nontoxic material; should avoid unfavorable chemical and radioactive sources.
d. Working area must measure up to the hospital construction safety requirement and fire protection requirement. Water and electricity supply should be guaranteed. Air disinfection tools should be equipped in every room.

e. Main sites requirements:
a. Ultrasound room functional space should be no less than 15 square meters. Indoor environment should follow Ministry of Health Medical Sites III Standard.
b. sperm treatment room neighboring to sperm dealing room, functional space no less than 5 square meters, with hand-washing facilities.
c. Sperm dealing roomfunctional space no less than 10 square meters
d. Egg harvesting room to do the egg harvesting operation functional space no less than 25 square meters. Indoor environment should follow Ministry of Health Medical Site II Standard.
e. IVF Lab functional space no less than 30 square meters and buffer area. Indoor environment should follow Ministry of Health Medical Site I Standard. To suggest to install laminar air flow room. Embryo area must achieve the hector-standard.
f. embryo transfer room functional space no less than 15 square meters, Indoor environment should follow Ministry of Health Medical Site II Standard.

4) Equipment criteria
a. B ultrasound equipment: 2-bench;
b. Vacuum extractor;
c. Vaginal examined bed;
d. Superclean bench: 3-bench;
e. Anatomical microscope;
f. Biological microscope;
g. Inverted microscope(include homeothermic bench);
h. SFA equipment;
i. CO2 incubator(at least 3);
j. CO2 concentration measurement;
k. Homeothermia flat and tube rack;
l. Refrigerator;
m. Centrifuge;
n. Comments in Lab: pH meter, osmometer, scale, electric heating drier;
o. Gametes and embryos frozen equipments include freezing meter, LN storing cask, LN transfer cask, et al. To report to ICSI organization, it should have a micromanipulation meter.

5) Other Criteria
Organizations operating IVF-ET and related technologies must also meet following requirements:
a. Clinic routine control(including routine biochemistry, blood and urine routine, imaging examination and reproductive immunological examination);
b. Reproductive endocrinal Lab and related equipment;
c. Cyto- and molecular genetic diagnosis Lab and related equipment, The PGD organization must have the prenatal diagnosis certificate;
d. Operation condition;
e. Inpatient care condition;
f. Sterilization and sewerage.

B. Regulation
1). Organization operating IVF-ET and deriving technologies, must obey national population and family-planning legislation and policies, and ask infertile couples to sign relevant informed consent and consent on selective embryo reduction of multifetal pregnancies.
2) Organization must first carefully inspect the couple's ID, marriage certificate and original copy of the qualification of pregnancy certificate issued under national population and family-planning legislation and policies. Photocopies of the mentioned documents should be saved for the records. International marriage and foreigners should show passports and marriage certificate; photocopies should also be obtained and saved

3) Organizations must carry out self-inspection on a routine mode, and provide necessary documents and annual reports to the Ministry of Health.
4) All patient records and relevant documents kept by the organization should be closely regulated according to the WYF[2002]No 193 "Requisition on printing and distribution of 'Regulation of Medical Organization's Patient Record'", issued by Ministry of Health and State Administration of Traditional Chinese Medicine
5) Organization must provide provider sperm bank with timely and accurate information on recipients' pregnancy and relevant information on the offspring.
6). Regulation and management system

Organization should establish following regulations
a. System of reproductive medicine ethical review board
b. System of patient record management
c. System of medical follow-up
d. System of division of work and responsibility
e. System of quality control on access to gametes and embryo's laboratory material
f. General code of practice
g. Management on special pharmaceuticals
h. Management on appliances
i. Sanitization and isolation management j. Management on materials

7) Clinical safety requirement
a. Organization is required to have basic facilities manage clinical emergency, include the equipments of ventilation and trachea cannula and other commen first-aid medicine and equipmets;
b. The organization applying anaesthesia should equip with surveillance, rescuing facilities and personnel;
c. Subjects should be asepsis, asordes and asepsis and accord with quality standard;
d. Deionised ultrapure water in laboratory;
e. The number of embryo transfer per cycle can't beyond 3 and 2 below 35 years old in the first cycle;
f. It should be unretrieval material which contact with gametes and embryos;
g. The donated sperm IVF-ET and derivation organization should carry out the technique according to the rules on artificial fecundation.

C. Indications and Contraindications
1) Indications
a. IVF-ET indications
a. Gametes transporting disorders induced by female factors;
b. Ovulation disorders;
c. Endometriosis;
d. Oligozoospermia and asthenozoospermia;
e. Unexplained subfertility;
f. Immunologic subfertility.
b. ICSI indications
a. Severe oligozoospermia, asthenozoospermia and teratozoospermia;
b. Irreversible obstructive azoosperatism;
c. Spermatogenesis disturbance(exculde genetic diseases);
d. Immunologic subfertility;
e. IVF failure;
f. Perforatorium abnormal;
g. Need PGD.
c. PGD indications: mainly used in monogenetic heredity diseases, chrompsomal diseases, sex-link inheritant diseases and the high risk patients of bearing abnormal babies.
d. Oocytes donated acceptors indications:

a. Loss the ability of oocytes producing;
b. Women carrying or suffering with severe genetic diseases;
c. Having the evident causes affecting the oocytes' quality and quantity.
e. Basic criteria for ovum donation
a. Ovum donation is a humanitarian act. Any form of organization or individual's attempt on commercializing ovum donation is prohibited.
b. Ovum donation is limited only to the spare ovum from ART treatment
c. A related health check is required for ovum donor (refer to sperm donor's health check standard)
d. Ovum donor should be fully informed on donated ovum's usage, her rights and liabilities. Signed informed consent is required.
e. Every ovum donor can contribute to 5 women's pregnancy at most
f. 100% clinical follow-up with the ovum donors

2) Contraindications
a. IVF-ET and related technology should not be conducted, in case of any one of the following situations:
a. Wife or husband has the severe mental disease, genitourinary system inflammation and sexually transmitted diseases;
b. According the Maternal and Infant Care Law, the couple have severe diseases inadvisable conception and PGD;
c. Any one of the couple has serious indulgence such as drug addiction.
d. Any one of the couple has had high intake of radiation, drug or medication that will lead to fetus abnormality and is still in its effective period.
e. The uterus has no function of conception, or the woman has severe disease to bear the conception.

E. Quality criteria
1) To protect patients' rights and interests, guard women and children's health benefits, promote population quality, prevent ART technology's industrialization and commercialization, and ensure a more regulated and standardized technology implementation, any reproduction organization's annual application of IVF-ET and related technology should not exceed 1000 oocyte-drilling cycles;
2) Clinical follow-up on IVF-ET newborns should not be lower than 95%;
3) IVF fertility rate should be more than 65% and ICSI more than 70%;
4) The clinic IVF-ET pregnant rate per cycle should be more than 15% within the first year and 20% from the second year; The clinic FET pregnant rate per cycle should be more than 10%. (The clinic ET pregnant rate = (clinic pregnant number/ET cycles)x100%);
5) With regard to multiple pregnancy, they need pregnancy reduction so as to avoid twins and forbid triplets.

2. The regulation on Artificial insemination
Artificial insemination technology is divided into two kinds of treatment by the source of the sperm, one is artificial insemination with husband sperm (AIH), the other is artificial insemination with donor sperm (AID)

A. General Standard
1) Organization and facility criteria
a. Specialized or general hospital holding the "License of Medical Institute", or family-planning services stations operate by provincial above (including provincial) authorities with "License of Family-Planning Service Station"
b. A Ministry of Health approval is required for conducting AID treatment, and approval from local province, autonomous region and municipality medical authority is required for conducting AIH treatment

c. Chinese People's Liberation Army medical organizations operating artificial insemination and related technology should follow the two “Measures”. For those applying for AIH treatment approval, all organizations should undergo following procedures: expert discussion, inspection, audition and apply to Ministry of Health for approval. All procedures are under the directorship of medical administrative authorities from the province, autonomous region, municipality or Hygienic Department of the General Logistics Department. For those applying for AID treatment, all organizations should undergo following procedures: expert discussion, inspection, and apply to Ministry of Health for approval. All procedures are under the directorship of medical administrative authorities from the province, autonomous region, municipality or Hygienic Department of the General Logistics Department.
d. The joint venture or international cooperative organizations must hold both the Ministry of Health Approval Certificate and the Certificate of Approval of Foreign-funded Enterprise from former Ministry of Foreign Trade (now Ministry of Commerce)
e. Organizations conducting artificial insemination treatment, must obtain sperms from sperm bank with “Human Sperm Bank Lincense” and sign sperm supply protocols. Organization must provide provider sperm bank with timely and accurate information on recipients’ pregnancy and relevant information on the offspring. The protocol should state clear of all parties rights and liabilities.
f. Organizations should abbey other legislation, regulation and management rules.

2) Staff requirement
a. No less than 2 specialized reproductive medicine practitioner, 2 laboratory professionals, 1 nurse. All should carry out good professional ethics.
b. All practitioners should have been qualified and licensed
c. Organization should have pointed CPR. CPR must be a lincenced gynecology practitioner with high clinical practice level specialized in reproductive medicine.
d. Other practitioners in the organization should have had training and experience either in clinical gynecology, reproductive medicine or and endocrinology. They also should have gynecologic ultrasound certificate and experience.
e. Laboratory professionals should have had training and experience on making semen analysis according to the WHO standard procedure.
f. Nurses should have been qualified and licensed
g. For organizations also conducting IVF-ET, a person should be assigned specially for that task, while other staff members can work on both sites.

3). Facility criteria Clinical sites includes waiting room, diagnosis and treat room, examination room, ultrasound room, IUI Lab, fertilized room and other assisted area. Total functional space is no less than 100 square meters and IUI Lab 20 square meters and fertilized room 15 square meters. For organizations conducting both artificial insemination and IVF-ET, no need for waiting room, diagnosis and treat room, examination room, ultrasound room, but IUI room and IUI Lab should be used specially and no less than 20 square meters. In addition, the related facilities include gynecological endocrinal test, imaginal examination, genetic test and or so.

4) equipment criteria
1) Vaginal examined bed(more than 2);
2) B ultrasound equipment: 1 bench;
3) Biological microscope;
4) centrifuge: 1 bench;
5) hectograde superclean bench: 1 bench;
6) CO2 incubator;
7) LN storing cask(more than 2);
8) Refrigerator;
9) SFA equipment;

10) water-bathe case: 1 bench;
11) the containers contacted with sperm should be atoxic irrepeated used materials.

B. Regulation

1) Before artificial insemination, infertile couples must sign informed consent and given consent on selective embryo reduction of multifetal pregnancies.
2) AID treatment can only obtain sperm supply from sperm banks approved by Ministry of Health.
3) Organizations should make timely record on infertile couple's treatment and closely regulated according to "Regulation of Medical Organization's Patient Record". Medical follow-up should be carried out on every patient.
4) Organization conducting AID must provide provider sperm bank with timely and accurate information on recipients' pregnancy, relevant information on the offspring, and the STD occurrence of the recipients. Records should be saved permanently.
5) Every sperm donor's sperm can only contribute to 5 women's pregnancy at most
6) All applications, either from individual or from any forms of organizations, on checking sperm donors or recipients record should be rejected. Exceptions are made for legislation organization with official letter or relevant parties with sufficient reason. In case of working requirements or other special reasons that made reviewing record necessary, approval must be obtained from the Person Responsible from sperm provider, and both donor and recipient's social status information should be concealed
7) Artificial insemination must have comprehensive and complete regulation protocols and technical operation brochure. Act accordingly.
8) Organization must have routine self-inspection on artificial insemination treatment, and should provide health administrations with necessary documents and annual report.

C. Indications and Contraindications

1) AIH
a. Indications
a. Oligozoospermia, asthenzoospermia, semen abnormal liquefection, sexual disturbance, genital malformation, et al;
b. Cervical subfertility;
c. Apareunia caused by genital duct malformation and pyschological factors;
d. Immunological subfertility;
e. Unexplained subfertility.
b. Contraindications
a. Either of the couple has the acute inflammation of genital and urinary system or STD;
b. Either of the couple has severe inherited, body or psychologic diseases;
c. Either of the couple contacts with enough ray, toxicant or medicine to lead to malformation in action period;
d. Either of the couple has severe hobbies, such as drug abuse.

2) AID
a. Indications
a. Irreversible azoospermatism, severe oligozoospermia, asthenzoospermia and teratozoospermia;
b. Failure of vasectomy reversal;
c. Dysspermatism;
d. The AID patients of the indication□□ □, except irreversible azoospermatism, should fully understand the following things: they can gain their genetic offspring through ICSI. If the patient himself insist in quitting this authority and sign the informed consent, the doctors can use AID to assist;
e. The husband and his family has the severe unfitable fertilized inherited diseases;
f. Maternofetal blood group incompatibility causes the disability of alive baby.

b. Contraindications
a. The female associated with acute GUS infection and STD;
b. The female associated with severe genetic, body and mental disorders;
c. The female contected with ray, toxicant and medicine led to fetal abnormal;
d. The female with drug abuse and other dyshobby.

D. Technical procedure and quality control

1) Technical procedure
a. Apply treatment closely according to indications and exclude contraindications
b. Artificial insemination in natural or ovulation induction cycle, but not lead to multiple pregnancy;
c. Use B ultrasound examination and hormone determination to monitor the follicle development;
d. Learn the ovulated time and do artificial insemination at the right moment;
e. The sperm used in IUI must be scrubbed and isolated. The total count of prosad movement is more than 20×10^6 /ml after scrubbed and isolated and not less than 10×10^6/ml;
f. Support corpus function after artificial insemination;
g. It needs 14-16 days to diagnose biaochemistry pregnancy and 5 weeks to diagnose clinicle pregnancy after artificial insemination;
h. Multiple pregnancy needs to do pregnancy reduction in the specialist centers;
i. The institution enforcing AID should identified the argreement of pregancy reduction with the patients, although it hasn't the certificate of pregnancy reduction.

2) Quality control
a. The frozen sperm used in AID should contain 40% of the total count of prosad movement after resuscitation;
b. The cycle clinicle pregnancy rate is not less than 15%(The cycle clinicle pregnancy rate=the number of clinicle pregnancy/the number of artificial insemination cycles).

3. The regulation for clinical practitioners
A. Must strictly follow National Population and Family-Planning legislations and policies
B. Must strictly follow the autonomy principle of informed consent, informed choice.
C. Must respect patients privacy
D. Gender selection without medical indication is prohibited
E. Surrogacy is prohibited
F. Embryo-gifting is prohibited
G. Application of human oocyte endochylema transfer and nuclear transfer in treating infertility is prohibited.
H. Forbidance of the hybridization between mankind and other species gatemes; Forbidance of the other species gametes, zygocytes and embryos in mankind; Forbidance of the mankind gametes, zygocytes and embryos in other species;
I. Forbidance of the genetic manipulation to the mankind gametes, zygocytes and embryos;
J. Forbidance of the close relative sperm and oocyte combination;
K. In the same treatment cycle, gametes and zygotes must be from the same male for same female
L. Gamete, zygote, or embryos being transferred to other individuals or to scientific research, without patient been informed or given consent, is prohibited.
M. ART treatment on single female or not qualified couples under national population and family-planning legislation and policies is prohibited
N. Human chimera embryo research is prohibited
O. Clone human is prohibited

5. Ethical Principles for Human Assisted Reproductive Technology & Sperm Banks

Promulgated by Ministry of Health, China

(Unofficial Translation)

I. Ethical Principles for Human Assisted Reproductive Technology

Human assisted reproductive technology is used as a medical treatment for infertility. To ensure safe, effective, and rational application of ART; and to protect the individual, family and offspring's rights and benefits, medical staff should comply to the following ethical guidelines:

A. Benefit to patient

1 Medical staff should make comprehensive analysis on patient's pathological, biological, psychological and social factors. Medical staffs have the liability to inform patient with all possible treatment choices, risks and benefits; and should point out the possible choices in patient's individual case and the most beneficial treatment scheme.
2 It is prohibited to stimulate ovulation with the purpose of multi-birth or commercialization of ovum
3 Infertile couple has the right to choose the disposals of gametes and embryos from ART process. Technical service organizations should keep detailed record on this and should obtain written informed consent from the husband, the wife or the couple
4 Patient's gametes and embryos can not be taken for any use, especially commercial use, without patient's informed consent.

B. Informed consent

1 ART should be conduct on the condition of obtaining autonomous and signed informed consent from both the husband and the wife.
2 Medical staff should informed the couple with indications of ART the following information: the necessity of application of this technology, the procedure, potential risks and means to eliminate the risks, success rate of this particular medical clinic, estimated total cost of one cycle, import and domestic pharmaceutical choices and other practical information that will facilitate patients decision making.
3 Couple receiving ART treatment has the right to stop further application of treatment at any time in the procedure; and this will not effect their future treatment.
4 Medical staff must inform recipient couple of ART and their born offspring the necessity of medical follow up.
5 Medical staff must inform donor the necessity of a health check and should obtain a written informed consent from the donor.

C. Protecting offspring

identification of the donor. Confidentiality means to conceal the fact of recipient's participation of the treatment and recipients related information.

3. Medical staff has the obligation of informing donor that the donor is not allowed to know all information on recipient and the offspring; medical staff should also obtain signed informed consent.

F. Non-commercialization

Organization and medical staff should closely follow ART clinical indications, and should not conduct ART with financial incentives Donation of semen and ovum is only a conduct of altruism. Commercialization is strictly prohibited, but compensation on wage, traffic and medical treatment can be made to donors

G. Ethical review and surveillance

1 To ensure the enforcement of above guidelines, organization conducting ART treatment should establish reproductive medicine ethical review board and been directed and supervised by the board
2 Members of the reproductive medicine ethical review board should be persons with background of medical ethic, psychology, sociology, law, reproductive medicine, nursing and public representative.
3 Reproductive medicine ethical review board should supervise ART treatment according to above mentioned guidelines; and should promote public education of ethics of reproductive medicine; should inspect, consult, discuss and give suggestion to all ethical problems arise from the procedure.

II. Ethical Principles for Human Sperm Bank

To promote safe, effective and rational collecting, preserving and providing sperms by sperm bank; and to protect the individual, family and offspring's rights and benefits, medical staff should comply to the following ethical guidelines:

A. Benefit to patient

1 Strict health check with sperm donors. All semen samples must be examined before use, so as to avoid or eliminate born defections and prevent the spreading of STD
2 It is prohibited to use commercial advertisement to recruit sperm donor. It should seek socially acceptable and civilized means and measures to enroll as large a population of sperm donors as possible. A complete set of donors' appearances record should be kept to respect recipients' right of choice.
3 Relevant psychology consultation service should be available to help with all possible psychology problems with donors or self-donors (sperm freeze only for the use of oneself)
4 Medical staff should do their best to understand and respect donor and self-donor's possible difficulties in the process of collecting samples, and should give best possible help.

B. Informed consent

1 Sperm donor should donate sperm out of his own will, and have the right to know the usage and the necessity of limit to the usage of his sperm (prevent offspring's consanguineous marriage). He should sign written informed consent.
2 Sperm donor has the right to cease donation under psychological, biological and other circumstances. After compensation of the examination and freezing fee to the sperm bank, sperm donor has the right to cease the usage of his frozen semen.
3 Self-donor can freeze his own sperm after given written informed consent. Medical staff has the liability to inform self-donor the necessity of this application, current thaw rate and possible medical outcome
4 Sperm bank is not allowed to collect, examine, preserve semen without signed informed consent.

C. Protecting offspring

1 Medical staff has the liability to inform sperm donor that he has no rights and obligations for the resulting offspring.
2 Comprehensive sperm donation system should be set up. Sperm bank has the obligation to give future ART offspring with anonymous medical information and marriage consultant.

D. Social goods

1 Comprehensive sperm donor management system should be set up. It is prohibited for one donor to donate on different sites and used in more than 5 women's pregnancy.
2 It is not allowed to select the X, Y chromosome without medical indication.

E. Privacy and confidentiality

1 To protect sperm donor's, recipient couple's and offspring's rights, donor and recipients should be double-blind; donor and the medical staff conducting ART should be double-blind; donor and offspring should be double-blind.
2 Sperm banks medical staff have obligation to ensure confidentiality with the donor, the recipient and the offspring. Sperm bank should establish system to ensure privacy is protected. Frozen semen should be coded when using. Recipient's identification should keep confidential by sperm bank

3. Recipient couple and ART medical staff have no rights to know the donor's identification. Donor have no rights to know the offspring's identification

F. Non-commercialization

1 Donation of semen is a conduct of humanitarianism. Commercialization is strictly prohibited, but compensation on wage, traffic and medical treatment can be made to donors
2 Sperm band can only provide frozen semen that meets the national qualification

standards, to organizations proved by Ministry of Health on conducting ART treatment

3 It is prohibited to market sperms. Sperm from sperm bank and not be used as commodity.

4. Sperm band cannot lower sperm quality for financial incentives.

G. Ethical review and surveillance

1 To ensure the enforcement of above guidelines, sperm bank should be supervised and examined by reproductive medicine ethical review board. Members of the reproductive medicine ethical review board should be persons with background of medical ethic, psychology, sociology, law, reproductive medicine, nursing and public representative.

2 Reproductive medicine ethical review board should supervise sperm bank according to above mentioned guidelines; and should promote public education of related ethics; should inspect, consult, discuss and give suggestion to all ethical problems arise from the procedure.

ICSCN International Consortium of Stem Cell Networks

Global Regulation of Human Embryonic Stem Cell Research and Oocyte Donation

	Prohibition of derivation of HESCs	Prohibition of derivation but allowing importation of HESC lines	Allowing derivation of HESCs from excess IVF embryos	Prohibition of creation of human embryos for research including SCNT	Allowing creation of human embryos for research including SCNT	No specific legislation regarding HESC Research	Regulations for Oocyte Donation	Policies and Further Information	Stem Cell Network, Society or Foundation
Australia			X		X		The National Health and Medical Research Council (NHMRC) has released revised *Ethical guidelines on the use of assisted reproductive technology in clinical practice and research* (ART guidelines). The revised ART guidelines provide ethical advice in areas such as: *human egg donation; research on embryos that are unsuitable for implantation; research on embryos created by somatic cell nuclear transfer; and proper consent in relation to the donation of human eggs and embryos.* The guidelines also provide ethical advice for the clinical practice of ART, including: *guidelines for the use of donated embryos; storage of gametes and embryos; information giving, counselling and consent and innovations, training and quality assurance.*	In late 2006 the Australian parliament voted to amend the legislation surrounding hESC regulation to allow SCNT and the derivation of hESC lines from embryos deemed unsuitable for implantation through PGD. "Research Involving Human Embryos Act 2002," "Prohibition of Human Cloning for Reproduction and the Regulation of Human Embryo Research Amendment Bill 2006." [PDF] -	Australian Stem Cell Centre: www.stemcellcentre.edu.au New South Wales Stem Cell Network: http://www.diabetes.unsw.edu.au/STEM/.
Austria	X			X					
Belgium			X		X			Belgium – *Law on research on human embryos in vitro*, (April 2003).	
Brazil			X	X				In March 2005, the Congress voted to permit research using embryos left over from in-vitro fertilization that had been frozen for at least three years. It upheld a ban on cloning embryos.	
Canada			X	X				Updated Guidelines for Human Pluripotent Stem Cell Research, June 28, 2006 http://www.cihr-irsc.gc.ca/e/31488.html	Stem Cell Network Canada www.stemcellnetwork.ca
China			X		X			Ministry of Science of Technology and Ministry of Health, "Guidelines for Research on Human Embryonic Stem Cells," January 2004. Authorized translation	

www.stemcellconsortium.org

Last updated: 14 August 2007

6. Global regulation of Human Embryonic Stem Cell Research and Oocyte Donation

	Prohibition of derivation of HESCs	Prohibition of derivation but allowing importation of HESC lines	Allowing derivation of HESCs from excess IVF embryos	Prohibition of creation of human embryos for research including SCNT	Allowing creation of human embryos for research including SCNT	No specific legislation regarding HESC Research	Regulations for Oocyte Donation	Policies and Further Information	Stem Cell Network, Society or Foundation
Cyprus				X		X			
Czech Rep			X					http://www.msmt.cz/Files/PDF/JJ Human stemcells.pdf.	
Denmark			X	X					Danish Stem Cell Research Center http://www.dasc.dk/. The Scan Balt Stem Cell Research Network has been established with representatives from all the 11 countries in the Scan Balt BioRegion. http://www.scanbalt.org/sw222.asp
Estonia			X	X					The Scan Balt Stem Cell Research Network has been established with representatives from all the 11 countries in the Scan Balt BioRegion. http://www.scanbalt.org/sw222.asp
Finland			X					Finland has no law neither prohibiting nor allowing SCNT.	The Scan Balt Stem Cell Research Network has been established with representatives from all the 11 countries in the Scan Balt BioRegion. http://www.scanbalt.org/sw222.asp
France			X	X			"Bioethics Law" (6 Aug 2004, amended Law No. 94-653 of July 29 1994, on Respect for the Human Body and Law No. 94-654 of July 29 1994, on the Donation and Use of Elements and Products of the Human Body, Medically Assisted Procreation, and Prenatal Diagnosis)	The new Bioethics Law received final approval of the government on 6 Feb 2006. The new law allows for 5 year licences to be issued to import HESC lines, to create new HESC lines from excess IVF embryos and to develop research programs. The law prohibits the creation of embryos for research including SCNT. www.agence-biomedecine.fr	

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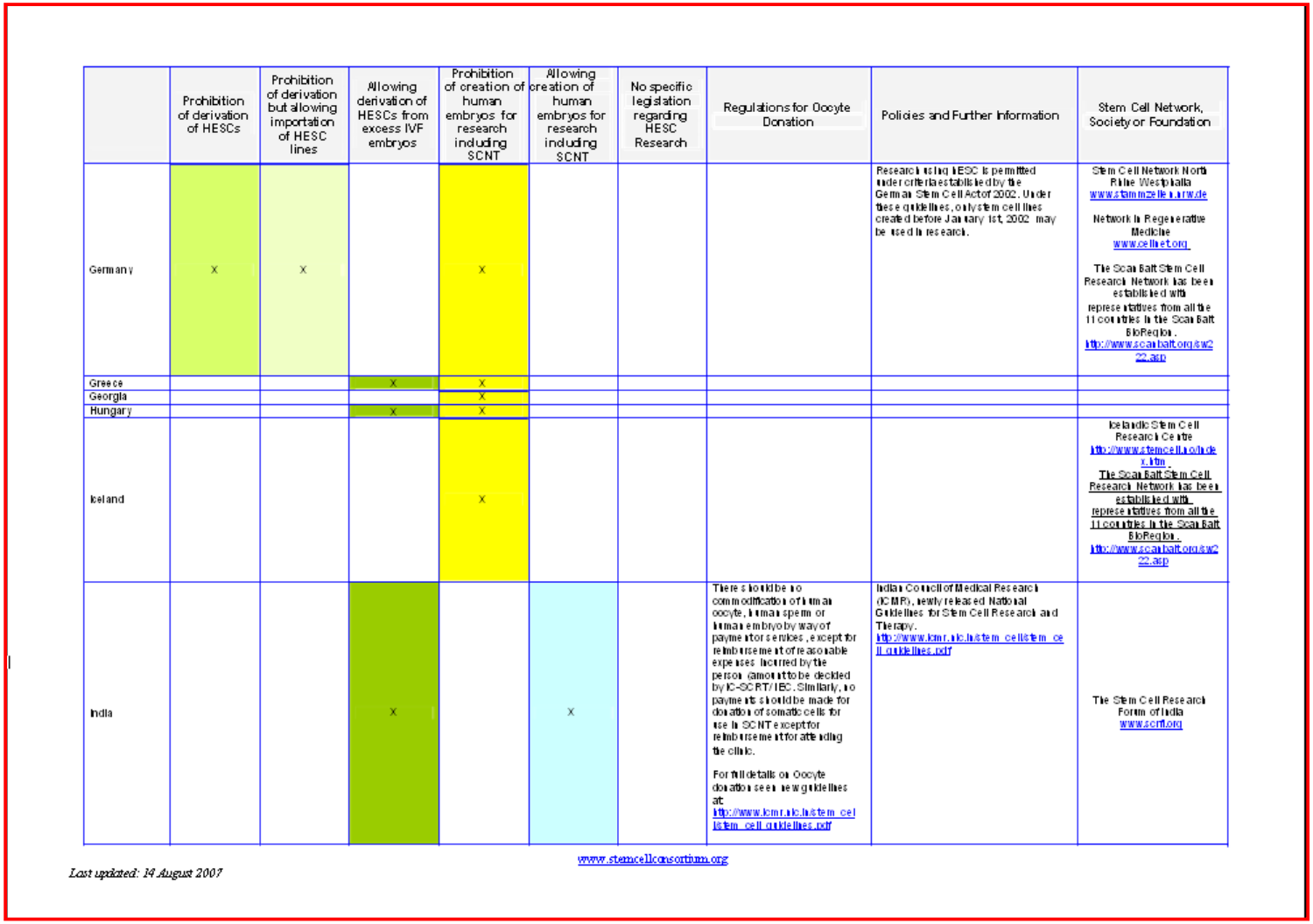

	Prohibition of derivation of HESCs	Prohibition of derivation but allowing importation of HESC lines	Allowing derivation of HESCs from excess IVF embryos	Prohibition of creation of human embryos for research including SCNT	Allowing creation of human embryos for research including SCNT	No specific legislation regarding HESC Research	Regulations for Oocyte Donation	Policies and Further Information	Stem Cell Network, Society or Foundation
Germany	X	X		X				Research using HESC is permitted under criteria established by the German Stem Cell Act of 2002. Under these guidelines, only stem cell lines created before January 1st, 2002 may be used in research.	Stem Cell Network North Rhine Westphalia www.stammzelle.nrw.de Network in Regenerative Medicine www.cellnet.org The ScanBalt Stem Cell Research Network has been established with representatives from all the 11 countries in the ScanBalt BioRegion. http://www.scanbalt.org/sw222.asp
Greece			X	X					
Georgia				X					
Hungary			X	X					
Iceland				X					Icelandic Stem Cell Research Centre http://www.stemcell.is/index.htm The ScanBalt Stem Cell Research Network has been established with representatives from all the 11 countries in the ScanBalt BioRegion. http://www.scanbalt.org/sw222.asp
India			X		X		There should be no commodification of human oocyte, human sperm or human embryo by way of payment or services, except for reimbursement of reasonable expenses incurred by the person (amount to be decided by IC-SCRT/IEC. Similarly, no payments should be made for donation of somatic cells for use in SCNT except for reimbursement for attending the clinic. For full details on Oocyte donation see new guidelines at: http://www.icmr.nic.in/stem_cell/stem_cell_guidelines.pdf	Indian Council of Medical Research (ICMR), newly released National Guidelines for Stem Cell Research and Therapy. http://www.icmr.nic.in/stem_cell/stem_cell_guidelines.pdf	The Stem Cell Research Forum of India www.scrfi.org

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	Prohibition of derivation of HESCs	Prohibition of derivation but allowing importation of HESC lines	Allowing derivation of HESCs from excess IVF embryos	Prohibition of creation of human embryos for research including SCNT	Allowing creation of human embryos for research including SCNT	No specific legislation regarding HESC Research	Regulations for Oocyte Donation	Policies and Further Information	Stem Cell Network, Society or Foundation
Ireland	X			X					
Israel			X		X		While SCNT for the derivation of cell lines is allowed, donation of oocytes is not permitted for research purposes, currently restricting this technology. From 9 May 07 the Knesset (Israeli Parliament) has started the process of approving egg donation for various purposes including research. The legal procedure is comprises of three following votes, the first of which has been accomplished	"Law 5759-1999 - Prohibition of Genetic Intervention (Human Cloning and Genetic Manipulation of Reproductive Cells)" (1999, amended March 2004).	The Israel Stem Cell Research Forum The Israel Stem Cell Society The Israeli Consortium Bereshith (Genesis) for Cell Therapy
Italy	X	X		X					
Japan			X					On 23 July 2004, Japan's Council for Science and Technology Policy (CSTP), the Government's top science and technology policy body approved the final report of its Bioethics Expert Panel on human embryo and stem cell research in Japan. The report recommended a change in Japanese policy to allow the creation of human embryos using therapeutic cloning techniques for stem cell research http://www.ottoglobalwatchonline.com/online_pdf/36704X.pdf http://www.ottoglobalwatchonline.com/online_pdf/36060X.pdf Japan's Ministry of Education, Culture, Sport, Science and Technology (www.mext.go.jp) is currently working to implement the reports recommendations. -	RIKEN Centre for Developmental Biology http://www.cdb.riken.jp/en/index.html
Lithuania	X			X					The Scan Balt Stem Cell Research Network has been established with representatives from all the 11 countries in the Scan Balt BioRegion. http://www.scanbalt.org/sw222.asp
Luxembourg						X			

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Latvia				X					The Scan Balt Stem Cell Research Network has been established with represe ntatives from all the 11 countries in the Scan Balt BioRegion . http://www.scanbalt.org/sw22.asp
Malta						X			
Mexico			X		X			Mexico reversed a previous ban on stem cell research in June 2004, creating the National Institute of Genomic Research (www.inmegen.org.mx) and permitting research on supernumerary embryos and allowing SCNT. .	
Netherlands			X	X					
Norway				X		X			Norwegian Center for Stem Cell Research http://www.stemcell.no/hcs.htm The Scan Balt Stem Cell Research Network has been established with represe ntatives from all the 11 countries in the Scan Balt BioRegion . http://www.scanbalt.org/sw22.asp
Poland						X			The Scan Balt Stem Cell Research Network has been established with represe ntatives from all the 11 countries in the Scan Balt BioRegion . http://www.scanbalt.org/sw22.asp
Portugal				X		X			
Russia			X		X				The Scan Balt Stem Cell Research Network has been established with represe ntatives from all the 11 countries in the Scan Balt BioRegion . http://www.scanbalt.org/sw22.asp

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Singapore			x		x		The Prohibition of Cloning and Other Prohibited Practices Act contains the following clause: Prohibition of commercial trading in egg, sperm and embryo This prevents the giving of valuable consideration such as money or gifts in exchange for a supply of egg, sperm or embryo, but does not refer to the reasonable reimbursement of expenses incurred or services provided in the collection, storage or transport of the tissue.	Human Cloning and Other Prohibited Practices Act came into effect on 1 October 2004	Singapore Stem Cell Consortium www.stemcell.edu.sg
South Africa			x		x			South Africa passed the National Health Bill (http://www.doh.gov.za/docs/bills/b32b.pdf) in late 2003 permitting HESC research on supernumerary embryos and embryos created specifically for stem cell research. SCNT is permitted and reproductive cloning is banned.	
South Korea			x		x			The Ministry of Science and Technology (http://www.most.go.kr/) coordinates research, both private and public. The Bioethics and Biosafety Act implemented in January 2005 prohibits reproductive cloning and the creation of embryos for non-reproductive purposes, but allows the use of supernumerary IVF embryos for research purposes, and SCNT.	
Spain			x		x			Spain's parliament passed a law to allow SCNT in June 2007.	The Spanish Ministry of Health (MSC), together with the Autonomous Communities, approved the creation of three research centres (July 2006): Cataloni a (CMRB), Andalusia (CABIMER) ,Valencia (Centro de Investigación Principe Felipe) www.cmrb.e.t, http://www.ocloa.ffb.es

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Sweden			X		X		This statute and the *In Vitro* Fertilization law of 1988 govern embryo research. Any research, which seeks to genetically modify the embryo, is prohibited. The statute implicitly prohibits embryo and oocyte cloning with criminal sanction. In December 2001, the Swedish Research Council declared that creating embryos through somatic cell nuclear transfer for therapeutic purposes "can be ethically defensible" which would require formulation of a legal framework by the Swedish government. http://www.ursr.se/fileserver/Index.asp?fil=LCK7HDEK3U6H		The ScanBalt Stem Cell Research Network has been established with representatives from all the 11 countries in the ScanBalt BioRegion. http://www.scanbalt.org/sw22.asp
Switzerland			X	X					Swiss Stem Cell Networks http://www.unine.ch/science/biologie/blanklesc/
Slovenia			X	X					
Slovakia				X		X			
Taiwan			X	X				Department of Health, "Ethical Regulations for Embryonic Stem Cell Research," 2002. – New legislation pending.	Taiwan Society for Stem Cell Research http://www.tsscr.org.tw/
Thailand						X		Medical Council of Thailand, "Regulations on Human Cloning No. 21/2544," June 2002. The regulations ban human reproductive cloning.	
UK			X		X		In Feb 2007 HFEA changed the regulations so that women are now allowed to donate eggs for research. Compensation is set at £250 Source : www.hfea.gov.uk	"Human Reproductive Cloning Act 2001," UK Stat. 2001 c23 & 1, (in force 4 December 2001). http://www.legislation.hmso.gov.uk/acts/acts2001/20010023.htm .	UK National Stem Cell Network www.uknsc.org Scottish Stem Cell Network www.sscn.co.uk North East England Stem Cell Institute www.nesci.ac.uk East of England Stem Cell Network www.escn.org.uk London Regenerative Medicine Network www.regenmednetwork.com

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	Prohibition of derivation of HESCs	Prohibition of derivation but allowing importation of HESC lines	Allowing derivation of HESCs from excess IVF embryos	Prohibition of creation of human embryos for research including SCNT	Allowing creation of human embryos for research including SCNT	No specific legislation regarding HESC Research	Regulations for Oocyte Donation	Policies and Further Information	Stem Cell Network, Society or Foundation
USA						X	The US has no federal legislation regarding human cloning and stem cell research. The only existing federal policy in this area is the Presidential ban on the use of federal funds for research on, or the creation of, new stem cell lines subsequent to his announcement of the ban on 9 Aug 2001. For full details see the NIH website at: http://stemcells.nih.gov/research/registry/eligibility/Criteria.asp Within the individual US States there is a huge variation of laws between the states. From California which has permissive laws for HESC research to states with an outright ban on HESC research to other states with no laws at all. See the National Conference of State Legislators for more information: http://www.ncsl.org/programs/health/Genetics/rt-clict.htm The Stem Cell Blog has produced a useful guide to state legislation called *What Color Is Your State?* It can be found at http://thestemcellblog.com . The US has the most developed and least regulated internal market for oocytes. Trading of oocytes for reproductive purposes common practice. For example, in 2002 11.4% of or ART procedures used oocytes purchased for fees of around $5000 per cycle. Moreover premiums are paid to vendors with additional desirable characteristics of sums up to $100,000 per cycle. Whilst the US has a large number of stem cell companies and privately funded stem cell research, as the states step in to fund research not funded federally many are imposing restrictions on paying for oocytes for stem cell research. For example, California which has committed $3 billion to stem cell research through Proposition 71 prohibits the paying for oocytes for research funded by the state.	California Institute for Regenerative Medicine www.cirm.ca.gov New York Stem Cell Foundation www.nyscf.org . Harvard Stem Cell Institute http://www.hsci.harvard.edu/

Prepared by the Australian Stem Cell Centre. Please email any amendments to to rebecca.skinner@stemcellcentre.edu.au

Sources:

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The status of hESC research legislation throughout Europe, at: www.hescreg.eu

Isasi, Rand Knoppers, B (2005). 'Mind the Gap: Policy Approaches to Embryonic Stem Cell and Cloning Research in 50 Countries', European Journal of Health Law Vol. 13, 9-26.

ISSCR International Legislation on Human Embryonic Stem Cell Research, at: http://www.isscr.org/public/regulationsindex.cfm .

StemCellWorldMap, at: http://www.lemsen.org/mapworld.cfm .

Stem Cells World Map, at: http://www.mbrc.umn.edu/stemmap.html .

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Updated February 2007

Regulations in EU Member States regarding hES[1] cell research

	AT	BE	BG	CY	CZ	DE	DK	EE	EL	ES	FI	FR	HU	IE	IT*	LT	LU	LV	MT	NL	PL	PT	RO	SE	SI	SK	UK
Allowing procurement of hES cells from super-numary embryos by law		X			X		X		X	X	X	X								X		X		X			X
Specific legislation for human embryo research incl. supernumerary embryos but without specific reference to hES cells								X					X					X							X		
Prohibiting procurement of hES cells from human embryos but allowing importation of hES cell lines						X									X												
No specific legislation regarding hES cell research	X		X	X										X		X	X		X		X		X			X	
Allowing creation of human embryos for procurement of hES cells by law		X																						X			X
Prohibiting creation of human embryo for research purpose and for procurement of hES cells by law or by ratification of the Convention of the Council of Europe on Human rights and Biomedicine signed in Oviedo on 4 April 1997			X	X	X	X	X	X	X	X	X	X	X		X	X	X	X		X	X	X	X	X	X	X	

1) hES cells = human Embryonic Stem cells *IT has no law regarding the importation & IT scientists are working on imported hES cell lines

COUNTRY CODE KEY:

AT : Austria
BE : Belgium
BG: Bulgaria
CY : Cyprus
CZ : Czech Republic
DE : Germany
DK : Denmark
EE : Estonia
EL : Greece
ES : Spain
FI : Finland
FR : France
HU : Hungary
IE : Ireland
IT : Italy
LT : Lithuania
LU : Luxembourg
LV : Latvia
MT : Malta
NL : Netherlands
PL : Poland
PT : Portugal
RO: Romania
SE : Sweden
SI : Slovenia
SK : Slovakia
UK : United Kingdom

7. Regulations in EU Member States regarding hES Cell Research

8. PRC Regulations on Informed Consent and Protection of Human Subjects in Biomedical Studies

Note: *This translation by a Chinese scholar is unofficial and for information only. Only the Chinese text is official.*
(Source: http://www.usembassy-china.org.cn/sandt/PRCpatient-protection.html)

"Guidelines on Ethical Review of Medical Research" promulgated by the Committee on Research Involving Human Subjects, The Ministry of Health and enforced on December 1, 1998

Chapter 3: Informed Consent

Article 10: All biomedical research involving human subjects must obtain written informed consent from human subjects. For incompetent, guardian's consent or proxy consent must be obtained.

Article 11: In research involving children researcher must confirm:
- Children should not participate in the same research as adults;
- The purpose of the research is to obtain the knowledge that is necessary for their health;
- Researcher must obtain the written consent from parent or guardian of each child;
- The child's denial to participate in research must be respected;
- The possible harm or risk to children should be reduced to the minimum;
- In therapeutic research the efficacy should not be lower than existing therapy.

Article 12: In research involving mental patients researcher must confirm:
- For incompetent, researcher must obtain the written consent from guardian;
- In therapeutic research the efficacy should be lower than existing therapy;
- The purpose of the research is for obtaining the knowledge necessary for health need of mental patients;
- The patient's denial to participate in research must be respected;
- The possible harm or risk to patients should be reduced to the minimum.

Article 13: Biomedical research involving population
- The research should be relevant to the health need of the population;
- Necessary measures must be taken to guarantee full understanding of the research by the individuals in the population;
- Protocol must be reviewed and approved by Ethics Committee, and reported to the local health administration for review and approval;
- In the case that it is impossible to get the consent from individuals of the population, Ethics Committee should review whether the research can be conducted, and whether the research has taken measures to protect the safety of the population and individual privacy;
- The researcher must not take undue measures to force or influence those who are not willing to participate in the research;
- The researcher must obtain the written consent from individuals in the population. For those who are incompetent, the researcher must obtain the written consent from the guardian.

Chapter 4: Obligations of Researchers

Article 15: The researcher should respect human subjects.
Sufficient time should be given to human subjects to ask questions and give answers; must not use cheating, threat and other undue means to human subjects; must provide adequate and relevant information and knowledge to human subjects, and give them adequate time to consider, and then ask them to make decision of whether to consent to participate in the research; only when the informed consent signed by human subject is obtained, it can be judged that the human subject consents to participate in the research; when the procedure or condition of the research is changed, the change must be explained to human subjects in details, and the consent must be obtained again from them.

Article 16: Biomedical research involving pregnant and lactating women.
In principle, pregnant and lactating women cannot be human subjects of biomedical research, except the research for protecting and promoting the health of pregnant and lactating women, fetuses or newborns. All researches must not do harm to fetuses or newborns.

Chapter 5: Interests and Rights of Human Subjects

Article 17: Researcher should commit to give certain compensation or free medical services to human subjects, but the amount or services should not constitute an inducement to human subjects. Providing compensation or free medical services to human subjects must be approved by the Ethics Committee.

Article 18: Keeping confidentiality and protecting privacy. Perfect confidential measures must be taken to the research materials. The researcher must not disclose anything involving the privacy of human subjects to media. The researcher should disclose human subjects the use of future materials prior to the research, and report to the Ethics Committee.

Article 19: Financial compensation
Those human subjects who got temporary or permanent harm owing to participating the research should get treatment and financial compensation; if the death of human subject is caused, her/his family should get compensation. Any research, any institution or any individual must not deprive this right from human subjects.

Chapter 8: Administration

Article 25: The following researches and activities are prohibited:
- Scientific experimentation involving human asexual reproduction;
- Research of using human embryo and aborted fetus;
- Exchange aborted fetus and its organ with foreign countries;
- Buying and selling human cells, tissues and organs.

9. Revised Guidelines on Ethical Review of Biomedical Research involving human subjects, January 2007

With the establishment of a new Ethics Committee of the Ministry of Health, the Guidelines above were revised as follows:

Chapter 1: General Provisions

Article 1: The guidelines are stipulated for protecting human dignity, life and health, for abiding basic ethical principles and for promoting the development of biomedicine, molecular biology and genetic engineering.

Chapter 3: Informed Consent

Article 8: All biomedical research involving human subjects must obtain written informed consent from human subjects in advance. For incompetent, guardian's consent or proxy consent must be obtained.

Article 9: In research involving children researcher must confirm:

- Children should not participate in the same research as adults;
- The purpose of the research is to obtain the knowledge that is necessary for their health;
- Researcher must obtain the written consent from parent or guardian of each child;
- The child's denial to participate in research must be respected;
- The possible harm or risk to children should be reduced to the minimum;
- In therapeutic research the efficacy should not be lower than existing therapy.

Article 10: In research involving mental patients researcher must confirm:

- For incompetent, researcher must obtain the written consent from guardian;
- In therapeutic research the efficacy should not be lower than existing therapy;
- The purpose of the research is for obtaining the knowledge necessary for health need of mental patients;
- Researcher should obtain the consent from patients according to their competency.
- The patient's denial to participate in research must be respected;
- The possible harm or risk to patients should be reduced to the minimum.

Article 11: Biomedical research involving population

- The research should be relevant to the health need of the population;
- Necessary measures must be taken to guarantee full understanding of the research by the individuals in the population;
- Protocol must be reviewed and approved by Ethics Committee, and reported to the local health administration for review and approval;
- In the case that it is impossible to get the consent from individuals of the population, Ethics Committee should review whether the research can be

conducted, and whether the research has taken measures to protect the safety of the population and individual privacy;
- The researcher must not take undue measures to force or influence those who are not willing to participate in the research;
- The researcher must obtain the written consent from individuals in the population.
- For those who are incompetent, the researcher must obtain the written consent from the guardian or legal proxy.

Chapter 4: Obligations of Researchers

Article 12: Researcher must provide human subject the following information before obtaining consent from them:

- Purpose of the research and its method;
- Time of participation for human subject;
- Its possible benefits to human subject or other groups;
- Possible harms or discomfort to human subject;
- Whether there is other similar or better approach;
- How to keep confidentiality of her/his records;
- Scope of researcher's responsibility for providing health care;
- Providing free medical treatment for the harm relevant to the research;
- Compensation to human subject or her/his family members when disability or death is caused by the research;
- Human subject can deny to participate in research or withdraw at any stage of Research, researcher cannot use it as an excuse to infringe upon her/her rights and interests.

Article 13: The researcher should respect human subjects.
- Sufficient time should be given to human subjects to ask questions and give answers;
- must not use cheating, threat and other undue means to human subjects;
- must provide adequate and relevant information and knowledge to human subjects, and give them adequate time to consider, and then ask them to
- make decision of whether to consent to participate in the research;
- only when the informed consent signed by human subject is obtained, it can be judged that the human subject consents to participate in the research;
- when the procedure or condition of the research is changed, the change must be explained to human subjects in details, and the consent must be
- obtained again from them.

Article 14: Biomedical research involving pregnant and lactating women.
In principle, pregnant and lactating women cannot be human subjects of biomedical research, except the research for protecting and promoting the health of pregnant and lactating women, fetuses or newborns. All researches must not do harm to fetuses or newborns.

- Chapter 5: Interests and Rights of Human Subjects

Article 15: Researcher should commit to give certain compensation or free medical services to human subjects, but the amount or services should not constitute an inducement to human subjects. Providing compensation or free medical services to human subjects must be approved by the Ethics Committee.

Article 16: Keeping confidentiality and protecting privacy. Perfect confidential measures must be taken to the research materials. The researcher must not disclose anything involving the privacy of human subjects to media. The researcher should disclose human subjects the use of future materials prior to the research, and report to the Ethics Committee.

Article 17: Financial compensation
Those human subjects who get temporary or permanent harm owing to participating in the research should get treatment and financial compensation; if the death of human subject is caused, her/his family should get compensation. Any research, any institution or any individual must not deprive this right from human subjects.

10. Law on Practicing Doctors, promulgated by National People's Congress and entered into effect on on May 1, 1999.

Chapter: Legal Accountabilities

Article 8: Conduct experimental clinical treatment without the consent from the patient or her/his family member.

Article 9: Disclosure of patient's privacy and cause serious consequences.

Drug Clinical Trial Administration Norms

On September 1, 1999 Mr. Zheng Xiaoyu, the Director of National Drug Regulation Administration promulgated Drug Clinical Trial Administration Norms. The Administration stipulated that any drug that want to be marketed in China has to be passed in an authorized center for pharmaceutical clinical trial, and the protocol must be reviewed by the Ethics Committee.

Chapter 1: General Provisions

Article 1: In order to guarantee the standardization of drug clinical trials, make the results scientific and reliable, and protect the rights and interests of human subjects and safeguard their safety, laid down the Norms according to the Law of Drug Regulation of the People's Republic of China and with reference to international accepted principles.

Chapter 2: Preparation before Clinical Trial and Necessary Conditions

Article 4: All researches involving human subjects must comply to ethical principles in Helsinki Declaration and CIOMS' International Ethical Guidelines on Biomedical Research Involving Human Subjects, i.e. justice, respect, maximum benefits to human subjects, and avoidance of harms as far as possible.

Chapter 3: Guarantee the Rights and Interests of Human Subjects

Article 8: In the process of drug clinical trials the individual rights and interests of human subjects must be safeguarded, and the research must be scientific and reliable as well. Ethics Committee and informed consent are major measures to guarantee human subjects' rights and interests.

Article 9: In order to guarantee human subjects' rights and interests Ethics Committee should be set up in the medical institutions conducting clinical trials. Ethics Committee should have its members from non-medical profession, law and other institutions. The number of members is five at least with different genders. The composition and work of Ethics Committee should be relatively independent from and not be intervened by any researcher.

Article 10: Before the clinical trials the protocol should be reviewed, and approved by Ethics Committee with signatures, and then it can be performed. In the period of trial any change of the protocol should be approved by Ethics Committee, and then it can be performed. Any serious adverse event in the trial should be reported to Ethics Committee.

Article 12: Ethics Committee should strictly review the following points of the protocol from the perspectives of safeguarding the rights and interests of human subjects:

(1) Qualifications and experiences of researchers, whether they have sufficient time to conduct clinical trial in question, whether the personnel and equipments conform to the requirements.

(2) Whether the protocol is appropriate, including purpose, possible harm/risks and benefits to human subjects and others, and whether the design of trial is scientific.

(3) Whether the procedure of human subjects' enrollment is appropriate, the procedure of providing information to human subjects or her/his family member, or her/his guardian or legal proxy is full and understandable, and the procedure of obtaining her/his written informed consent is appropriate.

(4) Providing treatment and giving compensation when human subjects are harmed or died because of their participation in the trial.

(5)The acceptability of the revision of the protocol.

(6)Regularly review the risks to human subjects during the process of clinical trials.

Article 14: Researcher or her/his designated representative must explain the relevant information on clinical trial to human subjects:

(1) The participation of human subject in clinical trial is voluntary, and at any stage of trial, human subject has right to withdraw without discrimination or retaliation, her/his medical treatment and rights/interests won't be affected.

(2) Must make human subject understand her/his individual materials about her/his participation in, and obtained in the trial are confidential. Ethics Committee, Drug Regulation Administration and researchers can get access to these materials when necessary according to the regulations.

(3) Purpose, process and period of the trial, procedures of examination, expected possible harm/risks, inconveniences and benefits to human subject, and the possibility of her/his assigned to different groups in the trial.

(4) Human subject can get access to the relevant information at any time. Must give sufficient time to human subject to consider her/himself whether to participate in the trial. For incompetent human subject, information should be provided to her/his legal proxy. In the process of informed consent should be used the language and words that are understandable to human subject.

(5) When there is harm relevant to the trial, treatment and appropriate compensation will be provided to human subject.

Article 15: The written informed consent form be obtained after full and detailed explanation of the trial.

(1) The written informed consent form should be signed and dated by human subject or her/his legal proxy, and by the researcher or her/his representative too.

(2) In the case that the human subject or her/his legal proxy is illiterate, there should be one witness who is present in the all process of informed consent. After detailed explanation of the written informed consent form, human subject or her/his legal proxy expresses the consent orally, it should be signed and dated by the witness.

(3) If Ethics Committee agrees in principle with researcher who judges that the participation of incompetent human subjects in the trial will be in their interests, these patients are permitted to enter into the trial, and the informed consent form should be signed and dated by their legal proxy.

(4) If the informed consent is not obtained from human subject, witness or guardian, researcher must record this situation and the detailed reasons of why the consent is not obtained in the file and sign on it.

(5) If new important materials relevant to drug in trial are found, the informed consent form must be revised and submitted to Ethics Committee for approval, and be got consent form human subject again.

11. Management Methods on Clinical Applications of Medical Technologies

MOH, May 1, 2009 Information released by MOH and translated by RC-UK office

Recently, the Ministry of Health has released and distributed *the Management Methods on Clinical Application of Medical Technologies*, clarifying that the state shall set up regulations on entry and management of clinical application of medical technologies so as to manage the medical technologies by classes and grades. The Ministry of Health shall be responsible for the approval and clinical application management of Class III medical technologies with high risks, as well as formulation and adjustment of the Content of Class III Medical Technologies. The Methods will be implemented from May 1.

The gene cloning technology will not be applied clinically for the time being.

The heterogenic stem cell treatment technology, xenogeneic treatment technology, human body cell cloning technology and the like shall not be applied clinically for the time being. In addition, as for the Class III medical technologies that have been put into in clinical application before the Methods is promulgated, the medical institutions shall submit an inspection application to technology inspection and approval authority within 6 months after the Methods is promulgated. If any medical institution fails to do so or the health administrative authority determines not to register such medical technologies under the diagnosis and treatment items, the clinical application of all Class III medical technologies shall be stopped.

Before Class III medical technologies are clinically applied for the first time, they shall pass through the safety demonstration and ethical inspection organized by the Ministry of Health. Before Class II and Class III medical technologies are clinically applied, they shall pass through the technical inspection made by the third party. When the medical workers clinically apply Class I medical technologies, the medical institution can inspect such technologies by itself or comply with the regulations stipulated by health administrative authority at provincial level. The technology inspection authority designated or established by the Ministry of Health or health administrative authority at provincial level shall be respectively responsible for inspecting the clinical application capability of Class III and Class II medical technologies. The Ministry of Health can also appoint the health administrative authority at provincial level to inspect the designated Class III medical technologies.

The technology inspection authority shall establish expert database in line with actual needs. The inspection work system, procedure and list of the expert database shall be submitted to health administrative authority that appoints it to do the inspection for file. Members of the technical inspection expert database shall include experts in the fields of medicine, law, ethics, management, etc. Employment of such experts by the inspection authority will not be restricted by administrative regions. When members of the expert database inspect technologies, the Avoidance System and Responsibility Seeking System shall be implemented.

Class III medical technologies

Medical technologies involving significant ethical problems with safety and validity needing further demonstration by standard clinical tests and studies: Cloning

treatment technology, autogeneic stem cell and immunocyte treatment technology, gene treatment technology, treatment of drug addiction by operation in central nervous system, technology on treating insanity by stereotactic surgery, allogenic stem cell transplantation technology, tumor vaccine treatment technology, etc.

Medical technologies involving significant ethical problems, but with ensured safety and validity: homorganic transplantation, transsexual operation, etc.

Medical technologies involving high risks with safety and validity either needing further demonstration or already ensured: technology of ablation treatment by large-sized instrument and equipment such as particle generator, treatment technology of radioactive particle implantation, tumor hyperthermia technology, tumor cryotherapy technology, tissue and cell transplantation technology, artificial heart implantation technology, technology of auxiliary diagnosis and treatment by artificial intelligence, etc.

Other medical technologies that need special management: gene chip diagnosis and treatment technology, distraction osteogenesis treatment technology, xenogeneic organic transplantation technology, etc.

12. Ministry of Health Procedures for Ethical Review of Human Biomedical Research (Provisional)

Chapter 1: General Provisions

1. In order to protect human dignity, protect human lives and health, follow the basic principles of ethics, and promote the development of biomedicine, molecular biology, and genetic engineering, the Ministry of Health establishes the following provisions.

2. Ethical review is based upon the basic principles of ethics accepted by the international community. It takes into consideration the current status and future progression of medical, pharmaceutical, health, science, and technology development in China. It conducts review, and provides conclusive evaluations of medical scientific research related to human subjects.

3. Ethical review is a serious responsibility. It should be a principled, fact-based evaluation, conducted consistently. It should rely on expert knowledge, encourage consensus, and seek objectivity.

4. The Ethics Committee has responsibility for second review of the research process, the conclusion, and the thesis content, in addition to its responsibility for review of proposed scientific research projects.

5. The Ministry of Health regulatory authority manages ethical review of human research in all health professions. The health bureau regulatory authority in each province, autonomous region, and directly-administered city has jurisdictional authority for ethical review of human research.

6. The relationship between the administrative function of the Ministry of Health Ethics Committee for human biomedical research and the local government ethics committees is not superior-to-subordinate but one of professional guidance.

Chapter 2: Scope of Review

7. Scientific research projects to be financed by the Ministry of Health, and scientific research projects with international cooperation or introduced from abroad are the main scope of this review.

8. Mature health service technologies and products accepted in China and abroad without ethical dispute are not subject to this review.

9. Scientific projects that violate national law or regulatory code shall not be accepted for ethical review.

Chapter 3: Informed Consent

10. Human biomedical research requires informed consent from all subjects. For individual subjects who are not competent to give consent, consent must be given by a guardian or legal representative.

11. For all research involving children, the investigators must confirm that:

- Children do not participate in studies for adult subjects;
- The aim of the research is to gain knowledge of children's health needs;
- They obtain written informed consent from parents or legal guardians of all minor subjects;
- A minor subject's refusal to participate in the research is respected promptly, unless the equipment or procedure used in the study cannot be replaced by any other equipment or procedure;
- Investigators minimize the risk of harm to children, and balance any risk against the importance of the research data;
- Research of therapeutic efficacy has predicted efficacy no lower than currently available therapies.

12. For research on patients with mental diseases or behavioral disorders, investigators must confirm that:

- For patients who are incompetent to give informed consent, investigators obtain informed consent from a guardian or legal representative;
- Research on therapeutic efficacy has predicted efficacy no lower than currently available therapies;
- The research aim is related to obtaining specialized knowledge of the mental disease or behavioral abnormality;
- Investigators obtain consent based upon the capacity of patients to understand their choices, and that patient refusal to participate in non-clinical* research be respected;
- The risk imposed on patients by any research equipment or procedure be minimized, and not be higher than the importance of obtaining the research data.

13. Provisions of human biomedical research:

- Research must relate to human health;
- Measures must be taken to assure that individuals who participate in the study have sufficient understanding of the research;
- Research protocols must be reviewed and approved by the Ethics Committee, and submitted to the local health authority for approval;
- If investigators are unable to obtain individual informed consent from research subjects for objective reasons, the Ethics Committee should evaluate the research to determine whether accepting the patient without individually signed informed consent is consistent with ethical principles, and whether investigators have taken the necessary measures to protect human safety and privacy;
- If an individual is not willing to participate in the study, the investigator must not take any inappropriate measures to influence or coerce the subject to participate;

* The Chinese text reads “non-clinical,” but the translator believes it is in error, and should read “clinical.”

- The investigator must obtain written informed consent from each research subject. For individuals who lack comprehension, written informed consent must be obtained from the subject's guardian or legal representative.

Chapter Four: Investigator's Responsibilities

14. The investigator must provide each subject the following information before obtaining consent from the subject:
    - The aim of the research, and the procedures to be followed;
    - The expected duration of the subject's participation;
    - Anticipated benefits to the subject or others which may result from the research;
    - Description of any possibility of foreseeable risk or discomfort to the subject;
    - Description of any alternative procedures, or courses of treatment, if any, that might be advantageous to the subject;
    - Description of the extent of confidentiality of the subject's medical records;
    - Description of the range of medical treatments or services available to the subject;
    - Assurance that the subject will be treated without charge if the study procedure causes any injury or illness;
    - Whether any benefits or compensation will be paid to subjects or their survivors by the investigator in the event the study procedure causes death or disability to subjects;
    - Assurance that individuals have the right to refuse participation in the study, and subjects have the right to discontinue participation at any stage of the study, without penalty or loss of benefits to which they are otherwise entitled.

15. The investigator should respect subjects, allow subjects enough time to ask questions, and answer their questions. Investigators should not use deception, threat, or other inappropriate means to treat their subjects. Investigators may only ask subjects to consent to participate in the study after providing them sufficient information and knowledge relating to the study, and allowing sufficient time for consideration. Subjects are only considered to have consented to participate in the study after investigators have received signed informed consent documents from the subjects.

When the extent or conditions of the research changes, the investigator must explain the new facts to each subject individually, and re-obtain written informed consent.

16. **Issues concerning biomedical research on pregnant women and nursing women**. In principle, pregnant women and nursing women are forbidden to be the subjects of human biomedical research. There are, however, exceptions for research to protect and promote the health of pregnant women, nursing women, fetuses, and newborn children. Such studies, however, must not present risk to fetuses or newborn children.

Chapter 5: Subjects' Rights

17. Investigators should provide subjects reasonable compensation for participation, as well as medical treatment free of charge. However, the money paid and services provided to the subjects should not be so high as to create an enticement for subjects to participate in the study. Payments and the medical treatment provided by the investigator must be approved by the Ethics Committee.

18. **Confidentiality and privacy protection: study records**. The investigator must establish secure safeguards for the confidentiality of study records. The investigator must not release to the public media any information related to the subject's privacy. Prior to beginning the study, the investigator should fully disclose to the subjects the future use of the research data, as well as the regulatory authority to which the data are submitted.

19. **Compensation to the Subjects**. Subjects should receive adequate treatment and compensation for any trial-related injury, whether temporary or permanent. In the event of death, the subject's family should be compensated. The investigator and sponsoring organization or individual must not deprive subjects of this right.

Chapter 6: Ethics Committee

20. The Ethics Committee is established and approved by the Ministry of Health to be responsible for human biomedical research. The Committee consists of specialists and scholars in the field of health administration, science and technology management, genetics, law, philosophy, biostatistics, traditional Chinese medicine, pharmacy, modern medicine, biomedical engineering, and hygiene. Specialists in the same field as the proposed research should conduct the ethical review for any project related to human biomedical research. These projects include medical, pharmaceutical and health-science research projects that have bilateral or multilateral international collaboration. The Committee also is responsible for participation in ethics training programs. Review is conducted in meetings of the Committee.

21. Each provincial, autonomous-regional or directly-administered-city health bureau shall establish an Ethics Committee in accordance with Section 20. Provinces that have not met the conditions may entrust ethical review to a committee of experts.

Chapter 7: Review Procedures

22. For projects requiring ethical review, the sponsoring organization or individual must complete the "Application for Human Biomedical Research Ethical Review" in triplicate, and submit it to the Ministry or Health Ethics Committee or the sponsor's local Ethics Committee. The Ministry of Health provides the application format.

23. The Ethics Committee should provide a written response within three months of receipt of the application. There are three possible results: 1) approval, 2) rejection, and 3) approval after revision. Reasons for the decision are described separately. Approval documents must be signed by the director of the Ethics Committee.

24. Three copies of the approval document must be maintained: by the office of the Ethics Committee, by the science or technology regulatory authority responsible for the project, and by the applicant.

Chapter 8: Management

25. The following research and associated activities are forbidden:

- Scientific research related to human asexual reproduction (cloning reproduction);
- The use of human embryonic and fetal tissues from abortion or miscarriage, with the exception of placenta from natural birth, in research and development of products.
- International trade in fetal tissues from abortion or miscarriage, and internal organs;
- Buying or selling human cells, human tissue, and internal organs.

26. **Ethical review and management related to internationally-collaborative human medical experiments**. Before Chinese medical, pharmaceutical, or health-research organizations, or individual investigators apply to conduct human biomedical research in other countries, they must obtain approval of the Ministry of Health Ethics Committee and the approval of the Department of National Health Administration. Foreign organizations or individuals that apply to conduct human biomedical research in China must submit approval documents from the ethics committee or government department in their own country to the corresponding Chinese department, and apply for Ministry of Health Ethics Committee review and Ministry of Health approval.

Chapter 9: Legal Responsibility

27. When a violation of ethical principles in human experimental research is discovered by the Ministry of Health or a local Ethics Committee, it has the obligation to report the violation to the government science or technology regulatory authority, to stop the violation.

28. When violation of the principles of conducting human biomedical research causes significant human harm to the subjects or their fetuses, the investigator should be subjected to administrative and financial penalty. For serious cases, the matter shall be referred to the judicial system.

Chapter 10: Supplemental Principles

29. This interpretation of ethical review is courteously provided by the Ministry of Health Human Biomedical Research Ethics Committee.

30. These procedures are effective as of 1998.

Appendix 4: Ministry of Health Ethics Committee Regulations for Human Biomedical Research

1. In order to reinforce the management of biomedical research ethics, to meet ethical standards of biomedical research, and to be responsible for the public health, the Ministry of Health established the Ministry of Health Biomedical Research Ethics Committee based upon "Ministry of Health Ethics Review for Human Biomedical Research."

2. The Ministry of Health Biomedical Research Ethics Committee is entrusted by the National Health Administration regulatory authority to be the national consulting body for ethical review of biomedical research. Its professional leadership is guided by the Ministry of Health Department of Scientific Education.

3. The Committee has one director, one associate director, and nine committee members. Committee members include specialists in the fields of clinical medicine, preventive medicine, basic medicine, pharmaceuticals and medical devices, medical ethics, and law.

4. Appointment and dismissal of Committee members are determined by the Ministry of Health. Each term is for four years, and is renewable. To preserve continuity of the Committee's mission, no more than three new members should be appointed when the terms expire.

5. Administration of the Committee is established at the Center for Ethics Research at Beijing Medical University's office of Medical Technology Evaluation.

6. Committee responsibilities include:
   - To accept the research of the National Health Administrative regulatory authority for biomedical research related to ethical issues and provide consulting and opinions;

- To conduct ethical review of human medical research projects that are funded, and offered for competitive bid, by the Ministry of Health;
- To conduct ethical review of projects related to human medical and scientific research that are funded, and offered for competitive bid, by the national government through the Ministry of Health;
- To conduct ethical review of new medical technology including medical devices and pharmaceuticals introduced from abroad;
- To conduct ethical review of new medical technology that will be distributed throughout the country;
- To conduct ethical review of human biomedical scientific research projects in three forms of private enterprises (wholly-owned company, joint venture, and partnership) and state-owned enterprises located in the territory of the Peoples Republic of China;
- To sign and issue the ethical opinions of reviewed projects.

7. The director or associate director of the Committee convenes working meetings and project review meetings.

8. In the course of project review, the Committee members must hold serious, conscientious, and impartial attitudes towards the projects that are submitted for review, and offer objective review opinions.

9. Committee members shall deliver their opinions of projects submitted for review within three months after receipt of the review documents.

10. Projects that are submitted for review may be signed as approved, and issued, only after more than fifty percent of the members who participate give approval. The director of the Ethics Committee signs and issues the ethical review opinion for the biomedical research Ethics Committee.

11. The Ethics Committee members should avoid reviewing the document if there is any conflict of interest with the project under review. Committee members must not quote or reveal research data under review.

12. The Ministry of Health may move to dismiss any member who does not comply with this regulation or who is not capable of conducting the review. If more than two-thirds of the Committee members then vote to pass the motion, that member is removed from the Committee.

13. The Ministry of Health has sole authority to interpret these regulations.

14. These regulations are effective as of the date of approval by the Ministry of Health.

13. Regulations for Implementation of the Drug Administration Law of the People's Republic of China[1]

State Council, 2002

Chapter V: Control over Drugs

Article 28: Institutions for non-clinical safety evaluation and study of drugs shall implement the Good Laboratory Practice for Non-Clinical Laboratory Studies (GLP) and institutions for drug clinical trial shall implement the Good Clinical Practice (GCP). The GLP and GCP shall be formulated by the drug regulatory department under the State Council through respective consultation with the science and technology administrative department under the State Council and the health administrative department under the State Council.

Article 29: Clinical trials, manufacturing or importation of drugs shall be in conformity with the provisions in the Drug Administration Law and in the Regulations, and shall be reviewed and approved by the drug regulatory department under the State Council. The drug regulatory department under the State Council may authorize the drug regulatory department of the people's government of the province, autonomous region or municipality directly under the Central Government to conduct site inspection of research and development conditions of the drugs being applied, to conduct preliminary review of the submitted dossier, and to test the pilot samples. The specific measures therefore shall be formulated by the drug regulatory department under the State Council.

Article 30: Any clinical trial to be conducted for research and development of a new drug shall be subject to the approval by the drug regulatory department under the State Council in accordance with the provisions in Article 29 of the Drug Administration Law. When an application for conducting clinical trials is approved by the drug regulatory department under the State Council, the applicant shall select institutions for clinical trials from the lawfully certified ones to conduct the trials, and make a report thereof to the drug regulatory department and health administrative department under the State Council for the record. Prior to the drug clinical trial, the institution for drug clinical trial shall provide the subjects or their guardians with the truthful information on the trial, and obtain a written informed consent.

Article 31: For production of a drug admitted by national drug standards, an application shall, in accordance with the provisions of the drug regulatory department under the State Council, be submitted to the drug regulatory department of the people's government of the province, autonomous region or municipality directly under the Central Government or to the drug regulatory department under the State Council, and the relevant technical data and supporting documents shall be provided. The drug regulatory department of the people's government of the province, autonomous region or municipality directly under the Central Government shall, within 30 working days from the date it receives the application, review and make comments, and report the matter to the drug regulatory department under the State Council for review while notifying the applicant of its comments. If all the requirements are fulfilled upon review, a drug approval number shall be issued by the drug regulatory department under the State Council.

[1] http://eng.sfda.gov.cn/cmsweb/webportal/W45649038/A48335997.html

14. Drug Clinical Trial Guidelines (China)

Chinese State Food and Drug Administration, Promulgated 1999 / 2000
Unofficial translation published by the website of the Chinese bioethics network, sponsored by the Chinese Society for Philosophy of Science:
www.chinaphs.org/bioethics/regulations_&_laws.htm

Chapter 1: General Provisions

Article 1: In order to guarantee the standardization of drug clinical trials, to make the results scientific and reliable, and to protect the rights and interests of human subjects and safeguard their safety, stipulated the Regulations according to the Law of Drug Regulation of the People's Republic of China and with reference to international accepted principles.

Chapter 2: Preparation before Clinical Trial and Necessary Conditions

Article 4: All researches involving human subjects must comply to ethical principles in Helsinki Declaration and CIOMS' International Ethical Guidelines on Biomedical Research Involving Human Subjects, i.e. justice, respect, maximum benefits to human subjects, and avoidance of harms as far as possible.

Chapter 3: Guarantee the Rights and Interests of Human Subjects

Article 8: In the process of drug clinical trials the individual rights and interests of human subjects must be safeguarded, and the research must be scientific and reliable as well. Ethics Committee and informed consent are major measures to guarantee human subjects' rights and interests.

Article 9: In order to guarantee human subjects' rights and interests Ethics Committee shall be set up in the medical institutions conducting clinical trials. Ethics Committee shall have its members from non-medical profession, law and other institutions. The number of members is five at least with different genders. The composition and work of Ethics Committee shall be relatively independent from and not be intervened by any researcher.

Article 10: Before the clinical trials the protocol shall be reviewed, and approved by Ethics Committee with signatures, and then it can be conducted. In the period of trial any change of the protocol shall be approved by Ethics Committee, and then it can be conducted. Any serious adverse event in the trial shall be reported to Ethics Committee.

Article 12: Ethics Committee shall strictly review the following points of the protocol from the perspectives of safeguarding the rights and interests of human subjects:

(1) Qualifications and experiences of researchers, whether they have sufficient time to conduct clinical trial in question, whether the personnel and equipments conform to the requirements.

(2) Whether the protocol is appropriate, including purpose, possible harm/risks and benefits to human subjects and others, and whether the design of trial is scientific.
(3) Whether the procedure of human subjects' enrollment is appropriate, the procedure of providing information to human subjects or her/his family member, or her/his guardian or legal proxy is complete and understandable, and the procedure of obtaining her/his written informed consent is appropriate.
(4) Providing treatment and giving compensation when human subjects are injured or died because of their participation in the trial.
(5) The acceptability of the revision of the protocol.
(6) Regularly review the risks to human subjects during the process of clinical trials.

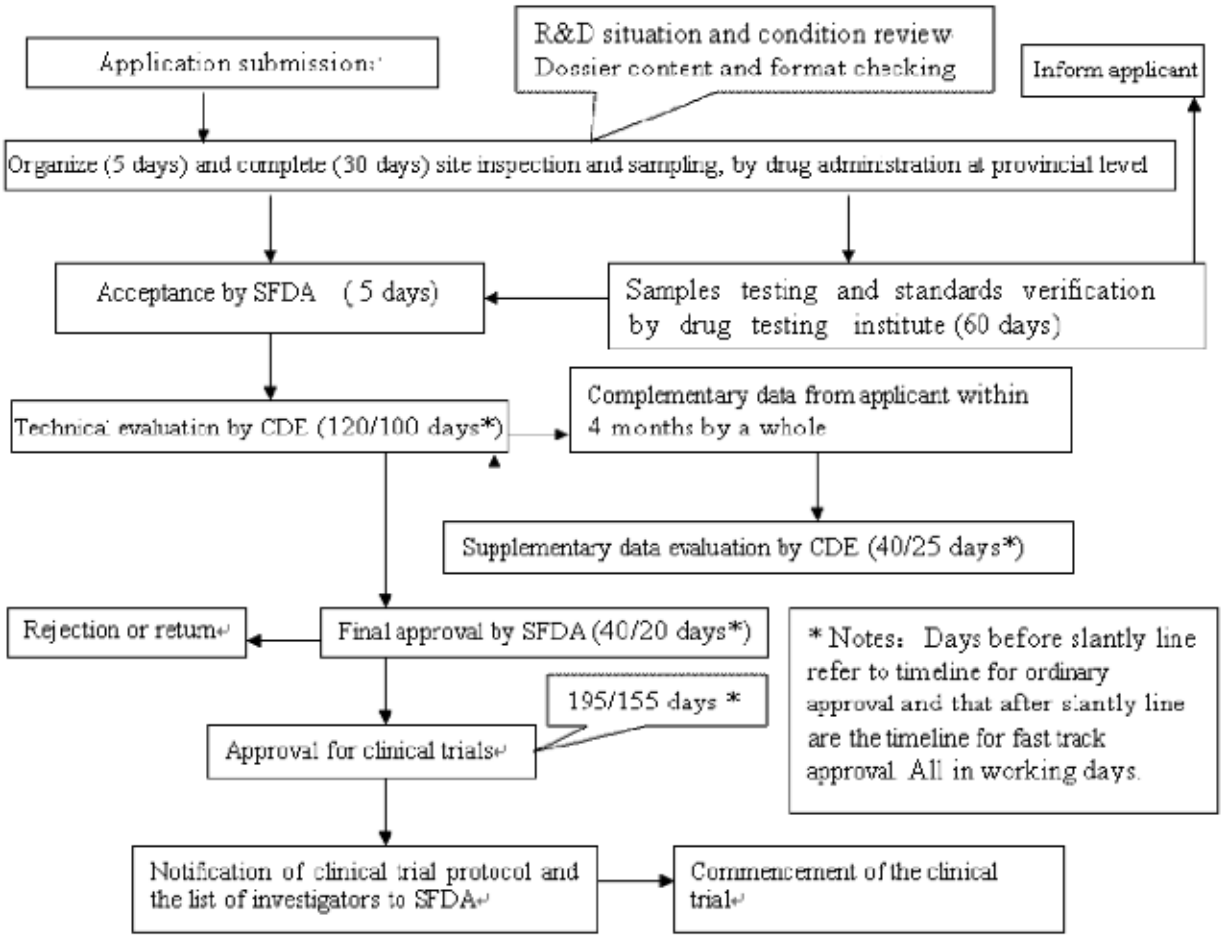
Article 14: Researcher or her/his designated representative must explain the relevant information on clinical trial to human subjects:
(1) The participation of human subject in clinical trial is voluntary, and at any stage of trial, human subject has right to withdraw without discrimination or retaliation, her/his medical treatment and rights/interests shall not be affected.
(2) Must make human subject understand her/his individual materials about her/his participation, and obtained in the trial are confidential. Ethics Committee, Drug Regulation Administration and researchers can get access to these materials when necessary according to the regulations.
(3) Purpose, process and period of the trial, procedures of examination, expected possible harm/risks, inconveniences and benefits to human subject, and the possibility of her/his assigned to different groups in the trial.
(4) Human subject can get access to the relevant information at any time. Must give sufficient time to human subject to consider her/himself whether to participate in the trial. For incompetent human subject, information shall be provided to her/his legal proxy. In the process of informed consent shall be used the language and words that are understandable to human subject.
(5) When there is injury relevant to the trial, treatment and appropriate compensation shall be provided to human subject.

Article 15: The written informed consent form shall be obtained after complete and detailed explanation of the trial.
(1) The written informed consent form shall be signed and dated by human subject or her/his legal proxy, and by the researcher or her/his representative too.
(2) In the case that the human subject or her/his legal proxy is illiterate, there shall be one witness who is present in the all process of informed consent. After detailed explanation of the written informed consent form, human subject or her/his legal proxy expresses the consent orally, it shall be signed and dated by the witness.
(3) If Ethics Committee agrees in principle with researcher who judges that the participation of incompetent human subjects in the

trial will be in their interests, these patients are permitted to enter into the trial, and the informed consent form shall be signed and dated by their legal proxy.

(4) If the informed consent is not obtained from human subject, witness or guardian, researcher must record this situation and the detailed reasons of why the consent is not obtained in the file and sign on it.

If new important materials relevant to drug in trial are found, the informed consent form must be revised and submitted to Ethics Committee for approval, and be got consent from human subject again.



15. SFDA Application and Approval Procedure for Clinical Trials.

16. Regulation on Research with Human Subjects

Chapter 1 General Principles

Article 1 In accordance with the "Regulations on Medical Practitioners of the People's Republic of China" and the "Regulations on Management of Medical Institutions", these "Regulations on Ethical Review of Biomedical Research Involving Humans" are promulgated to regulate biomedical research involving humans and practices of related technologies to protect human life and health, and human dignity, and to respect and protect the rights of the research subjects.

Article 2 All ethical review work on biomedical research involving humans should abide by these "Regulations".

Article 3 Activities referred to in these "Regulations" of biomedical research involving humans and related technologies include the following:
1) Research activities about the physical and pathological phenomena of a human body, using modern methods of physics, chemistry and biology, as well as research activities for disease diagnosis, treatment and prevention;
2) Activities of trial use on human bodies of medical and health technologies and products as biomedical research results. Not included in the review scope of these "Regulations" are clinical practices that have been used for more than two years before the "Regulations" comes into effect, or, the technologies that have already been approved by health authorities before these "Regulations" comes into effect.

Article 4 Reviews on ethics should comply with national laws and regulations, as well as life ethical principles commonly recognized, and reviews on ethics shall be carried out independently and objectively in a fair and transparent manner.

Chapter 2 Ethics Committee

Article 5 The Ministry of Health of China has its Medical Ethics Committee. Provincial health authorities have their steering consulting organizations of ethics reviews under their administration. Committees set up by the Ministry of Health and provincial health authorities are expert consulting organizations for medical ethics that consider important ethical issues and provide suggestions for policy-making and when necessary organize ethical reviews of important research projects; and that guide and monitor ethical reviews conducted by ethics committees in their administrative areas. A "Constitution" of the ethics expert committee set up by the Ministry of Health and provincial health authorities is to be made separately.

Article 6 Institutions that conduct biomedical research involving humans and application of related technologies, including medical and health institutions, scientific and research institutes, disease prevention and control institutions and women and child health care institutions, should establish their institutional ethics committees. Major responsibilities of the institutional ethics committees include the review and monitor of ethics for biomedical research and application of related technologies carried out by their own institutions or by organizations affiliated to their own institutions. Institutional ethics committees should also conduct reviews on ethics as requested and entrusted by social sectors and shall run training programs on ethics.

Article 7 Members of the institutional ethics committees should be chosen from fields such as biomedicine and management, ethics, law, sociology, etc. after opinions are sought widely by the organizations and institutions that are to have such ethics committees. Each ethics committee should consist of no less than five people, with a gender balance. In areas where minority ethnic groups live, minority ethnic people should be considered to serve as committee members.

Article 8 The term of each ethics committee member should be five years and can be reappointed. Each ethics committee should have a chairperson and several vice chairpersons, who are elected by members of the ethics committee and who can be re-elected. The organization or institution that sets up the ethics committee should give financial compensations for the members of the ethics committee based on the work they carry out.

Article 9 Responsibilities of the institutional ethics committee will be to review research protocols to maintain and protect the dignity and rights of the research subjects; to guarantee that any research project will not in any way put the research subjects in any risk; at the same time, to supervise and monitor the research projects that have been approved, and to cope with any complaints and incidents concerning research subjects.

Article 10 Institutional ethics committees have the following powers:
1) To require from the researchers proof of informed consent, or, as requested by the researchers, to approve the exemption of the requirement procedure for an informed consent;
2) To require the researchers to modify their research protocols;
3) To require the researchers to suspend or terminate their research activities;
4) To decide to approve, not to approve, or approve only after protocols are modified.

Article 11 Ethics committee members should keep all ethically reviewed research projects Confidential..

Article 12 Ethics committees should make their own decisions without any outside interferences; and review results should be timely made available or public.

Article 13 Ethics committees should be under the supervision and administration of their administrative regional and health authorities.

Chapter 3 Review Procedures

Article 14 Review principles for biomedical researches involving humans are:
1) To keep strictly to the informed consent procedure to respect and protect the rights of the potential research subjects so that they can make independent decisions to accept or reject the test, and never to cheat, allure, coerce the potential research subjects to agree, and to allow them to withdraw at any stage of a test;
2) The safety, health and rights of the research subjects should be considered first before scientific and social interests are considered so as to benefit, to the greatest extent possible, the research subjects and to avoid any possible injuries or damages to them;
3) To alleviate or exempt financial burdens resulting from the benefits research subjects receive from a test;
4) To respect and protect the privacy of the research subjects, to timely inform them of the storage and security measures concerning their personal data, and never to release those data to a third party not relevant or any media;
) To ensure that the research subjects receive free medical treatment and compensations for any possible injuries caused by a test;
6) To give special protection to those research subjects (vulnerable groups) who have lost or lack capability to protect their own rights, including children, pregnant women, mentally-retarded persons, mental patients, prisoners, and economically and educationally disadvantaged people.

Article 15 Research projects should submit the following materials to the ethics committees for ethical reviews:

1) The Application Form for Ethical Review;

2) The Application Protocol for Results of Research or Related Technologies;

3) A written informed consent of the potential research subject.

Article 16 Research project applicants must first obtain informed consent out of his or her own free will in writing from the potential research subject. If a written form is not obtainable, an oral informed consent must be first obtained, together with a written proof indicating that such an oral one is obtained. For those potential research subjects who are not able or not possible to make their own decisions, informed consent in writing must be obtained from their guardians or surrogates.

Article 17 In the process of obtaining informed consent, the applicants must provide the potential research subjects with comprehensive and understandable information relevant for the test, and the wording in the letter of informed consent should be easy to understand and can be in local language in minority ethical areas that is understood by the potential research subjects, and the potential research subjects should be allowed time long enough to consider whether or not to accept to be research subjects.

Article 18 When the practical procedure or a condition of a research project changes, another informed consent must be obtained, and a new application for ethical reviews must be submitted.

Article 19 Ethics committees should not accept any research project ethical review applications that are against national laws and regulations. If there is any interest conflict between an ethics committee and an applied project, the ethics committee concerned should actively refuse to get involved. If in any way refusal to get involved is not possible, the conflict of interest should be made clear to the applicants.

Article 20 Ethics committees should review the following:

1) Qualifications, competence and experience of the researchers meet the requirements for the research project;

2) The Research Protocol is of a scientific nature and complies with ethical principles;

3) Whether or not the balance between the risks and the benefits the research subjects may get is appropriate;

4) Whether or not the information provided to the potential research subjects (or their family members, guardians, and lawful surrogates) is comprehensive and understandable, and whether or not the methods used to obtain informed consent are appropriate;

5) Whether or not measures are taken to protect the confidentiality of the data of the research subjects;

6) Whether or not the standards for selection and rejection of the potential research subjects are appropriate and justified;

7) Whether or not the rights which the research subjects should enjoy have been made clear to them, including the right to withdraw from the test without a reason and without reprisal;

8) Whether or not the research subjects will get appropriate financial compensations, and if and when they are injured or die in the test, whether or not the medical treatment and financial compensation are appropriate;

6) Whether or not there are designated personnel in the research team who are responsible for dealing with matters related to the informed consent and the safety of the research subjects;

7) Whether or not protective measures are taken for possible risks in a test for the tested persons;
8) Whether or not there is a conflict of interest between the researchers and the research subjects.

Article 21 Ethics committees should make decisions to approve, not approve or reconsider a review application after modifications are made. Decisions made by ethics committees must be agreed to by two-thirds of the ethics committee members. Reasons must be given why a specific decision is made. When the probability of an injury or discomfort for a research subject is no higher than that in one's daily life or regular treatment (namely, projects with risks lower than the minimum risk level), the research project can be ethically reviewed by the committee chairperson, or by one or several committee members designated by the committee chairperson.

Article 22 When a research project approved by the ethics committee needs to be changed while being carried out, this must be reported to the ethics committee for approval. Any grave negative responses from the research subjects or negative incidents during the application of an approved research project must be reported to the ethics committee.

Article 23 Without the approval of the ethics committee, no applied research projects should be conducted.

Chapter 4 Supervision and Management

Article 24 The supervision and management of the ethical review of biomedical research involving humans should be included in the scientific and research work scope of health authorities at all levels. The supervision and management work should include the following:
1) Whether or not an ethics committee is established as required in an institution that carries out biomedical research involving humans;
2) Whether or not the institutional ethics committee conducts ethical reviews in accordance with the ethical review principles;
3) Whether or not the ethical review contents and procedures meet the requirements;
4) Whether or not there is a dispute over the implementation of the reviewed results

Article 25 The Ministry of Health manages in a macro way the ethics committees nationwide, makes and perfects regulations on ethical reviews, researches on and makes relevant policies. Provincial health authorities shoulder the responsibility for the supervision and management of the work of the ethics committees in the provinces.

Article 26 Foreign institutions or individuals that have obtained their national or regional approval to carry out biomedical research involving humans within China should apply to ethics committees set up under these "Regulations" for a review.

Article 27 At the conclusion of a biomedical research project involving humans, the project responsible person must submit a certificate indicating that the research project has undergone ethical reviews by the ethics committee. Before a research paper about a biomedical research project involving humans is published, the author(s) must submit a certificate indicating that the research project has undergone ethical reviews by the ethics committee.

Article 28 Any individual or organization has the right and obligation to report any breach of the regulations or unethical activities.

Article 29 When a breach of the regulations or an unethical activity is found, the institution and health authorities where the research project is carried out has the power to penalize the researchers related, to give them an open criticism, and to abolish their qualifications for rewards; and to suspend the application of the research project according to the seriousness of the misconduct, and transfer the case to courts if it is against national laws.

Chapter 5 Supplementary Article

Article 30 These "Regulations" will come into effect on the day it is announced.

Note:
These "Regulations" were made by the Ministry of Health of China and came into effect on January 11, 2007. This English version is translated by the Chinese Medical Association.

17. MRC China-UK Research Ethics Report: Recommendations

(Full report at URL
http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC006303)

Summary of findings

Chinese laws and guidelines cover many aspects of medical research. The regulation of research is rapidly evolving in China and many of these guidelines and regulations have been produced within the last decade. Ongoing review of the regulatory situation in China (and indeed the UK) is required to ensure that collaborations are governed appropriately, in accordance with the regulatory systems of both countries.

Recent Chinese guidelines draw extensively on international guidance, such as the International Committee on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use Good Clinical Practice Guidelines (ICH GCP). Chinese regulations bear a marked resemblance to UK regulation in areas such as embryonic stem cell research. Most of the underlying principles governing the conduct of medical research in China are broadly similar to those that guide UK regulation, although there are particular challenges, for example, interpreting individual informed consent in a culture that places high value on family involvement in decision making. However, some aspects of medical research are much more closely regulated in the UK than in China, such as uses of human tissues and data protection.

The key difference between the two countries is in the implementation of regulation: for this reason this Committee recommends close review of potential research collaborations. Although the elite scientists and institutions that we visited in China were committed to implementing international standards, the situation elsewhere remains unclear and the implementation and enforcement of regulation is not as consistent as it is in the UK.

The two countries differ greatly in their approaches to enforcing guidelines for the conduct of research at the national level. In China, although there is some scrutiny of clinical trials, there is comparatively little inspection or review of compliance. Moreover, although sanctions exist for violations of guidelines, it is not clear how they would be applied.

The absence of national oversight places the onus on individual institutions and researchers to ensure the appropriate conduct of research. In contrast, the UK has many regulatory agencies overseeing and, in some cases, licensing and inspecting aspects of research – including uses of human tissue and embryos. There are also separate regulatory processes for gene therapy research and some research involving patient data. These additional layers of oversight may be viewed as a burden by the UK research community, but they provide considerable assurance regarding the appropriate conduct of research.

There are also important differences between the UK and China in terms of the institutional structures that conduct ethical reviews. China has followed the US model of institutional review boards (IRBs) and has no equivalent to the UK's National

research ethics Service (NRES) to administer these committees and ensure consistency of procedure.

Our report details significant differences between review committees in the UK and China. For example, there is a clear requirement in the UK that Research Ethics Committees (RECs) include members who are independent of the research teams, but this is not the case in China. Chinese IRBs are largely composed of professionals associated with the institution and are often chaired by the Director or a senior member of the research staff of that institution.

In addition to its general overview of the regulation of medical research, the Committee undertook a detailed analysis of three areas of particular interest. Their findings were as follows:

1. Stem cell research: Particular attention must be paid to the source of tissue used in research, including embryos, and procedures for obtaining consent, which should be compatible with both Chinese and UK regulation. The situation in China regarding the regulation of human admixed embryos is uncertain and future proposals involving such work need to be assessed in relation to the guidelines in place at that time. Any proposal involving the translation of stem cell research into clinical practice needs to be reviewed with great care, as the regulatory situation in China lacks clarity and it is important to ensure that this is not exploited.
2. Research involving clinical trials: All such research should be reviewed carefully, including the protocol, procedures for approval, recruitment and consent, and the issue of post-trial benefits. The MRC should ensure that there are adequate monitoring mechanisms in place. China's State Food and Drug Administration (SFDA) performs a similar role to the UK Medicines and Healthcare products Regulatory Agency (MHRA) in reviewing applications for clinical trials, but the MHRA has a system of inspection that is more transparent and covers a greater proportion of clinical trial sites. The SFDA is undergoing a programme of reform and further review will be needed in future to determine if this has fully addressed previous concerns.
3. Traditional Chinese Medicine: Attention needs to be paid to the quality, purity and standardisation of product to be used, the selection of participants and the use of placebo and control groups. Consideration should be given to the issue of concurrent traditional or Western treatments being taken by participants.

3. Summary of recommendations
The MRC must ensure the highest possible standards of governance of China-UK collaborations. If the UK, or specifically the MRC, is perceived to have been involved in unethical research, the negative effects on the reputation of the MRC and on future China-UK collaborations could be considerable. The followings recommendations address how these high standards can be established and implemented in such collaborations.

MRC engagement with Chinese research ethics policy
Recommendation 1
The MRC should continue to discuss research ethics with Chinese counterparts and maintain the lines of communication developed through the CURE project.

Recommendation 2

If there is a lack of confidence in monitoring and inspection procedures in China in areas of strategic relevance to the MRC, the MRC should take steps to remedy this by reviewing the situation and, where necessary, engaging with researchers and policy-makers to improve capacity.

Recommendation 3

The MRC should seek to involve China in discussions about how to manage 'first-in-human' trials for innovative therapies.

MRC engagement with potential Chinese collaborative partners

Recommendation 4

The MRC should focus on established centres of excellence when funding collaborations with China and seek to build durable relationships with these centres. In evaluating potential collaborations, we recommend that the MRC should look for both an international reputation in research, indicated by publications in international journals and funding from overseas funding agencies known to require tight ethical regulation, and for markers of good institutional governance. Such markers would include an international scientific review committee and well-constructed Institutional Review Boards with an appropriate proportion of independent members recruited from outside the institution. Outside these established centres of excellence, the MRC will need to take proactive measures in all stages of planned collaborations to ensure that high standards of research ethics are maintained.

Recommendation 5

MRC should consider funding research to develop knowledge of institutional governance and matters relating to research ethics in relation to proposed MRC-funded China-UK collaborations.

Recommendation 6

Under no circumstances should the MRC fund research that has not been judged acceptable by a UK ethics committee. All proposed collaborations should be fully scrutinised by both countries, following the relevant Chinese and UK procedures.

Recommendation 7

The MRC must ensure that appropriate procedures for informed consent are in place. A research proposal could seek to remedy uncertainty in this area by incorporating elements such as reviewing consent procedures. Such additional work would also require approval of the ethics committees in China and UK.

Pre-funding review

Recommendation 8

It is important that the MRC seeks clarity, from the outset, regarding the reasons to collaborate on both sides of a proposed collaboration and an understanding about benefit sharing.

Recommendation 9

The MRC and research ethics committees should review the specific piece of research for which funding and/or ethics approval is sought in the context of the whole programme of research, of which the specific project may be part.

Recommendation 10

The MRC's pre-funding review process for China-UK collaborations should include review by one or more experts with experience and knowledge of Chinese regulation and science.

Recommendation 11
The MRC should review research protocols to ensure that they are sensitive to cultural differences and social context.

Recommendation 12
The MRC should review the level of payments or nature of inducements in any collaborative projects to ensure that they conform with current MRC policy and are not 'undue' inducements.

Recommendation 13
The MRC should require all participating institutions and researchers to demonstrate that they have all necessary licences from the appropriate Chinese authorities to undertake their proposed programme of research.

Additional funding
Recommendation 14
Potential MRC-funded collaborations should be able to apply to the MRC for funding for an initial "Phase Zero", lasting six to twelve months.

This initial phase would be conceived as a period during which relationships and institutional developments might evolve before the research itself commences. It could provide knowledge relating to governance or ethics of the proposed project or allow for a period of capacity-building within the proposed team. Where there is uncertainty regarding governance structures, funding for the research could be made conditional on the satisfactory completion of "Phase Zero".

Recommendation 15
For larger projects or research in areas of particular concern or sensitivity, the MRC should provide funding for expert evaluation of the research governance structures.

Strategic issues
Recommendation 16
The MRC should consider further:

• Strategic issues in the funding of collaborative research – including the evaluation of different models for funding collaborative research in China.

• Possible mechanisms to support capacity building for ethics review in China-UK collaborations.

18. The Chinese Alternative to the Stem Cell Research Debate

By Sam Crane (China Daily)
Updated: 2006-07-28 09:24

Believe it or not, ancient Chinese philosophy can add to our understanding of the ethics of embryonic stem cell research.

Hear me out.

In the US, debate on stem cell research centres on the question of whether destroying an embryo is tantamount to killing an individual person. Opponents believe that, since an embryo has the potential to become a person, it should be treated as a person and not be subjected to scientific experiments that might cause its destruction. Supporters argue that embryos are not yet fully formed persons and thus can be used to harvest stem cells for scientific study. In addition, proponents of stem cell research would add that the social benefits of science outweigh the destruction of individual embryos.

The US controversy pits devout Christians, whose religious beliefs lead them to see embryos as persons, against utilitarian liberals, whose definition of an "individual" does not include fetuses before the third trimester of pregnancy. The issue has become politicised of late, with the US Congress ready to pass legislation supporting embryonic stem cell research and the President threatening a veto.

Unsurprisingly, the US debate has called upon various strands of Western philosophy and religion. But Daoism and Confucianism can add something to the conversation. A modern-day philosophical Taoist would likely be sceptical of the entire scientific research enterprise. The Dao De Jing has this to say in passage 29: "Longing to take hold of all beneath heaven and improve it; I have seen such dreams invariably fail. All beneath heaven is a sacred vessel, something beyond improvement. Try to improve it and you ruin it. Try to hold it and you lose it."

Religious Daoists (dao jiao) are famous for their search for a death-defying elixir of life. Philosophical Daoists (dao jia), however, are more accepting of the inevitable demise of the human body. Zhuang Zi is marvellously free of anxiety and resentment about death. Indeed, the notion that purposive human activity can overcome the natural aging process is contrary to the general Daoist attitude to do nothing (wu wei) that might get in the way of Way.

If confronted with the question of stem cell research, therefore, a philosophical Daoist might say: "why bother?" It may help a few people with certain maladies, but it will not fundamentally transform the human condition. Such Daoists would generally dissent, not because embryos might be persons, but because science cannot define destiny.

Contemporary Confucians, on the other hand, would probably find themselves aligned with supporters of stem cell research, but for somewhat different reasons.

For a Confucian, persons are defined socially. Our identities are shaped through our daily cultivation of our closest social relationships. The question of whether an embryo is a person is, therefore, nonsensical: how could it be a person if it was not yet actively engaged in social relations. A person becomes a person at birth.

Furthermore, if stem cell research helped to cure disease, allowing people to better perform their social roles and duties, then the science would be advancing the cause of Humanity (ren), the highest Confucian virtue. Confucians would emphasize, even more than Western liberals, these sorts of social benefits. It is less about individual rights and accomplishments for a Confucian, and more about the mutual realization of individual and social morality.

We learn more when we consider the widest possible range of ideas in any debate. Adding Confucian and Daoist perspectives to the American discussion of embryonic stem cell research gives us insights into the issues, and into ourselves, that we might otherwise overlook.

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