Roche

Roche Annual Report 2005

Part 1

Business Report

We Innovate Healthcare




Innovative solutions spanning the healthcare spectrum

Predisposition | Early detection | Prevention | Diagnosis | Therapy | Monitoring

Our combined capabilities in diagnostics and pharmaceuticals enable us to meet needs across the entire healthcare spectrum. From identifying disease susceptibilities and screening for disease in at-risk populations to prevention, diagnosis, therapy and treatment monitoring, our innovative products are advancing the fight against disease on a wide range of fronts, and making a real difference for patients and health professionals.

At Roche our commitment to innovating healthcare is matched by a commitment to corporate social responsibility. Sustainability is one of our company's guiding values. We recognise that economic, social and environmental concerns are intertwined and that progress in each of these sectors requires progress in all three. As a research-intensive company with a long-term strategic focus, Roche strives to deliver sustainable value to all its major stakeholders.

Predisposition Page 8

'It's so good to know my medication really can help me.'

Early detection Page 16

'We couldn't have stood the uncertainty any longer.'

Prevention Page 42

'The medication helps against my osteoporosis, and I only have to take it once a month.'

Diagnosis Page 64

'Suddenly I realised my life was hanging by a thread.'

Therapy Pages 70 and 84

'The feeling that I had regained control over my disease gave me a huge psychological lift.'

Monitoring Page 100

'I've got my independence back.'

Table of Contents

Business Report 2005

Key figures

Roche Group

	2005 (mCHF)	2004 (mCHF)	% change (CHF)	% change (LC)	2005 as % of sales	2004 as % of sales
Sales[1]	35,511	29,522	+20	+19	100	100
Research and development[1]	5,705	5,154	+11	+11	16.1	17.5
Operating profit before exceptional items[1]	9,025	6,766	+33	+33	25.4	22.9
Net income	6,730	7,063	–5		19.0	23.9
Net cash	11,215	3,909	+187			
Equity	41,743	33,283	+25			

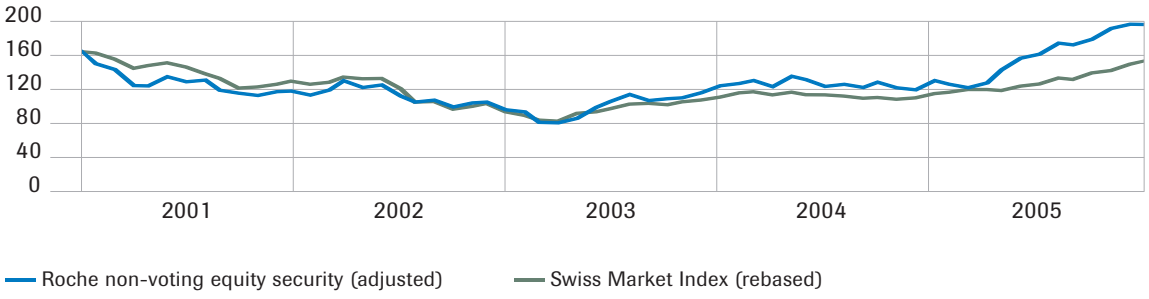
	2005	2004	Change
Equity ratio (in %)	60.2	56.9	+6%
Core earnings per share (in CHF)	7.68	5.72	+34%
Dividend per share[2] (in CHF)	2.50	2.00	+25%
Number of employees (at 31 Dec. 2005)	68,218	64,594	+3,624

1) Continuing businesses.

2) Proposed by the Board of Directors.

LC = local currencies.

Price development of non-voting equity security *(Genussschein)* in CHF



The year 2005 in brief

Group

- Roche Group increases its sales by 6 billion Swiss francs to a record high of over 35 billion Swiss francs.
- Operating profit margin up 2.5 percentage points to 25.4%.
- Net income at virtually the same level as the year before, despite income of 2.3 billion Swiss francs in 2004 from the divested consumer health business.
- Group awarded credit ratings of AA+ (Standard & Poor's) and Aa1 (Moody's).
- Roche reselected for inclusion in the Dow Jones Sustainability Indexes.
- Board to propose 19th consecutive dividend increase: 25% to 2.50 Swiss francs per share and non-voting equity security.

Pharmaceuticals

- Pharmaceutical sales advance 25%, four times the global market growth rate.
- Sales of anticancer drugs up 42% to 11 billion Swiss francs, further strengthening Roche's market leadership in oncology.
- Tamiflu production expanded significantly to meet huge need for pandemic readiness supplies.
- Positive results from phase III clinical trials in rheumatoid arthritis and breast, lung and pancreatic cancers.

Diagnostics

- Roche Diagnostics maintains its global market leadership with sales growth of 4%.
- Operating profit remains at previous year's record level; margin down slightly from 2004.
- Next generation of Accu-Chek diabetes management products launched worldwide.

Outlook for 2006

- Above-market sales growth, with double-digit increases for the Roche Group and the Pharmaceuticals Division.
- Core earnings per share growth target in line with sales growth.

Visit http://www.roche.com for additional information on Roche.

All growth rates are based on local currencies.
Operating profit margins are stated before exceptional items.

Letter from the Chairman

Dear Shareholders

Your company had an outstanding 2005. Innovative Roche medicines and diagnostics helped advance the fight against serious diseases. Operationally and financially the Group posted strong results, with substantial market share gains and a further significant improvement in operating profitability. At the General Meeting of Shareholders the Board of Directors will propose a dividend increase of 25% to 2.50 Swiss francs per share and non-voting equity security. If approved, this will be the Group's nineteenth dividend increase in as many years.

Sales by the Roche Group rose 19% in local currencies and for the first time exceeded 35 billion Swiss francs. The Pharmaceuticals Division accounted for most of this increase. Its sales were up 25% for the year, four times the average market growth rate. The Diagnostics Division maintained its leadership position in a difficult market, but fell slightly short of its performance goals.

Group operating profit before exceptional items rose by one-third to a record high of 9 billion Swiss francs. At 6.7 billion Swiss francs, net income came close to matching the previous year's figure, despite income of 2.3 billion Swiss francs recorded in 2004 from the divested consumer health business. This strong earnings performance will enable us to continue investing heavily in research and development and in expanding our production base. With Group expenditure on research and development totalling more than 5.5 billion Swiss francs annually, ours is one of the world's most research-intensive companies. During the next several years we

will additionally be investing about 2 billion Swiss francs in new biotech manufacturing facilities to keep pace with rising demand for our products.

Roche is in excellent financial health. In 2005 we further strengthened our balance sheet and significantly increased net cash. Over the last three years our ratio of equity to total assets has risen steadily from 40% to 60%. This increased financial strength gives us the strategic flexibility to selectively expand our core pharmaceuticals and diagnostics businesses. In late 2005 Standard & Poor's and Moody's awarded Roche credit ratings of AA+ and Aa1, respectively – the second highest ratings assigned by these agencies.

For the Pharmaceuticals Division 2005 was the best year in Roche history. Despite the expiry of the US patent on Rocephin, once Roche's top-selling medicine, the division increased its sales by a truly impressive 5.5 billion Swiss francs to over 27 billion Swiss francs. For the first time ever, seven Roche medicines generated annual sales of more than 1 billion Swiss francs each – in some cases significantly more. The division's operating profit margin before exceptional items also showed another significant improvement, advancing from 25.0% to 27.4%.

Our powerful oncology portfolio was the key driver behind these superb results. Roche is the only healthcare company with five medicines for cancer on the market that have been shown to increase patient survival. Within the space of just a few years, a new generation of more targeted, less toxic anticancer medicines have made Roche the global market leader in oncology. We reinforced this leadership last year with sales growth of 42%. The innovative new additions to our oncology portfolio – Avastin for colorectal cancer and Tarceva for lung cancer – are already very well established.

New Roche medicines were also launched successfully in other therapeutic areas, and supplemental approvals for new indications spurred a significant increase in prescriptions of some of our existing drugs. Last year Roche captured the attention of health professionals and the public with some exciting new clinical data. These include data showing that Herceptin can make a significant difference in the early-stage treatment of aggressive breast cancers. In clinical trials involving nearly 13,000 women, adding Herceptin to standard therapy halved the risk of cancer recurrence compared with standard therapy alone. And in a trial of MabThera/Rituxan in lymphoma patients, maintenance therapy with the drug was shown to increase survival so dramatically that the tide may now also be turning in the battle against certain forms of this disease. A claim like this would have been unthinkable a few years ago.

As these examples illustrate, drug research and development does not and should not stop as soon as a drug is approved in its first indication. Taking the development of anticancer drugs to a new level is one of the core missions of our global research organisation.

We also made significant progress on projects to develop novel biotherapeutics for rheumatoid arthritis, a common disease characterised by progressive inflammation, and in most cases progressive destruction, of the joints. Clinical trial data have confirmed that our top-selling anticancer medicine, MabThera/Rituxan, offers a completely new approach to treating rheumatoid arthritis. And a product being developed by our Chugai subdivision has also been shown in clinical trials to slow joint damage significantly and dramatically improve the disease's painful, disabling symptoms. The chances are good, I believe, that Roche will soon be a major player in this disease area.

Responding to the threat of a potential flu pandemic was one of the year's greatest challenges. Roche has acted energetically and responsibly to meet increased global demand for its leading influenza drug, Tamiflu. Among other steps, we promptly initiated a massive scale-up of pro-

duction capacity at our own risk and adopted a pricing policy that provides significant discounts on deliveries of the drug for pandemic use, and we have given over five million packs of Tamiflu to the World Health Organization as a rapid response stockpile for use at the epicentre of a potential pandemic and to help establish regional stockpiles of the drug. In addition, we have granted our first sublicences for production of the drug for pandemic use and are holding in-depth talks with a dozen companies that could provide additional manufacturing support if necessary.

For Roche Diagnostics 2005 was a year focused on launching new products, particularly for diabetes management. And it was also a year in which the division expanded into markets where it had never competed before – notably DNA sequencing. While market conditions continue to be difficult, Roche Diagnostics maintained its leading market position, with sales advancing 4% in local currencies to 8.2 billion Swiss francs. The division's immunodiagnostics and molecular diagnostics portfolios were the main growth drivers.

Roche Diagnostics posted an operating profit of 1.7 billion Swiss francs before exceptional items, matching the all-time high of the previous year. Divisional profitability remained high for the industry, despite a slight decrease in the operating profit margin, to 20.5%. Strong pricing pressures, production start-up costs and the costs related to the many new products launches during the year were the main reasons for this decline.

As the global market leader, we feel we have an obligation to supply advanced diagnostics that make a significant contribution to effective, cost-efficient patient care. Our new generation of Accu-Chek products for improved diabetes management, which we began launching worldwide in 2005, is a perfect case in point. The response has also been very strong to the European and US launches of our AmpliChip CYP450 Test, a product that takes us another step closer to personalised medicine. Using this DNA microarray test, doctors can gauge a patient's ability to metabolise certain drugs based on the patient's genetic profile – information which can then help guide drug selection and dosing decisions. Additional DNA microarray tests, for cancer screening, are currently in late-stage development.

Reflecting the Group's strong performance, we created 3,600 new jobs last year, bringing the total number of Roche employees worldwide to over 68,000. I would like to take this opportunity to express my thanks to all our people for their dedication and professionalism. The value they create every working day is vital if Roche is to continue to invest in developing innovative solutions for areas of unmet medical need. By helping to make patient care more effective, and hence more cost-efficient, our clinically differentiated medicines and diagnostics will play an increasingly important role in easing the pressure on healthcare budgets.

For decades Roche has been actively committed to socially and environmentally sustainable development, as well as to delivering long-term benefits to patients. At the end of last year not only were we reselected for inclusion in both Dow Jones Sustainability Indexes and the FTSE4Good Index, we were also ranked second in the pharmaceutical industry category. This is a tribute to our sustainability efforts, and something I am very pleased about. I am equally pleased that several highly respected publications, including *Fortune* and *Science,* have included us in their lists of the best companies to work for.

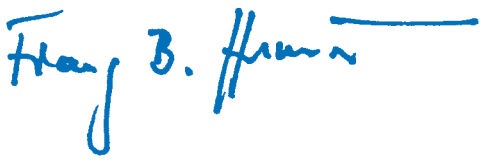
Roche has always striven to be a responsible corporate citizen as well as a healthcare innovator. The action we are taking to ensure the availability of Tamiflu in the event of a pandemic is a recent example of how seriously we take our wider responsibilities as a company. We also set high standards with our policies and practices regarding transparency in clinical research. We disclose negative as well as positive results from our late-stage trials, and early last year we also began publishing data

from all our clinical trials on the Internet. In addition, Roche has established an independently hosted, publicly accessible online trial protocol registry that provides information in clear, simple language.

Our commitment to corporate social responsibility also extends to the world's least developed countries. Ours is one of the few companies still doing research on HIV/AIDS, and it is also one of the few companies that supplies medicines at cost and does not enforce patent rights in the poorest developing countries. In addition, in early 2006 we announced that we would provide the technical expertise to manufacture the AIDS drug saquinavir to interested manufacturers in Least Developed Countries at no cost.

Clearly, the greatest contribution we can make to sustainability is to continue developing new and better solutions for unmet medical needs. But we also recognise that our continued viability and success as an innovative company depend on our doing business in a socially and environmentally responsible way.

Our outlook remains very positive. Thanks to a portfolio of innovative products, we are well positioned to continue creating value. In 2006 we expect both divisions to achieve above-market sales growth in local currencies, and our target is for core earnings per share to rise in line with Group sales.



Franz B. Humer

'It's so good to know my medication really can help me.'

Predisposition | Early detection | Prevention | Diagnosis | Therapy | Monitoring




A novel test brings personalised medicine closer

When British scientist Anneke Westra was diagnosed with manic depression, it was the start of a ten-year nightmare. Her doctors prescribed a succession of drugs, but she had serious adverse reactions to them all. Some even caused her to have hallucinations and blackouts. Though Anneke had been fighting depression for most of her life, she hadn't let that stop her from earning a PhD in biotechnology, registering a patent and giving lectures all over the world. But now the medicines she was on left her feeling drained and worn out. At one point she even attempted suicide.

Obviously, things couldn't go on like this, so Anneke began doing some investigating on her own. That's when she found out about the AmpliChip CYP450 Test, a test to predict people's ability to metabolise certain drugs. In Anneke's case, the test showed that her body was breaking down and clearing her medicines too slowly, allowing them to accumulate at harmfully high levels.

Nothing can give Anneke back all those lost years, but the test results did enable her doctor to adjust her medication to a dosage that works for her. Now 41, Anneke is being treated with a low-dose combination of three medicines and finally feels fine.

Predisposition

Cytochrome P450 genes code for drug-metabolising enzymes found primarily in the liver. The AmpliChip CYP450 Test detects variations in two of these genes that can make a patient a poor or a rapid metaboliser of many widely prescribed drugs. This information can help physicians make better, more personalised drug selection and dosing decisions for their patients. And that means more effective treatment with fewer side effects.

Roche Group

Group results

The Roche Group posted very strong operating results in 2005. Group sales increased significantly to 35.5 billion Swiss francs, a gain of 19% in local currencies (20% in Swiss francs and in US dollars). The Pharmaceuticals Division was the key growth driver. Its sales increased four times as fast as the global market average and significantly ahead of the growth rates in North America, Europe and Japan, the division's three most important markets. In the Diagnostics Division sales in local currencies increased 4%, in line with global market growth.

Strong top-line growth had a very positive impact on the Group's earnings performance in 2005. Operating profit before exceptional items rose 33% in local currencies to 9 billion Swiss francs, and the corresponding operating profit margin improved substantially, rising 2.5 percentage points to 25.4%. The excellent sales growth during the year more than offset significantly increased investments in launch and pre-launch activities and in the Group's strong development pipelines. For the first time, the operating results for 2005 and the restated prior year figures include costs for the Group's equity compensation plans for employees, which are recorded as an operating expense. The Group's improved earnings performance primarily reflects the Pharmaceuticals Division's significantly higher operating profit margin.

The Diagnostics Division's operating profit before exceptional items decreased 1% in local currencies to 1.7 billion Swiss francs, resulting in a margin decline of 0.8 percentage points to 20.5%. This was primarily due to heavy price pressure in the market, start-up costs for new manufacturing facilities, the many new products launched during the year and higher depreciation from an increased volume of instrument placements.

The Group's strong profitability is also reflected in other key figures: EBITDA rose 25% in local currencies to 11.4 billion Swiss francs, and cash flows from operating activities before taxes increased to 12.0 billion Swiss francs.

Net financial income showed a significant improvement over last year, thanks to the Group's strong positive cash flow and the restructuring of Group debt that has been carried cut over recent years. Roche posted a positive financial result for 2005, with net income from financial assets and foreign exchange management exceeding financing costs by about 300 million Swiss francs.

At 6.7 billion Swiss francs, Group net income was nearly as high as the year before (7.1 billion Swiss francs), despite income of 2.3 billion Swiss francs from the divested consumer health business in 2004. The Group's return on sales margin was 19%.

There was a further significant improvement in the Group's financial position. The ratio of equity to total assets is now 60%, and over 86% of total assets are financed long-term.

Outlook

Barring unforeseen events, Roche reaffirms its positive outlook for 2006. Sales in both the Pharmaceuticals and the Diagnostics Division are expected to grow ahead of the market in local currencies, and we anticipate continued double-digit growth for the Pharmaceuticals Division and the Group as a whole.

Sales growth is expected to be stronger in the second half of the year than in the first. The reasons for this include the patent expiries for Rocephin and Copegus and the fact that expanded production capacity for Tamiflu will result in an increase in deliveries of pandemic supplies of the drug in the second half of 2006. Our target is for core earnings per share and non-voting equity security to grow in line with sales, despite significant investments in the launch of new products and of major new indications for established products.

Group strategy

Healthcare in the 21st century

Evolving consumer needs, innovation and market dynamics are likely to be the key drivers of change in healthcare in the years ahead. Despite enormous progress in the fight against disease, there are still many areas of high unmet medical need. And the demand for new and better healthcare products and services is bound to grow as a result of population ageing and other demographic changes. The advances that have occurred in science and technology in recent years clearly have implications for clinical practice, raising hopes that we may one day have better treatments for mankind's most serious diseases, and perhaps even ways of preventing or curing them. But as demand for healthcare grows, so will the pressures to control its costs, which may have the unintended effect of hampering innovation.

A distinctive strategy

Roche's major divestments over the last several years, most recently the sale of the consumer health business, have been aimed at focusing the Group's energies entirely on its two innovation-intensive divisions: Pharmaceuticals and Diagnostics. Today's Roche is a highly focused company, and as a result it is well positioned to be an industry pioneer in healthcare – from predisposition testing and prevention to diagnosis, therapy and treatment monitoring. Roche is a market leader in oncology, transplantation and virology and the world leader in *in vitro* diagnostics.

Roche aspires to be distinctive in its ability to drive value creation through the discovery, development and commercialisation of medically differentiated products. More specifically, Roche is pursuing industry leadership in the emerging field of personalised healthcare, which is gaining in importance as advances in areas such as genetic profiling enable earlier diagnosis and facilitate better patient stratification. Because of their clinical and economic benefits, preventive therapies and targeted medicines will appeal not only to consumers but to payers and regulators as well.

Our pharmaceuticals and diagnostics businesses, including our majority shareholdings in Genentech and Chugai, are the hub of the Roche innovation network. Because we are both a diagnostics and a pharmaceuticals company, we can capitalise on broad synergies in research, development and marketing. These capabilities are augmented by technology collaborations and a constellation of alliances to develop individual products and product portfolios.

Biotechnology is an important factor in our innovation strategy. Thanks to our early involvement and major investments in this sector, biologics currently account for approximately half of Roche's revenues. The Group owns a significant proportion of the world's biotechnology manufacturing capacity and is now the world's leading producer of therapeutic proteins and monoclonal antibodies.

Creating value for today and tomorrow

Our business model is focused on creating sustainable value for all our stakeholders: not just for our shareholders, but also for patients, our employees and society at large. We are currently developing a framework for measuring the value we create for each of these constituencies, and we expect it to be in place in time for our 2006 Annual Report.

Creating value for all our stakeholders

William Burns (CEO Division Roche Pharmaceuticals), Heino von Prondzynski (CEO Division Roche Diagnostics*) and Erich Hunziker (CFO) talk about Roche's strategy and its implementation.

2005 witnessed mounting pressures to control healthcare spending, several companies were hurt by safety concerns over high-profile products, and the healthcare sector experienced a slowdown in growth. Roche's sales, by contrast, have continued to grow strongly, and the company has a premium stock market rating. What makes Roche different?

Erich Hunziker. Roche has a strategy designed to help it excel in today's cost-conscious healthcare market. We are a market leader in high-growth areas like oncology, transplantation and hepatitis, and a world leader in *in vitro* diagnostics. Our aim is to supply innovative prescription drugs and diagnostics that are best-in-class. We're not out to develop 'me-too' drugs offering marginal benefits over what's already on the market, and we have no interest in following some of our competitors into the generics business. Also, investors are becoming increasingly risk-averse, which means they're paying close attention to the procedures companies have in place for risk management and sustainability. This includes areas like corporate governance, patents, access to products in the poorest developing countries and ethics in business. Thanks to its sound policies and procedures and transparent reporting, Roche has come to be recognised as a leader in corporate sustainability.

'Innovative' and 'innovation' are words that are worked awfully hard. Everybody's an innovator nowadays, or claims to be.

William M. Burns. Our idea of innovation in healthcare centres on the patient. To be a genuine advance, a new medicine or diagnostic has to meet patients' needs better than anything else that's available. Certainly, in these cost-conscious times, payers' needs have to be addressed too. But we believe that the needs of payers, and of healthcare systems as a whole, are met most effectively by addressing patients' needs. At Roche Pharmaceuticals we use the phrase 'clinically differentiated medicine' to describe drugs that treat a particular patient population with a significantly higher degree of success or fewer side effects than other options. Or that are simply much easier to take. We have five anti-cancer medicines proven to extend patients' lives – a claim no other healthcare company can match. These are exactly the kinds of products we're after.

Heino von Prondzynski. Roche supplies pioneering diagnostic devices for a wide range of uses – from predisposition screening and early detection to response monitoring and prognostic testing. And because they contribute to better medical decision-making right down the line – helping doctors make better decisions faster at virtually every stage in the fight against disease – they can promote meaningful savings while at the same time substantially improving patient outcomes.

We're already a leader in major segments like molecular diagnostics and diabetes monitoring, and we're doing pioneering work on biomarkers for cancer and heart attack.

EH. There are different ways and degrees of aspiring to be an innovator. At Roche we've embraced innovation as our greatest strength, the core of our competitive advantage. And we've put an innovation model in place that's like no other in the industry. To be an innovator, obviously you have to have access to cutting-edge science and technology. We got into biotechnology early on, acquiring a majority stake in Genentech back in 1990, because even then we could see the potential of protein therapeutics.

* Until the end of 2005.

Technological advances are certainly one of the major drivers of innovation. What role does biotechnology play in the innovation process at Roche?

WMB. As our understanding of the molecular basis of disease grows, it's increasingly clear that diseases like cancer, and even diabetes, are far more diverse than anyone once suspected. And while this may sound like discouraging news, it's in fact cause for hope, because it means that the likelihood of identifying optimal molecular targets for new drugs is increasing. Biotechnology has opened up completely new therapeutic approaches, particularly in oncology. We're pursuing these new possibilities very aggressively and are confident that they will be a major source of future innovations – which of course means that we also expect them to be a key growth driver for us. This doesn't mean that we intend to stop working on new chemical therapeutics – not by any means. Our chances of developing truly differentiated medicines are greatest if our drug discovery efforts include small molecules and proteins.

EH. One of Roche's great strengths is its ability to craft a long-term strategy and follow through on it. Our lead in biotechnology is a result of strategic choices made over the course of the last ten to 15 years. Our unique innovation model, combining strong in-house R&D, majority shareholdings in Genentech and Chugai and partnerships with scores of other biotechs and universities, gives us broad access to the technologies that spur innovation. We're already a major player in biotechnology, and we're poised to become even stronger.

What is the strategic rationale behind Roche's commitment to diagnostics, an industry that is clearly less dynamic than pharmaceuticals?

HvP. Right now Roche Diagnostics is at the forefront of another revolution in medicine. Our products are helping to address two of healthcare's most critical challenges: namely, drug safety and efficacy on the one hand, and cost containment on the other. As personalised medicine comes of age – as it certainly will – Roche's combined expertise in diagnostics and therapeutics will play a key role in pioneering new medical breakthroughs.

William M. Burns, CEO Division Roche Pharmaceuticals

WMB. Our twin focus on pharmaceuticals and diagnostics will continue to serve us well in the future, particularly given the industry trend away from 'one size fits all' products to more individualised therapeutic options – a trend, I might add, in which Roche has clearly been a leader. Clinically documented therapeutic benefits are increasingly what count. Our strengths in biotechnology, our unique research network and our lead in diagnostics R&D are all major competitive advantages.

When will personalised medicine be a reality?

HvP. What seemed like a distant vision a few years ago is now coming within reach. Roche has already launched the world's first commercially available pharmacogenomic test, the AmpliChip CYP450 Test. It helps physicians select the medicines and dosages most suitable for their patients. One of the key technologies powering the test is the polymerase chain reaction, or 'PCR' for short. The other is the DNA microarray. We're now developing microarray-based tests for the diagnosis and monitoring of cancer, osteoporosis and other complex diseases. Particularly in oncology, our aim is to enable treatments to be tailored more closely to the genetic profiles of specific patient populations. Our leukemia microarray, for example, will be a major step forward in discriminating between leukemia subtypes quickly and reliably. And our AmpliChip p53 Test could one day help physicians reliably

Erich Hunziker, Chief Financial Officer

determine how aggressive a cancer is and decide which therapies will work and which ones won't.

WMB. Our divisions have been working together on biomarkers for several years now. Biomarkers have the potential to increase our understanding of drug efficacy and safety, and as Heino just indicated, they're playing an increasingly significant role in drug discovery and development. For instance, we're currently collaborating with our colleagues over in Diagnostics on a biomarker that will predict which patients with rheumatoid arthritis are most likely to benefit from treatment with MabThera/Rituxan or Actemra. Rheumatoid arthritis is an emerging area of strength for Roche. Given the growing range of treatment options for rheumatoid arthritis, it would be extremely useful to have a test that predicts how different patients might respond to different drugs. Personalising medicine also means developing more targeted drugs. At present we're pursuing the development of cancer drugs for adjuvant use very aggressively. These aren't palliative treatments any longer – we're moving from extending patients' lives to curing cancers. Despite recent advances, however, the war on cancer is still, unfortunately, far from being won.

Focusing on 'high-end' medical innovations is commercially risky given the huge investments involved and the inherent uncertainty of R&D. How does Roche counterbalance these risks?

EH. Despite heavy investments in R&D, production and marketing, there are no guarantees of success. Generally speaking, we'll continue to pursue a rather conservative financial investment strategy, since that helps counterbalance the commercial risks associated with our high-tech operating businesses.

WMB. Maintaining the right balance between in-house and external R&D in our innovation network can be viewed as a kind of 'risk spreading' strategy. Our majority stakes in Genentech and Chugai and our many other alliances and partnerships complement and augment our internal capabilities in a variety of ways. Among other things, by reinforcing a corporate culture that promotes creativity. And of course they have significantly enhanced the depth and quality of our development pipeline, which is an important aspect of risk management. We need to continue refining the structures and skills that have enabled us to build and manage our innovation network so successfully. We need to ensure that we have the capabilities to recognise promising emerging technologies very early on as well as the partnership and governance structures that will continue to make us a preferred partner for product and technology alliances.

Right now Roche is enjoying strong operating earnings and expects them to continue. What do you propose to do with all the cash? What are the priorities?

EH. Repaying debt and increasing our net liquidity are high on the list of financial priorities, and certainly some of our strong cash flow will go for that. Good as our balance sheet currently is, we want to make it even better, which will give us greater flexibility to strengthen our core businesses. And we'll continue to make carefully selected acquisitions – primarily to strengthen the Group strategically and gain access to new technologies. That's what our financial resources are for. Our goal isn't to maximise quarterly earnings – it never has been and never will be. That's a trap we've managed to avoid, and it would be at odds with the long development cycles in our businesses.

HvP. The healthcare market will change significantly over the next decade, and in ways that are fairly easy to predict. Ageing populations and population growth are certain to fuel demand for healthcare, while increasing the pressure to contain its costs. And it seems equally certain that personalised medicine will become a growing part of mainstream medical practice. Ten years from now we want to be a company that consistently brings clinically differentiated products and services to market. And we want to be acknowledged by regulators and payers as a company with a steady eye on delivering benefits that justify the costs. Our distinctive combination of strengths gives us a strategic edge here by enabling us to develop novel products and services spanning the entire healthcare spectrum. We believe there have to be improvements at every step in the healthcare process, starting with predisposition screening and early detection; and at Roche we'll carry on making significant contributions on all these fronts.

WMB. Achieving our ambitions will require us to continue our strong financial commitment to research and development – something we have every intention of doing. World-class research is the backbone of our strategy of creating value through innovation. It's what enables us to deliver advances in healthcare, creating superior value for patients and for all our other stakeholders. And that means that we'll have to keep an especially close eye on new and emerging developments in science and technology, so that we can continue to anticipate trends and adjust and refine our strategy accordingly.

Heino von Prondzynski, CEO Division Roche Diagnostics*

* Until the end of 2005.

'We couldn't have stood the uncertainty any longer.'

Predisposition | Early detection | Prevention | Diagnosis | Therapy | Monitoring

How a test for HIV spared two parents months of worry

'You have a healthy baby' are first words parents want to hear after the birth of a child. Ruth and Colin Webb were no different. The British couple were HIV-positive when their daughters were born. There was a time when the Webbs would have had to wait an agonising 18 months after their daughters' births to find out whether the girls had HIV. That's how long it took for the less sensitive tests used at that time to detect the virus in a child's body.

HIV-positive mothers like Ruth Webb make a huge effort to give birth to healthy children. To reduce the risk of mother-to-child transmission, Ruth took Fortovase during her pregnancies to lower the amount of HIV in her blood, and her doctor closely tracked her viral load with an HIV monitoring test. There was no way of knowing whether the babies would be alright until they were born, but at least they were spared all those additional months of anxious waiting.

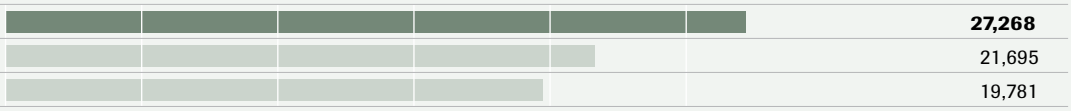
An HIV-1 DNA test provided initial reassurance within a few weeks of birth. For the Webbs their girls' test results were an enormous relief. Sarah and Anna, now five and seven years old, were both HIV-negative.

Early diagnosis

PCR-based tests can detect even tiny amounts of HIV, making it possible to diagnose infection long before any symptoms appear. Besides resolving uncertainties about perinatal HIV transmission, this can give HIV-positive patients and their doctors a critical time advantage in fighting the virus. The earlier therapy is started, the better.

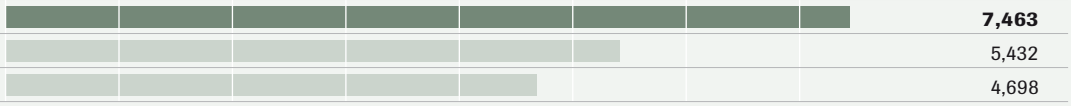
Pharmaceuticals Division in brief

Sales *in millions of CHF*



2005	**27,268**
2004	21,695
2003	19,781

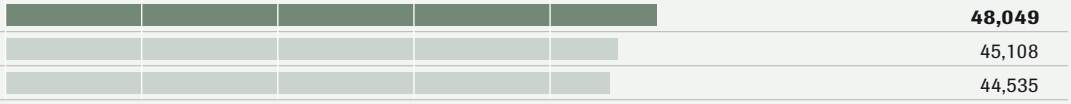
Operating profit before exceptional items[1] *in millions of CHF*



2005	**7,463**
2004	5,432
2003	4,698

1) From 2004 including charges for all equity compensation plans.

Number of employees



2005	**48,049**
2004	45,108
2003	44,535

Key figures

	In millions of CHF	% change in CHF	% change in local currencies	As % of sales
Sales	27,268	26	25	100
– Roche Pharmaceuticals	16,955	21	20	62
– Genentech	6,614	46	46	24
– Chugai	3,699	15	17	14
EBITDA	8,997	30	29	33.0
Operating profit[1]	7,463	37	37	27.4
Research and development	4,986	12	12	18.3

1) Before exceptional items.

Pharma Executive Committee *1 January 2006*

William M. Burns	CEO Division Roche Pharmaceuticals
George C. Abercrombie	North America
Jennifer Allerton	Informatics
Eduard Holdener	Development
Peter Hug	Partnering
Jonathan K.C. Knowles	Research
Dominic Moorhead	Finance and Controlling
Paul Newton-Syms	Human Resources
Charles Sabbah[1]	Strategic Marketing
Pascal Soriot[2]	
Claude Schreiner	Western Europe
Jan van Koeveringe	Technical Operations

1) To 28 February 2006.
2) From 1 March 2006.

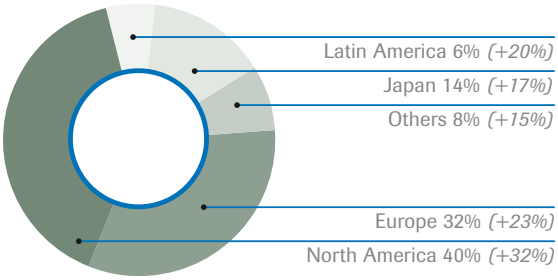
Pharmaceuticals

Results

In 2005 the Pharmaceuticals Division recorded its best result ever, exceeding the high, above-market growth of the previous year. Sales for the full year rose 25% in local currencies (26% in Swiss francs and 25% in US dollars) to 27.3 billion Swiss francs, four times as fast as the global market. The gains also more than offset the decline of the Group's former top-selling medicine Rocephin following the expiry of its US patent in July. As in 2004, growth was driven primarily by strong demand for the division's flagship oncology portfolio, now boosted by the innovative cancer treatments Avastin and Tarceva, and by strong sales of CellCept (transplantation) and Pegasys (hepatitis B and C). The anti-influenza drug Tamiflu, which many governments are stockpiling as part of pandemic readiness programmes, also contributed to growth. The division's oncology, transplantation and virology franchises significantly outpaced their respective markets.

Operating profit before exceptional items increased again, by 37% to 7.5 billion Swiss francs. The operating profit margin before exceptional items gained 2.4 percentage points, rising from 25.0% in 2004 to 27.4% in 2005. This improvement was achieved despite higher investments in R&D, continued product launch activities and, by comparison with 2004, much lower gains from product divestments. EBITDA totalled 9 billion Swiss francs or 33.0% of sales, compared with 32.0% the previous year.

Sales by region



Italic = growth rates.

Therapeutic areas

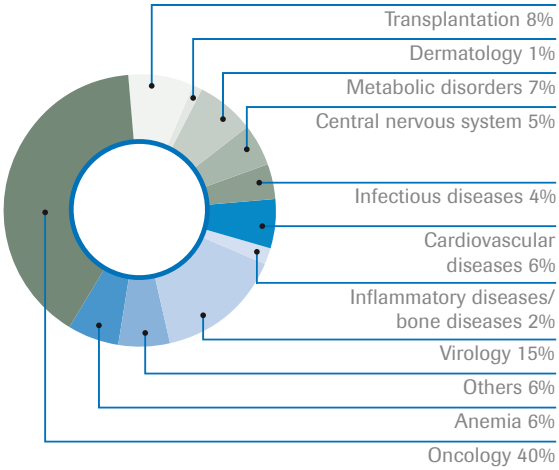
Oncology

Cancer is one of the main causes of death in industrialised countries, and the Roche Group is at the forefront of the search for better solutions for patients and physicians in this important area of unmet medical need. Roche is pioneering a number of advances in cancer treatment, including targeted therapy. MabThera/Rituxan, Herceptin, Avastin, Tarceva and Xeloda are all examples of the Roche Group's innovative cancer treatments.

Two thousand and five was an outstanding year for the Roche Group's oncology portfolio[1]. Sales of oncology products grew 42%[2] and now account

1) Oncology portfolio: MabThera/Rituxan, Herceptin, Avastin, Xeloda, Tarceva, Bondronat, Kytril, Furtulon, Neupogen, NeoRecormon (36%), Roferon-A (70%), Neutrogin, Picibanil, Vesanoid.
2) Unless otherwise stated, all growth rates are in local currencies.

Sales by therapeutic area



for 40% of divisional sales. All major brands contributed to this result, which has substantially reinforced the Group's position as the world's leading provider of cancer medications.

Non-Hodgkin's lymphoma (NHL), a group of malignancies of the lymphatic system, affects approximately 1.5 million people worldwide and claims an estimated 300,000 lives each year. Sales of MabThera/Rituxan (rituximab), for the treatment of indolent and aggressive forms of NHL, were strong throughout the year, driven by a steady rise in prescriptions for both forms of NHL in Europe. In August Genentech and Biogen Idec filed a supplemental application with the US Food and Drug Administration (FDA) for approval of the product for use in untreated patients with intermediate grade or aggressive NHL. A pivotal international phase III clinical trial has shown that two years of maintenance therapy with MabThera/Rituxan dramatically improves the chances of survival of patients suffering from indolent non-Hodgkin's lymphoma, regardless of their initial therapy. Based on these results, Roche filed an application with EU regulators in December to expand the product's indications to include maintenance treatment in patients with indolent NHL. (See *Major development activities,* pp. 26–29, for information about ongoing clinical development programmes with MabThera/Rituxan and other products.)

Breast cancer is the most common cancer among women worldwide, with over 1 million women newly diagnosed and almost 400,000 dying from the disease each year. There are different types of breast cancer, and knowledge of tumour characteristics is essential for determining appropriate treatment. Herceptin (trastuzumab) is designed specifically for a particularly aggressive type of tumour (HER2-positive) that accounts for approximately 20–30% of all breast cancers. Sales of Herceptin, the only targeted treatment approved for HER2-positive breast cancer, showed impressive gains in all key markets in 2005. Strong growth in the US and Europe was driven by extensions in treatment duration and increased first-line penetration. Herceptin is also supported by a considerable, and growing, body of clinical data showing that the product offers significant survival benefits in the advanced and early disease settings. As a result of very strong data reported in 2005, Herceptin is already being used and reimbursed in some countries in the adjuvant (early disease) setting in advance of approval. (See also *Major development activities, Oncology,* p. 27, *Setting new standards in cancer treatment,* p. 30, and patient story, p. 71.)

Skeletal complications, including hypercalcemia, bone lesions and fractures, are often associated with cancer. Following the rollout of Bondronat (ibandronic acid) in major European markets for the prevention of skeletal events in patients with breast cancer and bone metastases, sales increased strongly, by 108% to 79 million Swiss francs.

Colorectal cancer – cancer of the large intestine or rectum – accounts for over 1 million new cases (around 10% of all newly diagnosed cancers) worldwide each year. It is the second most common cause of cancer deaths in Europe. The main treatment is surgery, which may also be combined with radiotherapy and chemotherapy.

Avastin (bevacizumab), the first anti-angiogenic drug for the treatment of cancer, generated an impressive 1.7 billion Swiss francs in sales in its first full year on the market. Already approved in the US for the treatment of advanced colorectal cancer, Avastin received EU approval for the same indication in January 2005 and has now been launched in

Oncology professionals moved at ASCO

More than 20,000 oncology specialists and other professionals attended the 41st American Society of Clinical Oncology (ASCO) Meeting in Orlando, Florida, last May. Also present was Jonas Marques, oncology/hematology sales manager at Roche Brazil, who was particularly interested in the special session on Avastin and Herceptin.

Both products were featured in a packed session that clearly moved the attendees, who considered the studies presented extremely important because of their impact and consistent findings. During the Herceptin presentation, one of the world's leading oncologists remarked, 'Biology has spoken, and we must listen,' and added, 'Herceptin has ushered in a new era of breast cancer treatment.'

The presentation's impact was evident. 'After the session,' says Jonas 'one Brazilian specialist called his clinic to prescribe Herceptin as adjuvant therapy for patients he had already treated for breast cancer in the last six months.'

Oncologists were also very impressed with the data on Avastin, which appears to have potential for treatment of cancers other than colorectal. It is currently awaiting approval in Brazil.

The 7,000 attendees responded with a standing ovation. 'This is the first time I have seen this at any type of data presentation,' says Jonas. 'I think it says a lot about the impact of these products on the cancer world.'

Jonas joined the Roche Brazil oncology team in 2002 and has always been aware of the importance of his work to patient care. 'The Herceptin presentation at the 2005 ASCO Meeting has given my job new meaning. Women with HER2-positive breast cancer may now have a real chance for long-term survival.'

key European markets. Sales in the US continue to show rapid growth, while uptake in Europe has also been very strong. (See patient story, p. 85.)

Sales of Xeloda (capecitabine) continued their strong upward trend in 2005, with impressive gains in all major markets. Growth has been fuelled by recent US and EU approvals for the use of the product for adjuvant treatment (after surgery) of colon cancer.

With an estimated 1.2 million new cases annually, lung cancer is the most common cancer worldwide. It is the leading cause of cancer deaths in the world and in Europe. Pancreatic cancer, one of the most aggressive malignancies, kills a higher proportion of patients in the first year after diagnosis than any other cancer. It is often resistant to chemotherapy and radiotherapy and tends to spread quickly to other parts of the body. Pancreatic cancer is the fifth leading cause of cancer deaths in the developed world and the tenth most frequent cancer in Europe, where it kills some 78,000 people per year.

In its first full year on the market, Tarceva (erlotinib), a novel targeted cancer drug with proven survival benefit in advanced non-small cell lung cancer and pancreatic cancer, generated robust

sales. Market response to the product has been very positive. Following US approval late in 2004 for second- or third-line treatment of non-small cell lung cancer, the product received EU approval for the same indication in September 2005. It has already been launched in several European countries, with rollouts in further markets scheduled throughout 2006. In November the FDA approved Tarceva for the treatment of advanced pancreatic cancer; a filing for this indication was submitted to EU regulators in October.

Anemia

Anemia occurs when the number of red blood cells falls below normal, starving organs and tissues of oxygen. It is seen in over 80% of patients with impaired renal function due to chronic kidney disease and in up to 60% of patients with cancer. The potential long-term effects of anemia include cardiovascular disease in renal patients and reduced survival in patients with cancer. Anemia can be fatal if left untreated.

Sales of Roche's NeoRecormon and Chugai's Epogin (epoetin beta), for the treatment of anemia, showed healthy growth in 2005. NeoRecormon retained its leadership position in its markets despite sustained pricing pressure, with both indications (cancer-related anemia and renal anemia) contributing to an 11% increase in sales. In the oncology setting NeoRecormon continued its strong market penetration, posting growth of 21%, well ahead of the market (9%), thanks primarily to continued adoption of the convenient once-weekly prefilled syringe formulation. NeoRecormon is now indicated for the treatment of anemia in patients with all solid and lymphoid cancers receiving any form of chemotherapy.

Transplantation

Some 70,000 people worldwide receive life-saving organ transplants each year. Thanks to advances in surgical procedures and immunosuppressive therapy to prevent organ rejection, transplant recipients can now survive for many years with their new organs. This means increased demand for effective, low-toxicity immunosuppressant drugs like CellCept (mycophenolate mofetil), which has proven long-term organ and patient survival benefits. Zenapax (daclizumab), which prevents the acute rejection of newly transplanted organs, and Valcyte (valganciclovir), for the prevention of cytomegalovirus (CMV), a dangerous infection associated with transplantation, complete the Roche transplantation portfolio. Roche supports basic transplantation research through its funding of the independent Roche Organ Transplantation Research Foundation.

The Roche Group maintained its global leadership in the transplantation market in 2005. The Group's transplantation portfolio generated total sales of 2.2 billion Swiss francs, a rise of 19% over the previous year. The immunosuppressant CellCept posted solid double-digit gains globally and in its key regions, maintaining its leadership of the mycophenolic acid market (with a market share of over 95%) despite the entry of a new competitor.

Valcyte, the market leader for prevention of CMV disease, showed consistent growth throughout the year. A solid double-digit gain was recorded for combined sales of Valcyte and Cymevene (ganciclovir).

Virology

The liver is one of the body's most important organs, performing over 500 vital functions. The hepatitis B and C viruses (HBV, HCV) both cause acute and chronic liver disease, potentially leading to liver failure, cirrhosis and cancer. Worldwide, 350 million people are thought to be chronically infected with HBV, a highly infectious pathogen that is responsible for an estimated 1 million deaths annually. More than 170 million people around the world are infected with HCV, and 3 to 4 million new cases occur each year. Hepatitis C is the main reason for liver transplantation.

Combined sales of Pegasys (peginterferon alfa-2a) and Copegus (ribavirin) showed strong growth in 2005. In particular, higher sales volumes in Europe were driven by market share increases and market expansion as a result of new indications. Significant approvals towards the end of 2004 and early in 2005 have given the Pegasys plus Copegus combination the broadest range of hepatitis C indications

Meeting world demand for Tamiflu

The World Health Organization (WHO) recommends that governments stockpile antivirals in preparation for a possible influenza pandemic as part of their overall pandemic plans. Roche is assisting governments by dramatically expanding Tamiflu production capacity to respond to this critical need.

Armin Knoblich, global supply chain leader for Tamiflu, is proud to be part of an international task force of Roche specialists who have been working around the clock to ramp up supply quickly. 'To be able to produce over 300 million treatments annually by 2007,' he says, 'we are expanding our network of suppliers, third-party manufacturers, and licensees and selectively investing in our own facilities. That way, we can meet the demand for Tamiflu while keeping our manufacturing network flexible enough to respond to the situation in future.'

New production processes will also play a role. For example, shikimic acid, the starting material for Tamiflu, is extracted from star anise, a plant native to four provinces in China. But shikimic acid can also be produced in large quantities by a special fermentation method that does not rely on star anise. By expanding production of shikimic acid by fermentation, Roche is helping to ensure that Tamiflu production is not held back by a crop failure or other disruption of supply.

of any product or combination, including use in patients co-infected with HIV and in those with normal liver enzyme levels. An application for approval of combined Pegasys and Copegus in hepatitis C by Chugai has been designated for priority review by the Japanese authorities. Pegasys is also approved for the treatment of hepatitis B in over 50 countries worldwide.

Worldwide sales of Tamiflu (oseltamivir) rose to 1.6 billion Swiss francs, driven by a severe influenza season in Japan early in the year and increased orders for pandemic readiness supplies. Over 60 countries have now placed orders for pandemic stocks of Tamiflu, with some purchasing enough to cover 25–40% of their populations. Roche has agreed to donate over five million packs of Tamiflu to the World Health Organization (WHO): two million packs to be kept in regional stockpiles for use in the event of outbreaks of avian influenza and another three million packs in central storage, reserved for use as a rapid response stockpile to contain an influenza pandemic outbreak. Roche continues to substantially expand its Tamiflu production capacity and will be able to produce over 300 million treatments annually by 2007, using a collaborative network of its own facilities and those of a significant number of independent companies. In October Roche announced its willingness to enter discussions with governments and other manufacturers on the production of Tamiflu for emergency pandemic use. Roche has since signed sublicensing agreements with Shanghai Pharmaceuticals for China and Hetero Drugs in India and is in discussion with twelve additional partners to enhance the Tamiflu production network. At the end of the year the FDA approved and the EMEA and the Swiss authorities recommended approval of the product for prevention of influenza in children aged 1–12 years. (See *Meeting world demand for Tamiflu,* above, and *Access to medicines,* p. 31.)

Major product approvals and launches in 2005[1)]

Product	Generic name	Indication	Country
Avastin	bevacizumab	first-line treatment in combination with chemotherapy of metastatic colorectal cancer	EU
Bonviva/Boniva	ibandronic acid	osteoporosis, oral once-monthly formulation	EU, USA, Switzerland
		osteoporosis, intravenous formulation	USA
Invirase	saquinavir	HIV disease, 500 mg formulation	EU, Switzerland
Pegasys	peginterferon alfa-2a	chronic hepatitis B	EU, USA
		HCV-HIV co-infection	EU, USA, Switzerland
Tarceva	erlotinib	second- or third-line treatment of advanced non-small cell lung cancer	EU, Switzerland
		advanced pancreatic cancer, in combination with gemcitabine	USA
Xeloda	capecitabine	adjuvant colon cancer monotherapy	EU, USA Switzerland

1) Includes supplemental indications; updated to 6 January 2005.

HIV is a worldwide pandemic, and the number of people living with HIV continues to rise. The World Health Organization estimates that 40.3 million people, including more than 2.3 million children, were living with HIV/AIDS at the end of 2005. For almost 20 years Roche's innovative drugs and diagnostic tests have placed it at the forefront of efforts to combat HIV infection and AIDS, and we will continue working to improve the standard of HIV care worldwide. For information on Roche's HIV/AIDS initiatives, see *Access to medicines* (p. 30), *Ensuring access to healthcare worldwide* (p. 79), and visit www.roche.com.

Sales of Fuzeon (enfuvirtide) increased 53% to 259 million Swiss francs in 2005, helped by data from major studies showing the added value of Fuzeon when prescribed together with the latest anti-HIV agents. Recent updates to key treatment guidelines also support Fuzeon use in treatment-experienced patients and are expected to drive further uptake of the drug.

Primary care

Osteoporosis causes a gradual loss of bone density, making bones brittle and prone to break. It affects millions of people worldwide, especially women after the menopause.

Bonviva/Boniva (ibandronic acid), the first and only once-monthly oral bisphosphonate approved for the treatment of postmenopausal osteoporosis, was launched by Roche and its copromotion partner GlaxoSmithKline in the US in April and in Europe in September. Sales totalled 86 million Swiss francs and are expected to gain further momentum as physicians and patients recognise and prefer the simplicity and convenience of a once-monthly tablet. In January 2006 Boniva Injection became the first intravenous medication to be approved in the US for the treatment of postmenopausal osteoporosis, providing the proven bone-strengthening benefits of bisphosphonate therapy to more women. Given once every three months, Boniva Injection is designed to meet the needs of patients who are unable to take or tolerate oral bisphosphonates. The EU authorities are currently reviewing a marketing application for the same innovative formulation of Bonviva. (See patient story, p. 43.)

Top-selling pharmaceutical products — Roche Group

Product	Generic name	Indication	Sales in millions of CHF	% change in local currencies
MabThera / Rituxan	rituximab	non-Hodgkin's lymphoma	4,154	22
NeoRecormon, Epogin	epoetin beta	anemia	2,252	8
Herceptin	trastuzumab	metastatic breast cancer	2,146	48
CellCept	mycophenolate mofetil	transplantation	1,705	20
Avastin	bevacizumab	metastatic colorectal cancer	1,665	141
Tamiflu	oseltamivir	treatment and prevention of influenza A and B	1,558	370
Pegasys	peginterferon alfa-2a	hepatitis B and C	1,403	17
Rocephin	ceftriaxone	bacterial infections	927	–29
Xeloda	capecitabine	colorectal or breast cancer	796	47
Xenical	orlistat	weight loss, weight control	635	5
Kytril	granisetron	nausea and vomiting induced by chemotherapy or radiation therapy or following surgery	500	9
Nutropin, Protropin	somatropin, somatrem	growth hormone deficiency	476	6
Xolair	omalizumab	asthma	408	74
Copegus	ribavirin	hepatitis C	407	6
Cymevene, Valcyte	ganciclovir, valganciclovir	cytomegalovirus infection	394	19
Pulmozyme	dornase alfa/DNase	cystic fibrosis	393	15
Tarceva	erlotinib	non-small cell lung cancer, pancreatic cancer	387	2,224
Neutrogin	lenograstim	neutropenia associated with chemotherapy	364	15
Dilatrend	carvedilol	chronic heart failure, hypertension, coronary artery disease	326	–11
Activase, TNKase	alteplase, tenecteplase	myocardial infarction	310	11

Global sales of Xenical (orlistat) were up 5% in a flat market. In 2005 the product's EU labeling was expanded to include data on the use of the product in obese adolescents. Xenical is thus the first and only weight-loss medication in the United States and Europe with such information in the label. In February the existing agreement with GlaxoSmithKline was expanded to include promotion of prescription Xenical in the US by one of GSK's sales forces. In January 2006 an FDA advisory committee recommended approval of an application filed by GSK last June to market low-dose orlistat as an over-the-counter medicine for weight loss.

Other major products

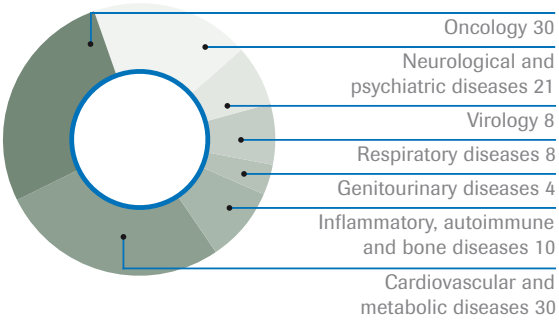
As expected, sales of Rocephin (ceftriaxone) declined markedly following the expiry of the product's US patent in July and the emergence of generic competitors in the second half of the year.

Research and development

Roche is committed to discovering and developing clinically differentiated medicines in key therapeutic areas, including oncology, inflammatory, autoimmune and bone diseases, virology and transplantation. The broad interdisciplinary approach made possible by the combined expertise of the Group's Pharmaceuticals and Diagnostics Divisions is helping to expand our understanding of diseases and biological processes and translate scientific advances into innovative medicines. Innovation in science and technology is the core of the Roche Group's focused R&D strategy.

The success of this strategy is reflected in the richness of the Group's pharmaceuticals pipeline. Its strength is expressed not only in the number of new molecular entities (NMEs) in the R&D portfolio. The success rate of the Group's late-stage clinical

111 research projects in major therapeutic areas
(31 December 2005)



trials – in 2005 fifteen out of fifteen phase III trials met their clinical endpoints – also makes Roche an industry leader. This is due in part to selection decisions based on aggressive screening and thorough profiling of compounds at the discovery, preclinical and early clinical stages.

Another cornerstone of our R&D strategy emphasises the value of leveraging key product assets by expanding their use into new indications. MabThera/Rituxan is a case in point: already established as a cancer medicine, it has now been tested in another important area of unmet medical need, rheumatoid arthritis (*see Rheumatoid arthritis and autoimmune diseases,* p. 29).

Roche is continuing to implement initiatives that aim to achieve better patient selection in clinical development programmes by developing predictive biomarkers. This is a key area of collaboration between the Pharmaceuticals and Diagnostics Divisions. Tests that enable predictions of how different patients might respond to particular drugs will allow identification of the most effective drug combinations for patient subpopulations while also limiting undesirable effects.

The acquisition of GlycArt Biotechnology, completed in July 2005, represents a significant addition of expertise in therapeutic antibody research and adds new, cutting-edge technologies and products to the Roche R&D organisation and pipeline. GlycArt's unique protein technology complements efforts to develop biological compounds that offer patients superior efficacy and safety.

R&D pipeline

At the end of 2005 the Pharmaceuticals Division's R&D pipeline comprised 108 projects, including 59 new molecular entities (NMEs) and 49 additional indications. Fourteen NMEs are currently in phase 0, 21 in phase I, 19 in phase II and five in phase III or filed for regulatory review. In 2005 13 projects entered phase I development, 12 entered phase II and 13 entered phase III. Seven projects moved out of the R&D portfolio following regulatory approvals.

Roche Pharmaceuticals currently has 111 projects in preclinical research across seven therapeutic areas and 78 development projects in nine therapeutic areas.

In 2005 four Roche-managed R&D projects were discontinued in phase 0 (one of which reverted to the R&D partner); eight were discontinued in phase I (with two reverting to R&D partners and two outlicensed); three were discontinued in phase II (of which one reverted to the partner). There were no discontinuations in phase III.

Partnering for success

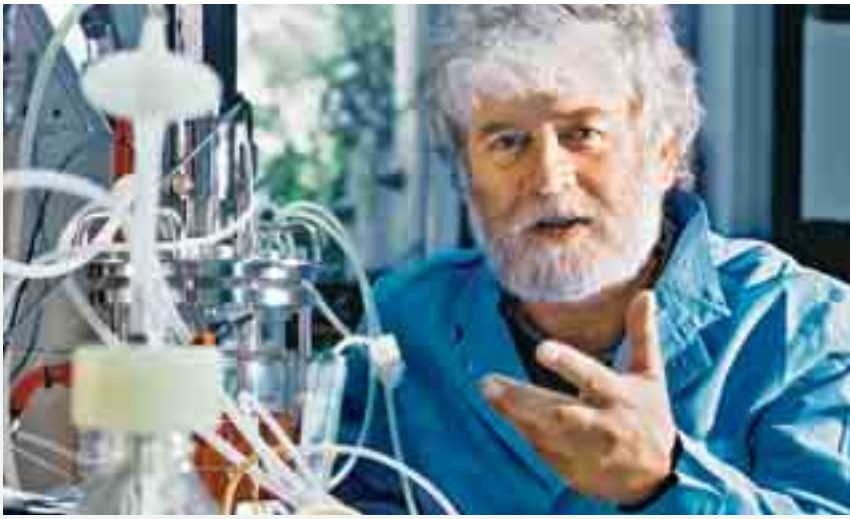
By pursuing innovative strategic alliances to complement the Group's strong internal research, the Roche Pharma Partnering unit continued helping to build a dynamic and robust pharmaceuticals portfolio (see *Partnering for innovation,* p. 28). In 2005 Roche Pharmaceuticals signed 31 new licensing agreements, including six product-related and 17 research and technology partnerships, and extended relationships with long-term partners such as GlaxoSmithKline, Protein Design Labs and Evotec.

Therapeutic proteins – building a stronger portfolio

Biopharmaceuticals are promising candidates for innovative therapies in a number of disease areas. However, creating protein-based drugs is a complex process that poses challenges very different to the manufacturing of small molecules. Roche Pharmaceuticals established the Therapeutic Protein Initiative (TPI) to build and expand its expertise in this area.

TPI is a global initiative, uniting contributions from many divisional functions, with protein discovery and development activities in Penzberg and protein formulation in Basel as its cornerstones. By acquiring and developing external and internal knowledge and skills, Roche has established novel technologies in cell-line development, automated product isolation and advanced analytical technologies.

Since its inception in 2001 TPI has helped increase Roche Pharmaceuticals' R&D productivity, with the number of protein-based projects rising from four to now more than 25. Most of these are in the key areas of oncology, inflammatory and autoimmune disorders and transplantation.



'Recombinant proteins, especially monoclonal antibodies, have demonstrated their value as novel therapeutic agents due to their high target specificity. They already provide safe and effective therapies for many patients,' says Stephan Fischer, Global Head of Biologics Research and Development at Roche. 'Our expertise and competence in all functions involved in protein research, development and manufacturing put the Roche Group in a unique position to keep delivering breakthrough medicines.'

Major development activities

Oncology

Major clinical development programmes are exploring the benefits of MabThera/Rituxan, Herceptin, Avastin, Tarceva and Xeloda in additional important indications.

Recent phase III data have shown that Avastin has significant survival benefit in metastatic non-small cell lung cancer and metastatic breast cancer, increasing the drug's potential to become a mainstay of cancer treatment (see *Setting new standards in cancer treatment,* p. 30). Regulatory filings for these new indications are planned for 2006. In addition, Avastin is being studied in phase III trials in the treatment of adjuvant colon cancer, advanced renal cell carcinoma, and pancreatic, prostate and ovarian cancer. It is also being tested in combination with Tarceva in non-small cell lung cancer (NSCLC).

Roche is evaluating MabThera/Rituxan in chronic lymphocytic leukemia (CLL) in two phase III programmes exploring its use as first-line treatment and in the therapy of relapsing CLL.

Phase III and IV trials with Herceptin are ongoing in the metastatic and adjuvant settings in breast cancer. Herceptin is also being evaluated in the treatment of gastric cancer. Data from four large clinical trials in patients with early-stage breast

R&D pipeline: all major development projects successfully brought forward

Therapeutic area	Project ID	Project/product (generic name)	Pharmacological class	Indication	Phase	Partner
Cardiovascular and metabolic diseases	R1438		enzyme inhibitor	type 2 diabetes	II	
	R1439			type 2 diabetes	I	
	R1440		enzyme modulator	type 2 diabetes	II	
	R1511			type 2 diabetes	0	
	R1579			type 2 diabetes	0	
	R1593			dyslipidemia	I	Nippon Shinyaku (NS-220)
	R1658		CETP inhibitor	dyslipidemia	II	Japan Tobacco (JTT-705)
	R1664			dyslipidemia	0	
	R483	insulin sensitiser	insulin sensitiser	type 2 diabetes	II	
Genitourinary disease	R1646			overactive bladder	0	
	R873		GPCR agonist	male erectile dysfunction	II	
Hematology and nephrology	R744	CERA	continous erythropoietin receptor activator	cancer-related anemia	II	
	R744	CERA	continous erythropoietin receptor activator	renal anemia	III	
Inflammatory, autoimmune and bone diseases	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	rheumatoid arthritis, DMARD inadequate responders	III	Genentech and Biogen Idec
	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	rheumatoid arthritis, anti-TNF inadequate responders	filed	Genentech and Biogen Idec
	R127	Valcyte (valganciclovir)	inhibitor of CMV replication	ulcerative colitis	I	
	R1295			rheumatoid arthritis	I	
	R1503		kinase inhibitor	rheumatoid arthritis	II	
	R1541			inflammatory bowel disease	I	
	R1569	Actemra (tocilizumab)	humanised anti-IL-6 receptor monoclonal antibody	rheumatoid arthritis	III	Chugai
	R1569	Actemra (tocilizumab)	humanised anti-IL-6 receptor monoclonal antibody	systemic onset juvenile idiopathic arthritis	III	Chugai
	R1594		humanised anti-CD20 monoclonal antibody	rheumatoid arthritis	II	Genentech (PRO70769)
	R1599			osteoarthritis	0	
	R3421			autoimmune diseases, transplantation	I	BioCryst
	R99	CellCept (mycophenolate mofetil)	IMPDH inhibitor	lupus nephritis	III	Aspreva
	R99	CellCept (mycophenolate mofetil)	IMPDH inhibitor	myasthenia gravis	III	Aspreva
Neurological and psychiatric diseases	R1450			Alzheimer's disease	0	
	R1647			depression	0	
	R1678			schizophrenia	I	
	R641			Alzheimer's disease	0	
	R7090			anxiety	I	
	R7118			schizophrenia	0	
Oncology	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	chronic lymphocytic leukemia, relapsed	III	Genentech and Biogen Idec
	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	chronic lymphocytic leukemia (1st line)	III	
	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	indolent non-Hodgkin's lymphoma – maintenance	filed	Genentech and Biogen Idec
	R1273	Omnitarg (pertuzumab)	anti-HER2 monoclonal antibody	ovarian cancer	II	Genentech
	R1273	Omnitarg (pertuzumab)	anti-HER2 monoclonal antibody	metastatic breast cancer	II	Genentech
	R1415	Tarceva (erlotinib)	EGFR inhibitor	glioblastoma multiforme	II	Genentech and OSI Pharmaceuticals
	R1415 + R435	Tarceva+Avastin (erlotinib + bevacizumab)	EGFR inhibitor + anti-VEGF monoclonal antibody	NSCLC (1st line) – maintenance	III	Genentech and OSI Pharmaceuticals
	R1415	Tarceva (erlotinib)	EGFR inhibitor	NSCLC (1st line) – combo with chemotherapy	III	Genentech and OSI Pharmaceuticals
	R1415 + R435	Tarceva+Avastin (erlotinib + bevacizumab)	EGFR inhibitor + anti-VEGF monoclonal antibody	NSCLC (2nd line)	III	Genentech and OSI Pharmaceuticals
	R1415	Tarceva (erlotinib)	EGFR inhibitor	pancreatic cancer	filed	Genentech and OSI Pharmaceuticals
	R1454			solid tumours	I	
	R1492		epothilone D	solid tumours	II	Kosan Biosciences (KOS862)
	R1507			solid tumours	0	
	R1530			solid tumours	I	
	R1550		monoclonal antibody	metastatic breast cancer	I	Antisoma
	R1594		humanised anti-CD20 monoclonal antibody	hematologic malignancies	I	Genentech (PRO70769)
	R1645		epothilone D	solid tumours	I	Kosan Biosciences (KOS1584)
	R340	Xeloda (capecitabine)	fluoropyrimidine	adjuvant breast cancer	III	
	R340	Xeloda (capecitabine)	fluoropyrimidine	adjuvant colon cancer – combo	III	
	R340	Xeloda (capecitabine)	fluoropyrimidine	metastatic colorectal cancer (1st line) – combo	III	
	R340	Xeloda (capecitabine)	fluoropyrimidine	metastatic colorectal cancer (2nd line) – combo	III	
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	NSCLC, squamous	II	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	adjuvant colon cancer	III	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	metastatic breast cancer (1st line)	III	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	metastatic breast cancer (1st line) – extension	III	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	metastatic colorectal cancer (1st line) – combo extension	III	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	renal cell carcinoma	III	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	NSCLC (1st line)	III	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	pancreatic cancer	III	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	ovarian cancer	III	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	prostate cancer	III	Genentech
	R547			solid tumours	I	
	R597	Herceptin (trastuzumab)	anti-HER2 monoclonal antibody	metastatic breast cancer – combo with hormonal therapy	III	Genentech
	R597	Herceptin (trastuzumab)	anti-HER2 monoclonal antibody	adjuvant breast cancer	III	Genentech
	R597	Herceptin (trastuzumab)	anti-HER2 monoclonal antibody	gastric cancer	III	
	R925	Bondronat (ibandronic acid)	bisphosphonate	metastatic bone pain	III	
Respiratory diseases	R35	(daclizumab)	anti-CD25 monoclonal antibody	asthma	II	PDL BioPharma
	R411		dual integrin antagonist	asthma	II	
	R667		nuclear receptor agonist	emphysema	II	
Transplantation	R35	(daclizumab)	anti-CD25 monoclonal antibody	transplant maintenance	I	PDL BioPharma
Viral and other infectious diseases	R1206			HIV	0	
	R1558		antibiotic	bacterial infections	II	Sankyo (CS023)
	R1626			HCV	I	
	R1656			HCV	I	Pharmasset
	R7025			HCV	0	Maxygen
	R7128			HCV	0	Pharmasset
Participation through Chugai	SG-75	Sigmart (nicorandil)		acute heart failure	filed	
	EPOCH	Epogin (epoetin beta)		chemotherapy-induced anemia	III	
	CHS13340		recombinant parathyroid hormone	osteoporosis	II	Daiichi Asubio Pharma
	ED-71		activated vitamin D derivate	osteoporosis	III	
	AVS	Antevas (nicaraven)	hydroxyl radical scavenger	subarachnoid hemorrhage	filed	
	CAL		humanised anti-PTHrP monoclonal antibody	bone metastases	II	
	CHC12103			solid tumours	I	Cell Therapeutics
	CGS20267	Femara (letrozole)	aromatase inhibitor	breast cancer	filed	Novartis
	GM-611	(mitemcinal fumarate)	motilin agonist	gastroparesis, irritable bowel syndrome	II	
	VAL	(valine)		post-hepatectomy	II	
Participation through Genentech		Raptiva (efalizumab)	anti-CD11a antibody	adult atopic dermatitis	I	
		Lucentis (ranibizumab)	antibody fragment to VEGF	age-related macular degeneration	filed	Novartis Ophthalmics
		Xolair (omalizumab)	anti-IgE antibody	pediatric asthma, peanut allergy	II, III	Novartis and Tanox
Opt-in opportunities	PRO128115	VEGF	topical VEGF	diabetic foot ulcer	I	Genentech
		BR3-Fc	BAFF inhibitor	rheumatoid arthritis	I	Genentech
	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	primary progressive multiple sclerosis	III	Genentech and Biogen Idec
	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	relapsed remitting multiple sclerosis	II	Genentech and Biogen Idec
	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	lupus nephritis	II	Genentech and Biogen Idec
	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	ANCA-associated vasculitis	III	Genentech and Biogen Idec
	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	systemic lupus erythematosus	III	Genentech and Biogen Idec
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	glioblastoma multiforme	II	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	adjuvant breast cancer	II	Genentech
	G-024856		topical hedgehog antagonist	basal cell carcinoma	I	Genentech and Curis
	PRO1762	Apo2L/TRAIL		cancer	I	Genentech
	R1564		vascular targeting agent	solid tumours	II	Antisoma (DMXAA)
	R1668		E2F modulator	solid tumours	I	ArQule (ARQ501)
	R1583	GLP-1	GLP-1	type 2 diabetes	II	Ipsen (BIM51077)
	R1524		calcineurin inhibitor	renal transplant	II	Isotechnika (ISA247)
	R1495		non-nucleoside reverse transcriptase inhibitor	HIV	0	Medivir
	R1589			Alzheimer's disease	I	Memory Pharmaceuticals

At the end of 2005 the Pharmaceuticals Division's R&D pipeline comprised 108 projects, including 59 new molecular entities (NMEs) and 49 additional indications. Fourteen NMEs are currently in phase 0, 21 in phase I, 19 in phase II and five in phase III or filed for regulatory review. In 2005 13 projects entered phase I development, 12 entered phase II and 13 entered phase III.

Blue type signifies first indication, black type additional indications.
Current as of 31 December 2005.

■ Therapeutic protein
■ Small molecule

Phase 0: Transition from preclinical to clinical development
Phase I: Initial studies in healthy volunteers and possibly in patients
Phase II: Efficacy, tolerability and dose-finding studies in patients
Phase III: Large-scale studies in patients for statistical confirmation of safety and efficacy

Partnering for innovation

Partnering is a key element in Roche's strategy to develop innovative, differentiated medicines for patients. Pharma Partnering (PP), the company's business development and licensing department, analyses over 1,500 external opportunities each year to find cutting-edge science to complement Roche's own R&D.

How does Roche find external innovation? 'We focus on emerging, innovative science,' says immunologist and marketing veteran Hari Kumar, one of PP's 'finders'. 'Strategy teams tell us what they need, be it a drug for a condition with no effective treatment or a technology, and we go out and look for it.'

Finders are specialists who combine scientific expertise with business acumen. Their job is to identify opportunities that could lead to new treatments, including new uses for existing Roche products.

Once a finder identifies an opportunity, a larger PP team assesses it based on three key questions: Is the science viable and differentiated? Will the opportunity complement Roche's overall strategy? What is its commercial potential? Senior management then make a decision based on the answers.

PP's alliance directors take over once a deal is approved. While the contract is being negotiated, they prepare Roche for the project's integration and ensure that communication with partners is open and clear.

Throughout the process Roche relies on its core partnering values: flexibility, respect for partners' culture and autonomy, and commitment that both sides will benefit from the collaboration. An organisation-wide partnering culture helps ensure our continued access to a broad range of external innovation and expertise.

cancer (adjuvant setting) have shown that adding Herceptin to chemotherapy significantly reduces the risk of cancer recurrence in this population. US and EU filings for this indication are planned for the first quarter of 2006.

Tarceva, a human epidermal growth factor receptor (HER1/EGFR) inhibitor, is designed to interfere with a molecular signal that plays a significant role in tumour cell growth in numerous types of cancer. It is currently being tested in the first-line and adjuvant NSCLC settings and in combination with Avastin in second-line NSCLC. Tarceva is also being evaluated in the treatment of glioblastoma multiforme, one of the most aggressive types of primary brain tumour.

Extensive late-stage programmes studying Xeloda in adjuvant breast cancer, in combination with chemotherapy in the adjuvant colon cancer setting, and in first- and second-line therapy of metastatic colorectal cancer are continuing. Recent interim analysis of a large collaborative group study of the drug as first-line treatment for advanced pancreatic cancer showed that adding Xeloda to standard chemotherapy (gemcitabine) significantly extends patient survival and improves quality of life.

A head-to-head phase III study comparing Bondronat and zoledronic acid in the treatment of metastatic bone pain has commenced, with results expected in 2007. Filings for this indication are planned in the US and Europe.

Hematology and nephrology (anemia)

Clinical development of CERA, the first continuous erythropoietin receptor activator for the treatment of anemia, is progressing on track. The phase III renal programme for this product includes six trials involving over 2,400 patients with chronic kidney disease (both on dialysis and not on dialysis). The first four phase III trials in dialysis patients were successfully completed at the end of 2005. CERA is the only anti-anemia drug ever studied using long dosing intervals (once every four weeks) in all patients for its initial filing. Roche plans to file marketing applications worldwide for CERA in renal anemia in 2006. Roche does not view the patent infringement litigation initiated by Amgen in the US as an impediment to the development and launch of CERA in the United States.

Rheumatoid arthritis and autoimmune diseases

Rheumatoid arthritis (RA) is an autoimmune disorder characterised by joint inflammation that, even when treated, can result in progressive joint destruction and, ultimately, loss of function. Its exact cause is unknown, and as yet there is no cure. Within two years of developing RA, up to 70% of patients have X-ray evidence of joint destruction, and within ten years 80% are unable to work or perform everyday tasks. RA is one of the most common autoimmune disorders and is now thought to affect over 21 million people worldwide. Current treatments include disease-modifying antirheumatic drugs (DMARDs) and biologic therapy such as the anti-TNF drugs.

In 2005 Roche significantly advanced the development of two medicines with the potential to substantially improve the treatment of RA.

MabThera/Rituxan is the first selectively targeted B cell therapy to be studied in this disease. The US and EU filings in August and September for the product's first rheumatoid arthritis indication represent a significant milestone. The filings, based on data from the pivotal REFLEX trial, cover the use of MabThera/Rituxan in patients who have failed to respond adequately to current biologic therapies, the subgroup of RA patients considered to be the most difficult to treat. Positive outcomes have also been seen in a phase IIb clinical trial (DANCER) with patients who had previously failed treatment with one or more DMARDs.

Development of Actemra (tocilizumab, formerly MRA) in RA is progressing well. Phase III data from Japan were presented at the American College of Rheumatology meeting in November. They show that treatment with Actemra significantly reduces the progression of joint damage and improves RA signs and symptoms. Based on these data, Chugai plans to file a marketing application for Actemra for RA in Japan in the first half of 2006. Patient recruitment for international phase III trials is proceeding as planned. Regulatory filings in the US and EU are expected in 2007. In 2005 Chugai launched Actemra in Japan in its first indication, Castleman's disease, a rare condition that causes severe enlargement of the lymph nodes.

CellCept is being developed in collaboration with Aspreva Pharmaceuticals for autoimmune applications, including the treatment of lupus nephritis (kidney complications associated with the autoimmune disease lupus erythematosus) and myasthenia gravis (a chronic autoimmune disease characterised by episodes of muscle weakness). Phase III clinical trials of the drug in both indications are under way. CellCept is the first potential new treatment for either of these debilitating and sometimes fatal conditions in many years. In January 2006 CellCept was designated an orphan drug in the treatment of myasthenia gravis by the FDA.

Diabetes

Roche has now completed the two-year animal carcinogenicity programme for the insulin sensitiser R483, required by the FDA for all members of this class of agents. A final decision on the commencement of phase III clinical testing of the compound in type 2 diabetes will be taken once the FDA and other agencies have completed their reviews of the carcinogenicity data.

Two other compounds being developed for the treatment of type 2 diabetes moved into phase II clinical testing in 2005, a glucokinase activator and a dipeptidyl peptidase (DPP-IV) inhibitor.

Setting new standards in cancer treatment

At the 41st meeting of the American Society of Clinical Oncology (ASCO), in Orlando, Florida, in May Roche and its partners presented data from an unprecedented eight major phase III trials that had successfully met their primary endpoints.

Product (generic name)	Indication (clinical trial)	Benefit
Avastin (bevacizumab)	Metastatic HER2-negative breast cancer, 1st line treatment (E2100)	49% improvement in overall survival
	Metastatic non-small cell lung cancer, 1st line treatment (E4599)	30% improvement in overall survival
	Metastatic colorectal cancer, 2nd line treatment (E3200)	24% reduction in risk of death
Herceptin (trastuzumab)	HER2-positive breast cancer, adjuvant treatment (NSABP B-31 and NCCTG N9831, joint analysis)	52% reduction in risk of disease recurrence
	HER2-positive breast cancer, adjuvant treatment (HERA)	46% reduction in risk of disease recurrence
MabThera / Rituxan (rituximab)	Relapsed indolent NHL, maintenance treatment (GSLG)	100% improvement in response duration at 3 years
Tarceva (erlotinib)	Pancreatic cancer, 1st line treatment (PA3)	23% improvement in overall survival

Expanding biotech production capacity

In 2005 the Roche Group continued to reconfigure its manufacturing capacities to meet the requirements of a changing product portfolio and increase the efficiency of its global manufacturing operations. In particular, a shift from chemically derived active pharmaceutical ingredients towards biologics and a corresponding trend towards sterile liquid dosage forms are driving current activities in this area. Technical development activities also reflect the impact of the Pharmaceuticals Division's dynamic R&D portfolio (including development of in-licensed products by Roche). Ongoing projects to further reduce supply chain complexity and optimise inventory levels remain on track.

Four major new facilities were dedicated last year: new biotech production facilities for epoetin and CERA in Penzberg (Germany); a state-of-the-art packaging and storage facility for injectable drugs in Mannheim (Germany); and a plant for high-potency pharmaceutical products in Shanghai. The new Penzberg and Mannheim facilities have been operational since the middle of 2005. The Shanghai facility, the first of its kind in China, is scheduled to come on stream this year; it will produce CellCept and Xeloda for the Chinese market.

The Oceanside (California) facility acquired by Genentech from Biogen Idec last June is currently being converted to produce Avastin; manufacturing of bulk drug substance is expected to commence in 2006, with FDA licensure expected in the first half of 2007. In 2005 Genentech received FDA licensure for a new Avastin manufacturing facility in Porriño, Spain.

Work on the new Basel (Switzerland) and Penzberg production facilities for therapeutic antibodies, both scheduled for technical completion in 2007, is moving ahead as planned.

Access to medicines

While the primary role of the Roche Pharmaceuticals Division is to discover, develop and commercialise innovative medicines, the adoption of policies that extend access to critically needed products to people affected by poverty throughout the world is an integral part of healthcare's mission. Therefore, in addition to supporting local initiatives to expand healthcare access, Roche has implemented patent and pricing policies and joined major international efforts aimed at addressing this problem.

Roche does not file new patents for its medicines in the 50 Least Developed Countries (as defined by the UN), nor does it enforce patents it already holds in these countries. In response to the devastating HIV/AIDS pandemic, the company has extended this policy to sub-Saharan Africa, the poorest and hardest-hit region.

The prices Roche charges for its products in low and lower-middle income countries are below the corresponding prices in Switzerland at launch. Roche supplies the HIV medicines Invirase and Viracept at no profit to Least Developed Countries and sub-Saharan Africa. As a result, reduced prices for these products apply to 93% of all people living with HIV/AIDS worldwide.

In addition, Roche is a member of the Accelerating Access Initiative, which is helping increasing numbers of HIV/AIDS patients in developing countries to receive treatment. The company also supports two other HIV treatment access programmes, the CARE programme in four African countries and the Cambodian Treatment Access Programme. In addition to providing funding, medicines and diagnostics through these programmes, Roche has also contributed to providing training in HIV/AIDS care and treatment to hundreds of healthcare professionals from more than 14 African countries and Cambodia. (See also *Ensuring access to healthcare worldwide,* p. 79, and visit www.roche-hiv.com.)

In its most recent move to extend access to vital HIV/AIDS treatments in the world's neediest areas, Roche announced in January 2006 that, as part of its new Technology Transfer Initiative, the company will provide local manufacturers within sub-Saharan Africa and Least Developed Countries with the technical expertise required to produce generic HIV medicines. This assistance will be offered free and with no conditions attached.

The threat of an avian flu pandemic represents another critical global health challenge, and Roche is closely involved in ensuring that vital medicines are available where they are most needed. Following warnings by the WHO that the next global influenza pandemic is imminent, Roche has been doing all it can to ensure worldwide availability of its influenza drug Tamiflu for pandemic use. The steps taken include implementing a tiered pricing system with significant reductions for pandemic use and licensing agreements with local companies for production of the drug for pandemic use in India and China. In addition to taking unprecedented steps to ramp up Tamiflu production capacity (see *Meeting world demand for Tamiflu,* p. 23), Roche is working with the US National Institute of Allergy and Infectious Diseases and international virology experts to expand the information base regarding the optimal use of Tamiflu against the H5N1 avian influenza strain.

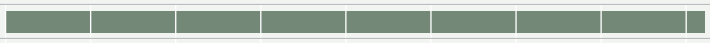
Access to medicines is an issue that affects more than the developing world – it can pose significant challenges in industrialised countries, as well. In the United States, for example, Roche is committed to making sure that every patient who needs a Roche drug has access to it, whether that patient is a senior citizen being treated for cancer, or a member of a working family facing an organ transplant. The Roche Patient Assistance Program, established in the 1960s, was the first in the industry to provide prescription drugs free of charge to qualifying patients who need them but lack prescription coverage and the means to pay for them.

Roche is also a founding member of the Partnership for Prescription Assistance, a programme sponsored by the Pharmaceutical Research and Manufacturers of America, which represents the country's leading pharmaceutical research and biotechnology companies. The programme offers a single point of access to over 475 public and private patient assistance programmes.

Similarly, Genentech provides its marketed products free of charge to eligible uninsured patients treated in the United States through the Genentech Access to Care Foundation and the Genentech Endowment for Cystic Fibrosis. Genentech is also a member of the Partnership for Prescription Assistance. To further support patient access to therapies for various diseases, in 2005 Genentech donated approximately 21 million dollars to independent, third party, public charities that offer copayment assistance to eligible patients.

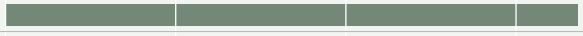
Diagnostics Division in brief

Sales *in millions of CHF*



2005	**8,243**
2004	7,827
2003	7,409

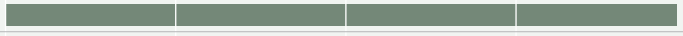
Operating profit before exceptional items[1] *in millions of CHF*



2005	**1,687**
2004	1,670
2003	1,405

1) From 2004 including charges for all equity compensation plans.

Number of employees



2005	**19,788**
2004	19,109
2003	18,302

Key figures

	In millions of CHF	% change in CHF	% change in local currencies	As % of sales
Sales	8,243	5	4	100
– Diabetes Care	2,886	4	3	35
– Centralized Diagnostics	2,906	6	5	35
– Molecular Diagnostics	1,171	6	5	14
– Near Patient Testing	718	6	5	9
– Applied Science	562	6	5	7
EBITDA	2,527	4	2	30.7
Operating profit[1]	1,687	1	–1	20.5
Research and development	719	2	2	8.7

1) Before exceptional items.

Diagnostics Executive Team *1 January 2006*

Severin Schwan	CEO Division Roche Diagnostics
Silvia Ayyoubi	Human Resources
Heiner Dreismann	Molecular Diagnostics
Christian Hebich	Finance and Services
Tiffany Olson	North America
Volker Pfahlert	Centralized Diagnostics, Applied Science
Burkhard Piper	Diabetes Care
Jürgen Schwiezer	EMEA (Europe, Middle East, Africa)
Robert Yates	Business Development

Diagnostics

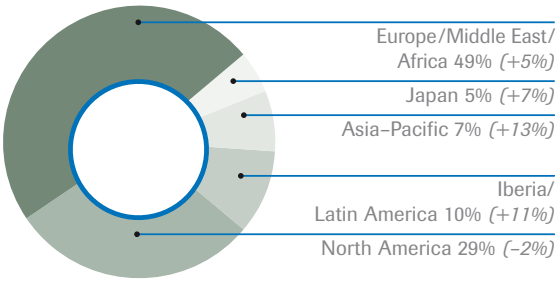
Results

Roche Diagnostics maintained its leadership position in a difficult market in 2005. Divisional sales rose 4% in local currencies (5% in Swiss francs and in US dollars), broadly in line with global market growth.

Worldwide, Roche Diagnostics launched more than 20 new products in 2005, including a complete new generation of products to replace older flagship offerings in the division's key diabetes management portfolio. During the year the division also expanded into several new, high-potential market segments, such as DNA sequencing.

Operating profit before exceptional items decreased 1% in local currencies to 1.7 billion Swiss francs, resulting in a margin decline of 0.8 percentage points to 20.5%. This was primarily due to heavy price pressures in the market, start-up costs for new manufacturing facilities and new products and higher depreciation charges. The higher depreciation resulted from an increase in instrument placements.

Sales by region



Italic = growth rate.

Business areas

Diabetes Care

Roche Diabetes Care, the market leader in diabetes management, posted sales growth of 3% in local currencies.

The business unit launched a number of innovative products in the second half of 2005. These included Accu-Chek Compact Plus, a glucose monitoring system with a built-in test strip drum and lancing device, and Accu-Chek Aviva, a successor to the Accu-Chek Advantage monitor. Also new on the market in 2005 was the Accu-Chek Spirit, a menu-driven insulin pump that sets new standards in flexibility and reliability. In addition, the business unit introduced Accu-Chek Pocket Compass 3.0, its latest software for mobile diabetes self-management. It features a bolus calculator module that enables users to calculate their bolus insulin requirements on the basis of current blood glucose, estimated food intake and several personal param-

Top selling product lines in 2005

Product line	Market segment	Business area	Sales in millions of CHF	% change in local currencies
Accu-Chek	Diabetes management	Diabetes Care	2,458	3
Cobas Integra[1)], Roche Hitachi[1)]	Clinical chemistry	Centralized Diagnostics	1,165	–1
Elecsys	Immunodiagnostics	Centralized Diagnostics	989	11
Amplicor tests, Cobas Amplicor	Clinical molecular diagnostics	Molecular Diagnostics	712	4
Cobas AmpliScreen	Nucleic acid-based blood screening	Molecular Diagnostics	311	11
CoaguChek	Coagulation monitoring	Near Patient Testing	183	13

1) Excluding HIAs (homogeneous immunoassays).

eters. With this new generation of products, Roche Diagnostics continues to lead the way in three key areas of effective diabetes management: glucose monitoring, insulin delivery and data management.

There is a growing body of evidence documenting the benefits of regular blood glucose monitoring. For the first time, a multicentre study has verified that glucose self-monitoring reduces morbidity and mortality among people with type 2 diabetes. Findings like these are expected to motivate people with type 2 diabetes to monitor their glucose more closely.

The Food and Drug Administration (FDA) has completed its inspection of the Roche Diagnostics facility in Burgdorf (Switzerland). The final decision on whether to lift the US import alert on pumps made at the facility is still pending.

Centralized Diagnostics

Roche Centralized Diagnostics supplies integrated total solutions for clinical laboratories. The business area reported 5% sales growth in local currencies, taking the lead for the first time in this important segment of the diagnostics market.

Growth was due primarily to the continued success of the immunodiagnostics portfolio. Roche is pursuing leadership in immunodiagnostics and in 2005 moved a step closer to achieving this medium-term goal. Placements of Elecsys and E170 systems advanced 24% for the year, reaching another record high; and thanks to strong demand for the Elecsys proBNP assay, Roche became the leading supplier of laboratory tests for cardiac markers. Sales of the Elecsys assay were helped by the more than 200 scientific papers published on NT-proBNP in 2005 and by inclusion of this marker in patient management guidelines. (See patient story on p. 65.)

Global trends such as mounting pressure on healthcare budgets, combined with a shortage of trained laboratory staff, mean that laboratories are increasingly dependent on automated, integrated laboratory systems that offer cost-efficiency and high performance. This creates an ideal market environment for the 2006 rollout of cobas 6000, a new generation of modular analysers for medium-size laboratories.

Investments in new technologies to automate the many tasks that precede and follow actual testing in the laboratory are beginning to pay off. An expanded cooperation agreement signed with the German company PVT Probenverteiltechnik in 2004 covering pre-analytical automation has strengthened our position as a leading provider of total laboratory solutions. RSD-800/A, a new system providing complete pre-analytical automation, has already been successfully launched in nine markets.

New markers point the way to better care

Immunodiagnostics represent a major share of the global *in vitro* diagnostics market – about one-fourth at last count and still climbing. Roche is tapping the potential of innovative immunodiagnostic markers to address unmet medical needs.

Immunodiagnostics exploit a basic feature of the body's natural defence system against disease. When viruses, bacteria or other foreign substances (collectively referred to as 'antigens') enter the body, it responds by producing antibodies that bind to the antigens and neutralise them. This response is highly specific: just as a key will normally fit only one lock, antibodies react only with the antigens that stimulated their production.

'Immunodiagnostic tests mimic this natural defensive reaction,' explains Joachim Eberle, Head of Research and Development at Roche Centralized Diagnostics. 'Because of their specificity, antibodies can be used to detect the presence of particular antigens in the body, and hence help in diagnosing disease.'

The immunoassay CA 15-3, for example, identifies a tumour marker protein in breast cancer patients. Early data from an ongoing study of the assay at Grosshadern University Hospital in Munich (Germany) are very encouraging. Following breast cancer surgery, a blood test is done to determine baseline levels of the tumour marker, and then further tests for the marker are repeated at six-week intervals. A rise in CA 15-3 levels can indicate the growth of new cancer cells from six to twelve months before a patient develops any symptoms – enabling physicians to take action sooner and save precious time. The natural mechanisms of antibody-antigen interaction are thus giving new hope to patients and health professionals.

Molecular Diagnostics

With sales growth of 5% and a market share of over 40%, Roche Molecular Diagnostics remains the clear leader in an increasingly competitive market environment. Blood screening (+11%) and virology (+8%) were again the main growth drivers.

In the five years since Roche Diagnostics entered the blood screening market, over 100 million blood donations have been screened using Roche's HIV and hepatitis C (HCV) tests. By 2004 Roche was already the global leader in this sector by volume of units tested, and in 2005 it became the first and only company to have tests for HIV-1, HCV and hepatitis B (HBV) approved by both the EU and the US authorities for screening living-donor and cadaveric organs and tissues as well as blood and plasma. Tissues from cadaveric sources, including skin, bone and ligaments, are used in roughly one million medical procedures per year and can transmit the same viral infections as blood. Tissues from a single donor are transplanted to an average of 50, and in some cases to as many as 100 recipients. This highlights the significance of the 2005 approvals. Towards the end of the year a regulatory filing was submitted in Europe for the next-generation cobas s201 blood screening system, which is expected to reach the market in 2006.

The core virology portfolio was strengthened in 2005 by the integrated Cobas AmpliPrep/Cobas TaqMan system, which offers laboratories new capabilities for fully automated sample preparation and DNA/RNA analysis. In addition, three viral load tests for use on this platform were approved for marketing in Europe; the tests measure the amounts of HIV, HCV and HBV in human plasma. Viral load is a key indicator for assessing disease progression, treatment response and drug resistance. US regulatory filings for all three tests are planned in 2006 and 2007.

Roche Diagnostics' LinearArray HPV Genotyping Test, which received CE mark approval in June, is the only commercially available test capable of identifying 37 high- and low-risk genetic variants of human papillomavirus (HPV). Although the majority of HPV infections clear spontaneously, persistent infection with high-risk HPV genotypes is recognised as a significant risk factor for development of cervical cancer. The new Roche test is expected to contribute significantly to the early identification of women at risk for cervical cancer.

In July 2005 Roche opened the world's largest manufacturing facility for PCR-based products in New Jersey (USA). PCR (polymerase chain reaction) is a technique that can produce millions of copies of virtually any DNA sequence in a short time and thus aid in detecting infectious agents and genetic variations quickly and very reliably. Over the last four years Roche Molecular Diagnostics has increased its kit output by 46%, and with the new facility now on line it will be able to continue to meet the steadily growing demand for these products.

The AmpliChip CYP450 Test, the first DNA microarray-based test for clinical diagnostic use, received US regulatory clearance in January 2005, following approval and launch in Europe in 2004. Three major laboratories in the United States have already added the test to their service offerings. The test helps guide physicians in selecting the medicines and dosages most suitable for their patients and marks a major step towards more personalised healthcare. (See patient story on p. 9.)

Near Patient Testing

Roche Near Patient Testing reported a 5% increase in full-year sales, with positive growth in its three core segments: cardiology, coagulation monitoring and blood gas/electrolytes. It is a leader in decentralised testing (testing outside the hospital laboratory) and patient self-monitoring.

Sales of coagulation monitoring products rose 13%, with especially strong growth recorded in the United States. A recent clinical trial has shown that patient self-monitoring with the CoaguChek S system can reduce the risk of severe complications and minor hemorrhages by up to 70% in patients on oral anticoagulant therapy and that it can reduce mortality after heart valve replacement by up to 60%. These results support the cost-effectiveness of patient self-monitoring and are further evidence of how modern diagnostics can help reduce the overall costs of healthcare. (See patient story on p. 101.)

The market launch of the Cardiac NT-proBNP test and out-licensing agreements for the marker NT-proBNP are expected to boost sales in the cardiology sector. Cardiac NT-proBNP is used in doctors' offices and intensive care units to rule out heart failure and to monitor heart failure patients.

Placements of Roche Diagnostics' blood gas and electrolyte analysers doubled compared with the year before.

Connectivity between remote testing devices is a critical element of point-of-care testing in hospital settings. Roche's cobas IT 1000 data management software, launched in 2005, is a technological milestone and already a worldwide commercial success. The software connects Roche and non-Roche point-of-care devices within a hospital or hospital network.

Applied Science

Roche Applied Science maintained its position in a fiercely competitive marketplace as sales rose 5% for the year. The business area supplies high-tech systems and reagents for research laboratories. Spurred by new product launches, sales gathered considerable momentum over the course of the

How diagnostics help take the squeeze off healthcare budgets

Diagnostics can help healthcare systems use precious resources more efficiently. The fact is, in addition to their medical benefits, diagnostic tests can create economic value.

Although diagnostic tests provide the basis for about two-thirds of all medical decisions, they account for only 1% of healthcare expenditure. For many years, new technologies were regarded as cost drivers. But looking at the treatment process as a whole, it is clear that innovative diagnostics can help make healthcare delivery more cost-effective while also providing a sounder basis for medical decision-making. And they can help physicians tailor treatment more closely to the individual needs of their patients. Modern tests, for example, can make it easier to determine the best medicine and dosage for a particular patient. As a result, patients receive better treatment and are less apt to suffer serious, costly adverse events.

Virology provides some excellent examples of the economic benefits of diagnostic products. Early diagnosis and effective treatment of hepatitis can prevent complications such as liver failure and liver cancer. Diagnostic instruments and test kits from Roche make it possible to detect the virus very early on. Another Roche test can then be used to establish the viral genotype, so that treatment – with a novel medicine like Pegasys – can be tailored to the infecting viral strain.

And once treatment is started, cutting-edge Roche diagnostics enable physicians to monitor patients' responses.

Roche Diagnostics is leading the way in researching and developing innovative diagnostic tests that will change the way medicine is practiced. As part of that, we are committed to promoting a better understanding of the value of diagnostic information among all stakeholders.

'At Roche Diagnostics we're proactively pursuing research that will document both the medical and the economic value of diagnostic information,' says Geoffrey Crouse, Head of Market Development and Governmental Affairs. 'In this context our key question is: How can we maximise the amount of health we get for the money we spend?'

year, with the business area reporting a double-digit increase in the fourth quarter.

Genome Sequencer 20 and LightCycler 480 were two of Roche Applied Science's most important new offerings in 2005. The Genome Sequencer 20 system enables researchers to sequence long DNA fragments and entire genomes up to 100 times faster than with other commercially available platforms and marks Roche's entry into the attractive sequencing research market. Employing an award-winning nanotechnology-based approach to sequencing, the system is the first product to emerge from a strategic alliance formed in 2005 between Roche and the technology's US-based inventor, 454 Life Sciences. Roche holds exclusive sales and marketing rights to 454 Life Science's sequencing systems for the life science market.

Major product launches in 2005

Business area	Product
Diabetes Care	Accu-Chek Aviva, high-end successor to the Advantage/Sensor blood glucose monitoring system
	Accu-Chek Pocket Compass 3.0, next-generation diabetes management software
	Accu-Chek Integra, blood glucose monitoring system with fully automated test strip handling
	Accu-Chek Compact Plus, blood glucose monitoring system, with integrated strip drum and lancing device for one-hand operation
	Accu-Chek FlexLink infusion set
Centralized Diagnostics	Cobas Integra 800 analyser with closed-tube sampling
	Dedicated HbA1c (glycated hemoglobin) analyser on the basis of Cobas Integra 800
	Improved reagents for prostate-specific antigen, myoglobin, troponin T and prolactin for Elecsys platforms
Molecular Diagnostics	Integrated Cobas AmpliPrep/Cobas TaqMan Instrument (HCV, HIV, HBV), first fully automated PCR system with assays for quantitative detection of HIV and hepatitis C and B
	Cobas AmpliPrep/Cobas Amplicor HCV Qual v 2.0 for qualitative detection of hepatitis C virus (US IVD)
	Cobas AmpliPrep/Cobas Amplicor HIV Monitor, test for monitoring HIV viral load (US IVD)
	Cobas AmpliScreen HCV, HBV and HIV-1 Tests for screening organ and tissue donations (US IVD, new indication)
	Cobas AmpliScreen HBV Test for detecting hepatitis B virus in human plasma (US IVD)
	Linear Array HCV Genotyping Test for determining hepatitis C genotype (CE IVD)
	Linear Array HPV Genotyping Test; identifies 37 genotypes of human papillomavirus (CE IVD)
	Cobas TaqMan 48 CT Test for *Chlamydia* (CE IVD)
	AmpliChip CYP450 Test, microarray for drug metabolism testing (US IVD)
	LightCycler 2.0 Factor II & V tests for factor II and V Leiden clotting disorders (CE IVD)
Near Patient Testing	Cardiac NT-proBNP, rapid and accurate assay for the quantitative determination of NT-proBNP; used for the diagnosis and management of heart failure patients
	CoaguChek XS, handheld system for coagulation self-monitoring
	OMNI S Version 5.0, software update for the OMNI S blood gas/electrolyte system
	cobas IT 1000, a new web-based data management solution for point-of-care testing in hospitals
Applied Science	Universal ProbeLibrary Set, innovative probe-based detection system for quantitative PCR tests
	Genome Seqencer 20, complete platform for high-throughput sequencing
	LightCycler 480, novel platform for gene expression and mutation analysis
	LightCycler 2.0, IVD version of the LightCycler 2.0 DNA amplification system (CE IVD)

IVD = for clinical use.
CE = European CE mark certification (Conformité européenne).

The LightCycler 480 real-time PCR system is a novel platform for gene expression and mutation analysis. Combining speed with exceptional accuracy, the new system supports all current probe formats and applications.

Research and development

Research and development expenditure totalled nearly 720 million Swiss francs (approximately 9% of sales), significantly more than the division's competitors spent. The molecular diagnostics, immunodiagnostics and diabetes care businesses accounted for the largest shares of expenditure.

Diabetes Care

Research and development efforts in this business unit are aimed at making diabetes management even simpler – for example by developing software geared to the special needs of frequent testers, who have to cope with huge amounts of data.

In addition, Roche is working on minimally invasive glucose measuring technologies requiring only a minute blood sample, or no sample at all, and on continuous blood glucose monitoring systems. The ultimate aim is to create an artificial pancreas, a system capable of mimicking the natural pattern of insulin release in healthy individuals.

Centralized Diagnostics

Roche Centralized Diagnostics develops total laboratory automation systems that increase laboratory productivity while reducing costs and reliable diagnostic tests that contribute to better patient care. Key areas of interest include cardiovascular disease, cancer and rheumatoid arthritis.

In addition, Roche is stepping up its research into new biomarkers of high diagnostic value in monitoring disease progression and evaluating treatment response. Biomarkers can be used singly or in combination as sources of information. Particularly in complex diseases like cancer, tests for multiple markers are often the only means of obtaining a conclusive result. Our next generation of systems will measure marker combinations using protein chips. A protein chip system (IMPACT) is currently undergoing feasibility studies and will be used initially to accelerate the clinical testing of new markers.

Molecular Diagnostics

Research activities at Roche Molecular Diagnostics are focused on further advancing PCR and related technologies to enable development of new gene-based tests on the TaqMan and AmpliChip platforms. Roche is also working on new approaches to increasing the total throughput of PCR-based analyses by testing for multiple viral or human genetic markers simultaneously in each run.

In September 2005 Roche and the Mayo Clinic in Minnesota (USA) signed an agreement to collaborate on developing an IT-enabled drug and dose selection system for use in treating psychiatric patients. Information provided by the system will be based on patient test data obtained with the AmpliChip CYP450 Test. Mayo Clinic will explore the use of the system for a wide range of psychotropic drugs. This is an area of clinical practice where several drugs often have to be tried over a long treatment cycle time in order to find the one that is best for a particular patient.

Molecular diagnostics are also steadily gaining in importance in oncology. Roche's efforts in this area are aimed primarily at developing tests for early cancer detection and risk stratification, particularly for solid tumours (such as cancers of the breast, prostate and colon) and leukemia. Candidate markers have been identified and are currently being evaluated for potential use in these important applications.

A large-scale, international clinical research programme investigating leukemia classification is under way and due to be completed in 2006. There are over 20 different subtypes of leukemia, and they do not all respond to the same treatments. Choosing the most effective available medication or type of therapy right at the outset for a particular leukemia subtype is particularly important in the acute leukemias, which progress very rapidly. The programme will compare results obtained with AmpliChip leukemia tests at different laboratories

Key product launches scheduled for 2006

Business area	Product
Diabetes Care	Accu-Chek Go S: Successor to the Accu-Chek Go meter, offering improved feature set and design
Centralized Diagnostics	cobas 6000 series: Consolidates clinical chemistry and immunochemistry testing for medium- to high-workload laboratories; modular, expandable and reconfigurable on site (up to 7 configurations), using cobas c501 and cobas e601 modules
	cobas 4000 series: Consolidates clinical chemistry and immunochemistry testing for small- to medium-workload laboratories; links cobas c311 and cobas e411 with the PSM data manager
	cobas c111 : Clinical chemistry and electrolyte analyser for extra-small-workload laboratories (stand-alone system)
	cobas IT 5000 solution: Laboratory information system that supports all steps of laboratory testing from order entry to result reporting; features connectivity, sample management, quality control and validation capabilities
	cobas IT 3000 solution: Central lab data management system (WAM/Middleware) for instrument interface consolidation, providing result-related reagent and test information
Molecular Diagnostics	LightCycler SeptiFast Test (CE IVD): The world's first diagnostic assay for detection of sepsis causing pathogens directly from blood
	cobas s201 MPV (CE IVD): Multiplex detection test for HIV, HCV and HBV for the cobas s201 blood screening system
	Cobas TaqMan 48 HCV v2.0: Test for monitoring HCV viral load
Applied Science	Genome Sequencer S 100 System: Next-generation system with capability to sequence larger genomes
	LightCycler 480: 96-well, including new software modules; extension of LC 480, allowing use in a broader range of applications

for inter-laboratory robustness and is also intended to confirm data from Roche gene discovery projects. A prototype test is expected to be ready for further research applications at the end of 2006.

Another microarray-based product currently in development is the AmpliChip p53 Test. Several research collaborations to investigate the potential clinical applications of this test are scheduled for 2006. The p53 gene is one of a family of genes called tumour suppressors, which code for proteins that prevent damaged cells from reproducing. Mutations of the p53 gene are found in virtually all tumour types. By identifying mutations that affect p53 function and activity, the AmpliChip p53 Test may one day help physicians select the anticancer medicines best suited to their patients' needs.

Near Patient Testing

One medium-term goal for Roche Near Patient Testing is to develop mobile devices that can perform urgent medical tests anywhere in a matter of minutes.

The business area plans to have a complete line of new instruments on the market by 2007 and has already begun refreshing its product portfolio with the pilot launch of the CoaguChek XS coagulation monitor. This user-friendly next-generation device has a built-in quality control system capable of detecting virtually any potential source of error during testing, thus making anticoagulant therapy safer than ever before.

Applied Science

Roche Applied Science focuses on developing high-quality systems and reagents for use in life science research, particularly in high-potential areas such as proteomics and DNA sequencing and analysis. For example, the business area is working to broaden the research uses of the new, highly versatile LightCycler 480 instrument. Innovative genotyping products and software upgrades will be introduced in 2006.

Products to expand the applications of the Genome Sequencer 20 are also due to reach the market in 2006 and 2007, and work is under way to make the system even faster.

Access to diagnostics

The AmpliCare programme is one of the ways Roche Diagnostics is helping to improve healthcare delivery to HIV/AIDS patients in those parts of the world where needs are greatest: in sub-Saharan Africa and other countries designated by the United Nations as 'least developed'. Since its inception in 2002, the programme has been supplying HIV viral load tests at sharply reduced prices, but tests are only part of the story. Because sustainability and continuity of care are so critical, we are contributing on other fronts as well – from providing expanded training and continuing education opportunities for doctors and nurses to supporting efforts to monitor health outcomes. We also strive to match our efforts to local needs. Working closely with laboratories and hospitals, for example, we determine what services or types of technical assistance are feasible and most suitable and then develop a targeted solution.

Roche Diagnostics plans to expand the AmpliCare programme to additional countries, with the focus now on reaching countries listed by the UN as having low-income economies. Preparatory talks have already been initiated for this purpose in Eastern Europe, Latin America and additional countries in Asia.

'The medication helps against my osteoporosis, and I only have to take it once a month.'

Predisposition | Early detection | **Prevention** | Diagnosis | Therapy | Monitoring

Growing older doesn't have to mean going slower

Senior sales account manager Ginger La Motta (62), from Branchburg (New Jersey), dotes on her four grandchildren and enjoys having them ride on her shoulders. But a diagnosis of osteoporosis five years ago made her realise that even simple pleasures like this could be a risk to her health.

Osteoporosis is a bone condition common among postmenopausal women. People tend to think of bone as hard and unchanging. In fact it's a dynamic living tissue that is constantly being broken down and rebuilt. After the menopause, rebuilding can be slower, and bone mass can decrease, making bones weaker and more likely to break. Ginger eats a healthy diet and exercises regularly. To keep her osteoporosis under control she takes once-a-month Boniva, the first once-monthly oral bisphosphonate.

Oral bisphosphonates must be taken in the morning on an empty stomach. Patients must then stay upright and not eat for at least another half-hour or hour. Because of her busy schedule, once-a-month Boniva was the ideal solution for Ginger. Now she can reduce her risk of fracture by taking just one tablet a month. And she's much more relaxed when playing with her grandchildren.

Prevention

Reducing the consequences of disease helps patients to maintain quality of life. Boniva (ibandronic acid) maintains and actually builds bone density, reducing the risk of fracture. Of course, patients need to stay on therapy to benefit. And with once-monthly Boniva, that's become a lot easier: patients take only 12 tablets a year.

Board of Directors and Executive Committee, Corporate Governance

Board of Directors and Corporate Executive Committee

Board of Directors

At the Annual General Meeting on 28 February 2005 John Bell, André Hoffmann and Franz B. Humer were elected to additional four-year terms on the Board of Directors.

The current Board terms of Rolf Hänggi, Peter Brabeck-Letmathe, DeAnne Julius and Horst Teltschik will end at the next Annual General Meeting, on 27 February 2006. At that meeting the Board intends to nominate Mr Brabeck-Letmathe, Ms Julius, and Mr Teltschik for re-election as directors for terms of four years.

Rolf Hänggi, who has served as Vice-Chairman of the Board since 1996, has declined to stand for re-election. Mr Hänggi has become increasingly active as a private investor in pharmaceutical start-up companies, a situation which could potentially give rise to conflicts between his own interests and those of Roche. This decision will help ensure his continued independence in his other capacities. The Board of Directors and Corporate Executive Committee extend their sincere thanks to Mr Hänggi for his many years of dedicated service to the Group.

In addition to the aforementioned three nominees for re-election, the Board will also recommend the election of Beatrice Weder di Mauro to Roche's highest governing body. A 41-year-old native of Basel, Ms Weder di Mauro, has been a professor of economics at the University of Mainz (Germany) since 2001 and has served on Germany's Council of Economic Experts since August 2004. Prior to that, she was an economist with the International Monetary Fund and the World Bank in Washington, DC.

If the Board's proposals are adopted, Chairman of the Board Franz B. Humer will continue to be the only director also serving in an executive capacity at Roche, and the majority of seats on the Board will be held by independent directors.

Corporate Executive Committee

Heino von Prondzynski, CEO Division Roche Diagnostics, has decided to leave Roche this year to pursue personal interests. Since joining Roche in March 2000 he has contributed significantly to the Diagnostics Division's achievements, providing the leadership that has helped the division expand its global market leadership so successfully. The Board of Directors would like to take this additional opportunity to thank Mr Prondzynski for his valuable contribution and to wish him all the best for the future.

Severin Schwan joined the Corporate Executive Committee as the new CEO Division Roche Diagnostics on 1 January 2006. Schwan, a 38-year-old Austrian with a doctorate in law and a degree in economics, began his career at Roche in 1993 in the Corporate Finance department in Basel. Following several international assignments, he served as Head of Global Finance & Services for the Diagnostics Division from 2000 until being put in charge of the division's regional operations in Asia–Pacific in 2004.

Board of Directors as of 1 January 2006 (from left): John Bell, Rolf Hänggi, Peter Brabeck-Letmathe, Bruno Gehrig, André Hoffmann, Franz B. Humer, Lodewijk J.R. de Vink, DeAnne Julius, Walter Frey, Andreas Oeri, Horst Teltschik

Name, year of birth			Term ends	First elected
Board of Directors				
Dr Franz B. Humer (1946)	D*, F	Chairman	2009	1995
Prof. Bruno Gehrig (1946)	C*, D, E	Vice-Chairman and Independent Lead Director	2008	2004
Rolf Hänggi (1943)**	A*, B, D, E	Vice-Chairman	2006	1996
Prof. John Irving Bell (1952)	C, E		2009	2001
Peter Brabeck-Letmathe (1944)	E		2006	2000
Lodewijk J.R. de Vink (1945)	A, E		2008	2004
Walter Frey (1943)	B, E		2008	2001
André Hoffmann (1958)	A, C, E		2009	1996
Dr DeAnne Julius (1949)	B*, E		2006	2002
Dr Andreas Oeri (1949)	B, E		2008	1996
Prof. Horst Teltschik (1940)	A, E		2006	2002
Secretary to the Board of Directors				
Dr Gottlieb A. Keller (1954)				
Honorary Chairman of the Board of Directors				
Dr Fritz Gerber (1929)				

A Finance and Investment Committee.
B Audit and Corporate Governance Committee.
C Remuneration Committee.
D Presidium of the Board of Directors/Nomination Committee.
E Non-executive director.
F Executive director.

* Committee chairperson.
** Will step down on 27 February 2006.

1 January 2006.

Burkhard G. Piper has been named to the Enlarged Corporate Executive Committee, an appointment which also became effective 1 January 2006. The 46-year-old German, who holds a degree in business administration, joined the Boehringer-Mannheim group, later acquired by Roche, in 1985. He held several management positions in marketing before being appointed General Manager of Roche Diagnostics Canada in 1999 and then Head of Roche Centralized Diagnostics in 2002. Mr Piper has headed Roche Diabetes Care since the end of 2005.

Mr Piper's predecessor, Staffan Ek, retired at the end of the year. The Board of Directors thanks Mr Ek for his very significant role in strengthening Roche's diabetes care business and his contribution to the success of the Group as a whole.

Effective 1 January 2006, Eduard Holdener, Peter Hug, Rolf Schläpfer and Osamu Nagayama were also appointed members of Roche's Enlarged Corporate Executive Committee. All four men had been assisting executive management as permanent participants on the Committee since 1 January 2005.

Corporate Executive Committee as of 31 December 2005 (from left): Jonathan K.C. Knowles, Pierre Jaccoud, Heino von Prondzynski (until 31.12.05), Staffan Ek (until 31.12.05), William M. Burns, Eduard Holdener, Franz B. Humer, Peter Hug, Erich Hunziker, Rolf Schläpfer, Gottlieb A. Keller, Osamu Nagayama

	Name, year of birth	Position
Corporate Executive Committee	Dr Franz B. Humer (1946)	CEO of the Roche Group
	Dr Erich Hunziker (1953)	Chief Financial Officer and Deputy Head of the Corporate Executive Committee
	William M. Burns (1947)	CEO Division Roche Pharmaceuticals
	Heino von Prondzynski (1949)[1]	CEO Division Roche Diagnostics
	Prof. Jonathan K.C. Knowles (1947)	Head Global Research
	Dr Gottlieb A. Keller (1954)	Head Corporate Services and Human Resources
Enlarged Corporate Executive Committee	Dr Eduard Holdener (1945)	Head Global Pharma Development
	Dr Peter Hug (1958)	Head Pharma Partnering
	Staffan Ek (1945)[2]	Head Business Area Diabetes Care
	Rolf Schläpfer (1956)	Head Corporate Communications
	Osamu Nagayama (1947)	President and CEO Chugai
Secretary to the Corporate Executive Committee	Pierre Jaccoud (1955)	Head Chairman's Office
Statutory Auditors of Roche Holding Ltd and Group Auditors	KPMG Klynveld Peat Marwick Goerdeler SA (since 2004) Principal auditor: John A. Morris (since 2004)	
Compliance Officer	Dr Andreas Greuter (1949) (direct dial number: +41 (0)61 688 75 37)	

1) From 1 January 2006: Dr Severin Schwan (1967).
2) From 1 January 2006: Burkhard G. Piper (1961).
End of 2005.

Corporate Governance

The Roche Group meets all of the requirements with respect to Corporate Governance complying with the existing legal regulations, the SWX (Swiss stock exchange) directives (including their Commentaries) and the Swiss Code of Best Practice for Corporate Governance as promulgated by the Swiss business federation 'economiesuisse'. The existing internal company regulations, in particular the company's Articles of Incorporation and Bylaws, consider all the principles that govern the management and supervision of our company including the necessary checks and balances in order to ensure good corporate governance[1].

We combine the printed Annual Report with key links to the Roche website (www.roche.com) which enables readers to gain both a snapshot at the reporting date and an up-to-date overview of the company's key corporate governance information. The Annual Report contains all the information available up to 31 December of the given year, while the Internet provides a source of permanent and constantly updated information. The company's Articles of Incorporation, the Bylaws and the curricula vitae of the members of the Board of Directors and the Executive Committee are regularly updated and made available on the Internet for all those who require information.

Organisational structure of the Board of Directors

Roche's Board of Directors is organised so as to ensure that the Group's businesses are conducted responsibly and with a focus on long-term value creation. Therefore, the Board of Directors of Roche Holding Ltd delegated certain responsibilities to several committees. As at 1 January 2006 these committees were:

- the Presidium of the Board of Directors/ Nomination Committee (Chairman: Franz B. Humer)
- the Audit and Corporate Governance Committee (Chairman: DeAnne Julius)
- the Finance and Investment Committee (Chairman: Rolf Hänggi)
- the Remuneration Committee (Chairman: Bruno Gehrig)

All the committees except the Presidium are chaired by independent directors.

The Bylaws of the Board of Directors, containing details on the internal structure of the Board, the allocation of authority and responsibilities, the mandates of the Board committees and the information and control mechanisms available to the Board in its dealings with corporate management, are published on the Internet.[2]

Under Articles 4.2.2 and 6.2/6.3 of the Bylaws of the Board of Directors, the Independent Lead Director may, at his own decision or at the request of any member, convene a Board meeting without the attendance of the Chairman. The Roche Board meets once a year to assess the Chairman's performance. This meeting, which is held in the absence of the Chairman, is chaired by the Independent Lead Director.

The Board of Directors periodically conducts a self-assessment of its performance. In 2005 a self-assessment focusing on a number of areas, including cooperation between the Board and the Executive Committee, was conducted with the assistance of a specialist consulting firm.

Remuneration

Remuneration of members of the Board of Directors

In 2005 the members of the Board of Directors received the remuneration shown in the table 'Remuneration of members of the Board of Directors' for serving on the Board.

1) http://www.roche.com/home/company/com_gov.htm
2) http://www.roche.com/home/company/com_gov/com_gov_bylaws.htm

Remuneration of members of the Board of Directors

	Remuneration 2005 (in CHF)	Additional compensation 2005 for committee members[3] (in CHF)
F. B. Humer	[300,000][4]	–
B. Gehrig	450,000[5]	–
R. Hänggi	400,000[6]	–
J. Bell	300,000	10,000
P. Brabeck-Letmathe	300,000	–
L. J. R. de Vink	300,000	10,000
W. Frey	300,000	10,000
A. Hoffmann	300,000	20,000
D. A. Julius	300,000	10,000
A. Oeri	300,000	10,000
H. Teltschik	300,000	10,000
Total	3,550,000	80,000

3) Per committee membership/year, excluding members of the Presidium and vice-chairmen: CHF 10,000.

4) The remuneration paid to the Chairman of the Board F. B. Humer (the only executive member of the Board of Directors) is deducted from his agreed salary (see 'Remuneration of members of the Corporate Executive Committee').

5) Remuneration for serving as Independent Lead Director and Vice-Chairman of the Board.

6) Remuneration for serving as Vice-Chairman of the Board.

Remuneration and additional compensation paid to non-executive members of the Board of Directors for serving in the aforementioned capacities totalled 3,330,000 Swiss francs in 2005 (previous year: 3,165,000 Swiss francs).

The non-executive members of the Board of Directors were not awarded any shares, non-voting equity securities (NES), Stock-settled Stock Appreciation Rights (S-SARs)[7] or stock options in 2005 and, as of 31 December 2005, held no unvested options awarded in previous years.

In connection with the acquisition of GlycArt on 25 July 2005 (see Finance Report, Note 8 and 34 to the Roche Group Consolidated Financial Statements 'Changes in Group organisation' and 'Related parties', page 53 and 88), the Group paid Rolf Hänggi 1,731,248 Swiss francs in consideration for his shareholding in GlycArt. This is equivalent on a per-share basis to the amounts paid to other shareholders for their GlycArt stock.

Otherwise, no additional remuneration was paid to members of the Board of Directors.

7) Refer to 'Stock options / Stock-settled Stock Appreciation Rights (S-SARs)', page 53.

Remuneration of members of the Corporate Executive Committee

The Remuneration Committee decides on the remuneration of the members of the Corporate Executive Committee (cash payments, bonus, stock options, S-SARs and [approving in principle] pension fund benefits) and the Board of Directors upon proposal of the Remuneration Committee decides on the Performance Share Plan (PSP).

The compensation components of the S-SARs and the PSP plan are intended to align compensation with the long-term success of the company.

In 2005 the members of the Corporate Executive Committee received the salaries, bonuses, stock options/Stock-settled Stock Appreciation Rights (S-SARs) and non-voting equity securities as shown in the following tables on page 50.

Members of the Corporate Executive Committee additionally receive annual expense allowances of 30,000 Swiss francs; the Chief Executive Officer receives an annual expense allowance of 50,000 Swiss francs. In 2005 the members of the Corporate Executive Committee in total received expense allowances totalling 200,000 Swiss francs.

Remuneration of members of the Corporate Executive Committee

A. Cash payments *(in CHF)*

	Annual salary 2005	Annual salary 2004	Annual salary 2003	Bonus 2005	Bonus 2004	Bonus 2003
F. B. Humer	6,030,000	6,030,000	6,030,000	1,000,000	1,000,000	1,000,000
W. M. Burns	1,425,000	1,200,000	1,200,000	900,000	800,000	600,000
E. Hunziker	1,567,500	1,470,000	1,470,000	900,000	800,000	600,000
G. A. Keller	662,500	530,007	417,498	350,000	300,000	120,000
J. K. C. Knowles	1,200,000	1,025,001	929,500	700,000	600,000	360,000
H. von Prondzynski	1,262,500	1,150,000	1,098,750	700,000	700,000	500,000
Total	12,147,500	11,405,008	11,145,748	4,550,000	4,200,000	3,180,000

B. Stock options / Stock-settled Stock Appreciation Rights (S-SARs)

	S-SARs[8] 2005 (value in CHF[9])	Stock options 2004 (value in CHF[9])	Stock options 2003 (value in CHF[9])
F. B. Humer	1,779,389	1,780,338	1,780,100
W. M. Burns	711,806	712,135	445,100
E. Hunziker	711,806	667,606	445,100
G. A. Keller	266,911	222,642	89 100
J. K. C. Knowles	533,823	489,652	311,600
H. von Prondzynski	667,310	578,709	356,100
Total	4,671,045	4,451,082	3,427,100

8) Refer to 'Stock options/Stock-settled Stock Appreciation Rights (S-SARs)', page 53.

9) Black-Scholes valuation as described in section 'Stock options/Stock-settled Stock Appreciation Rights (S-SARs)', page 53.

Richard T. Laube stepped down from the Corporate Executive Committee on 31 December 2004 and has left the company on 30 June 2005. In 2005 Richard T. Laube received continuing salary, bonus and severance payment totalling 1.86 million Swiss francs.

C. Performance Share Plan (PSP)

The members of the Corporate Executive Committee and other members of senior management whose performance has a major impact on Roche's ability to achieve its corporate objectives (some 50 individuals worldwide) participate in the new PSP programme 2005–2007, which was established at the beginning of 2005 for a three-year period. Under the provisions of this programme which replaced the PSP programme 2002–2004, a number of NES were reserved for the participants. The actual distribution of securities will depend on whether and to what extent an investment in Roche securities (shares and NES) will outperform the average return on investment in securities issued by a peer set[10] of 20 companies operating in the same industry during the three years in which this programme is in effect. Performance will be evaluated on the basis of market price and dividend yields, i.e. 'Total Shareholder Return'(TSR). In order to reduce the effect of any short-term market price fluctuation, the TSR is based on the average market values for the last three months (October until December 2004) before the beginning of the programme compared to the average of the last three months (October until December) in 2007. If an investment in Roche securities is equal to or outperforms 75% of the peer set and if Roche's own TSR increased at least 10% during the duration of the programme, the Board of Directors can elect to increase the number of NES awarded maximum up to two-fold. In the event that an investment in Roche securities underperforms the

10) Peer set: Abbott Laboratories, Altana, Amgen, AstraZeneca, Bayer, Becton Dickinson, Biogen Idec, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Johnson & Johnson, Merck, Novartis, Pfizer, Serono, Sanofi-Aventis, Schering AG, Schering-Plough, Takeda, Wyeth.

Performance Share Plan (PSP)

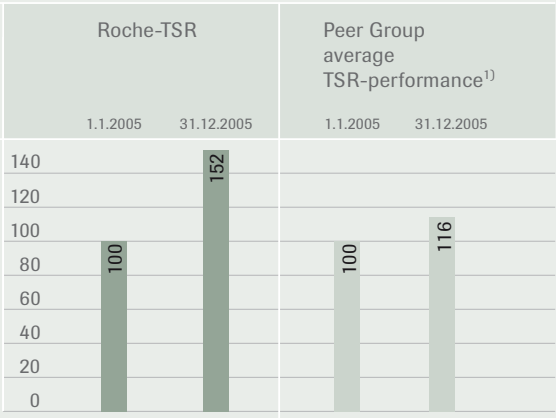
	Number of NES targeted under the PSP 2005-2007 (number)	Number of NES originally targeted under the PSP 2002-2004 (number)	PSP (2005–2007) value assumption[11] for 2005 (value in CHF)	PSP (2002–2004) value[12] for 2004 (value in CHF)
F. B. Humer	48,028	50,886	3,158,641	4,440,652
W. M. Burns	9,557	10,127	628,532	883,750
E. Hunziker	11,708	12,405	769,996	1,082,543
G. A. Keller	4,380	3,460	288,058	301,943
J. K. C. Knowles	8,363	7,173	550,007	625,964
H. von Prondzynski	9,159	7,088	602,357	618,546
Total	91,195	91,139	5,997,591	7,953,398

11) Value assumption for 2005: evaluated using the year-end price as of 31 December 2005 (CHF 197.30 per *Genussschein* [NES]), based on the number of NES originally targeted, subject to changes of the allocation and value of the number of NES originally targeted under the plan on 31 December 2007 and spread over the relevant period of time, i.e. $\frac{1}{3}$ for the year 2005. The Board of Directors will vote on the actual allocation of NES originally targeted on 31 December 2007 according to the TSR growth achieved.

12) Value for the year 2004 under PSP 2002–2004, after doubling of number of NES originally targeted according to the market value growth achieved and spread over the relevant years of the total period of the effective time of the plan.

average return delivered by the peer companies fewer or no NES will be awarded. In 2005 under the provisions of this programme NES have been reserved for members of the Corporate Executive Committee as shown in the table above. The Board of Directors will decide on the actual distribution of

Roche performance in 2005



Total Shareholder Return (TSR)
The value of CHF 100[1] invested on 1.1.2005

Roche market capitalisation *in billions of CHF*		113	171
Roche securities *in CHF*	Non-voting equity security (NES)	130.90	197.30
	Share	150.00	219.20

1) Prices translated at constant CHF exchange rates.
TSR = stock price plus dividend.

NES or cash equivalent under the plan after the close of the 2007 reporting year.

Over the last years Roche securities (shares and NES), including dividend yields, have outperformed the average return delivered by the peer pharmaceuticals and diagnostics companies.

Roche ranked second at the end of the PSP programme 2002–2004. During this time the market value of Roche increased from 102 billion Swiss francs to 113 billion Swiss francs, equivalent to a growth of 10.8% or 11 billion Swiss francs. The distribution of dividends totalled 3.8 billion Swiss francs.

Under the current PSP programme 2005–2007 (which is based on a moving three-month average at constant exchange rates) Roche after one year ranked number one (compared with the peer set of 20 companies operating in the same industry).

Roche's market value increased from 113 billion Swiss francs as per 31.12.2004 to 171 billion Swiss francs, equivalent to a growth of 51% or 58 billion Swiss francs as per 31.12.2005. The distribution of dividends in 2005 totalled 1.725 billion Swiss francs.

In 2005 the average Total Shareholder Return (TSR) of the peer set (at constant exchange rates) was significantly lower at 16%. Thus the TSR of Roche's securities at 52% in 2005 is 36% points higher than the average TSR of the peer companies at constant exchange rates.

D. Indirect benefits

Employer contributions that were made in 2005 to social security schemes, pension plans and a Group-wide employee stock purchase plan (Roche Connect) in respect of members of the Corporate Executive Committee are shown in the below table 'Indirect benefits'.

Under Roche Connect, a voluntary stock purchase plan, employees have the opportunity to buy Roche non-voting equity securities (NES) up to an amount equal to 10% of their annual salary at a 20% discount. NES purchased under this plan are subject to a holding period, which in Switzerland is four years.

E. Other remuneration, emoluments and loans to corporate officers

Gottlieb A. Keller has taken out a mortgage loan of 492,500 Swiss francs with the Pension Fund of F. Hoffmann-La Roche Ltd at an interest rate of 4.2% p.a. The interest rate on this loan is fixed until 31 December 2006.

Pension obligations to seven former members of the Corporate Executive Committee or their widows were transferred to the pension fund in 2005; a one-time payment of 1,536,688 Swiss francs was made to the fund to cover the resulting additional liabilities. Pensions totalling 1,946,568 Swiss francs were paid to two former Corporate Executive Committee members.

Otherwise, no additional remuneration was paid to current or former members of the Corporate Executive Committee.

Indirect benefits

	Pension funds/MGB[13] (in CHF)	AHV/IV/ALV[14] (in CHF)	Roche Connect (in CHF)
F. B. Humer	2,723,261	985,101	50,004
W. M. Burns	686,572	298,401	30,000
E. Hunziker	527,923	261,629	38,653
G. A. Keller	165,242	95,494	15,939
J. K. C. Knowles	854,960	173,804	22,500
H. von Prondzynski	850,648	217,518	27,916
Total	5 808,606	2,031,947	185,012

13) MGB: Stiftung der F. Hoffmann-La Roche AG für Mitarbeiter-Gewinnbeteiligung (employee profit-sharing foundation supplementing occupational pension benefits).

14) AHV/IV/ALV: Swiss social security programmes providing retirement, disability and unemployment benefits.

F. Highest total remuneration

The Chairman of the Board of Directors and CEO Franz B. Humer was the member of the Board and the member of the Corporate Executive Committee with the highest total remuneration in 2005 (please refer to 'Remuneration of the members of the Corporate Executive Committee'). Subject to changes in the allocation and computations relating to the three-year Performance Share Plan PSP 2005–2007 his salary was as follows:

Highest total remuneration *(in CHF)*

	2005	2004	2003
Cash payments	7,030,000	7,030,000	7,030,000
Stock options/S-SARs			
(value based on Black-Scholes formula[15] minus 11%)	1,779,389	1,780,338	1,780,100
Performance Share Plan[16]	(3,158,641)[17]	4,440,652	4,440,652
Pension funds/MGB[18]	(2,723,261)[19]	(2,740,991)[19]	(2,283,460)[19]
Roche Connect	50,004	50,004	40,629
Total (value)	14,741,295	16,041,985	15,574,841

15) Black-Scholes valuation as described in above section 'Stock options/Stock-settled Stock Appreciation Rights (S-SARs)'.
16) Refer to 'Remuneration of members of the Corporate Executive Committee, C. Performance Share Plan (PSP)', page 50.
17) Not paid out in 2005.
18) MGB: Stiftung der F. Hoffmann-La Roche AG für Mitarbeiter-Gewinnbeteiligung (employee profit-sharing foundation supplementing occupational pension benefits).
19) Payments into pension schemes.

Stock options/Stock-settled Stock Appreciation Rights (S-SARs)

At 31 December 2005 the members of the Corporate Executive Committee held options/(S-SARs as of 1 January 2005) as shown in the table on page 54.

All of the options shown in the table were issued by Roche as employee stock options. Each option entitles the holder to purchase one Roche non-voting equity security (NES; *Genussschein*).

Under the terms of this well established option plan, the strike price of the options shown was the closing price for Roche NES on the trading day prior to the Roche Annual Media Conference. All of the options shown are non-tradable. One-third of the options are subject to a vesting period of one year, one-third have a vesting period of two years, and one-third a vesting period of three years. Unvested options lapse without compensation if a member voluntarily leaves the company, while vested options must be exercised within a limited period of time. If they were tradable, the fair value of the options would be calculated at the date of issue based on the Black-Scholes formula and after deducting 11% for the average two-year vesting period.

Shareholdings

The Directors André Hoffmann and Andreas Oeri and members of the founder's family who are closely associated with them belong to a shareholder group with pooled voting rights. At the end of 2005 this group held 80,020,000 shares (50.01% of issued shares). André Hoffmann serves as spokesman of this shareholder group. Detailed information about this group will be found in the Finance Report, Note 34 to the Roche Group Consolidated Financial Statements ('Related parties', page 88) and in the Notes to the Financial Statements of Roche Holding Ltd (page 104). In addition, as of 31 December 2005 the non-executive members of the Board of Directors and persons closely associated with them held 176,475 shares; the members of the Corporate Executive Committee and persons closely associated with them held 546 shares at the same date.

Stock options/S-SARs

	Number of Stock options/S-SARs (as of 2005) held on 31 December 2005 by the members of the Executive Committee			
	2005[20]	2004	2003	2002
Total number	223,602	125,966	182,381	10,604
Strike price in CHF	123	129,50	77,80	115,50
Expiry date	3. 2. 2012	3. 2. 2011	25. 2. 2010	26. 2. 2009
Allotment value per stock option/ S-SAR as of 2005, in CHF (value based on Black-Scholes formula minus 11%)	20.89	31.92	16.27	30.10

20) S-SARs.

The S-SARs shown in the above table were issued by Roche on 1 January 2005 on the basis of the 'Roche Long-Term' program and instead of stock options. An S-SAR is the right to benefit financially from the increase in value of a non-voting equity security (NES; *Genussschein*) between the grant date and the exercise date. The strike price of the S-SARs under the terms of this perennial plan was the closing price for Roche NES on the trading day after to the Roche Annual Media Conference. On the third anniversary of the grant date, all remaining S-SARs shall be vested. One-third of the S-SARs are subject to a vesting period of one year, one-third have a vesting period of two years, and one-third a vesting period of three years. Vested S-SARs must be exercised within seven years after the grant date (i. e. exchange of S-SARs gain for NES) and unexercised S-SARs lapse without compensation. If they were tradable, the fair value of the S-SARs would be calculated at the date of issue based on the Black-Scholes formula and after deducting 11% for the average two-year vesting period.

The strike price, expiry date and allotment price are shown in the above table. The value of the options and S-SARs in the table 'Remuneration of members of the Corporate Executive Committee, B. Stock options/Stock-settled Stock Appreciation Rights (S-SARs)' on page 50, was based on the calculation method used at the time of issue.

Relationship to Group auditors and statutory auditors

At the Annual General Meeting of Roche Holding Ltd on 28 February 2005, KPMG Klynveld Peat Marwick Goerdeler SA (KPMG) was elected as Group auditors and statutory auditors (information on the appointment of the Group auditors and the date on which the principal auditor took up office is provided on page 47). The Group auditors and statutory auditors participate in the Audit and Corporate Governance Committee meetings. The auditors make written and oral reports on the results of their audits. The Audit and Corporate Governance Committee oversees and assesses the auditors and makes recommendations to the Board (for information on the responsibilities of the Audit and Corporate Governance Committee, see Article 8.1[21] of the Bylaws). The Group auditors and statutory auditors participated in three meetings of the Audit and Corporate Governance Committee in 2005.

The reports of the Group and statutory auditors are set forth on pages 95 and 107, respectively, of the Finance Report of this Annual Report.

KPMG received the following remuneration for their services as Group auditors and as statutory auditors of Roche Holding Ltd and other Roche financial companies:

21) http://www.roche.com/home/company/com_gov/com_gov_bylaws.htm

(in millions of CHF)	2005	2004
Auditing services	14.0	10.4
Audit-related services	1.9	1.7
Tax consultancy services	0.6	1.3
Total	16.5	13.4

The Group auditors and statutory auditors are elected each year by the Annual General Meeting. Ernst & Young Ltd received the following remuneration for their services as the auditors of Genentech and Chugai:

(in millions of CHF)	2005	2004
Genentech and Chugai audits	4.4	3.3
Other consulting services provided to Genentech and Chugai	0.5	1.0
Total	4.9	4.3

Additional information relating to corporate governance

Group structure and shareholders

- Roche's operating business is organised into two divisions: Pharmaceuticals and Diagnostics.
  The Pharmaceuticals Division comprises the three business segments Roche Pharmaceuticals, Genentech and Chugai.
  The Diagnostics Division consists of five business areas: Diabetes Care, Near Patient Testing, Centralized Diagnostics, Molecular Diagnostics and Applied Science. Business activities are carried out through Group subsidiaries and associated companies. Significant subsidiaries and associated companies are listed in the Finance Report, Note 37 to the Roche Group Consolidated Financial Statements ('Subsidiaries and associated companies', pages 92 to 94).
- Major shareholders are listed in the Finance Report, Notes 31 and 34 to the Roche Group Consolidated Financial Statements ('Equity attributable to Roche shareholders' and 'Related parties', pages 84 and 88) and in the Notes to the Financial Statements of Roche Holding Ltd (page 104).
- André Hoffmann and Andreas Oeri serve on the Board of Directors as representatives of the shareholders with pooled voting rights and receive the remuneration mentioned in 'Remuneration of members of the Board of Directors' above. No other relationships exist with the shareholders with pooled voting rights.
- There are no cross-shareholdings.

Capital structure

- Information on Roche's capital structure is provided in the Finance Report, the Notes to the Financial Statements of Roche Holding Ltd (page 104). Additional details are contained in the Articles of Incorporation of Roche Holding Ltd[22)].
- Changes in equity are detailed in the Finance Report, the Notes to the Financial Statements of Roche Holding Ltd (page 104).
- The Company has a share capital of 160,000,000 Swiss francs, divided into 160,000,000 fully paid bearer shares with a nominal value of 1 Swiss franc each. There are no limitations on the transfer of these shares and no cap on voting rights. Upon deposit, shares can be voted without any restrictions.
- There is no authorised or conditional capital.
- In addition, 702,562,700 non-voting equity securities (NES) have been issued in bearer form. They do not form part of the share capital and confer no voting rights. Each NES confers the same rights as one share to participate in available earnings and in any liquidation proceeds following repayment of the share capital. Roche's NES and rights pertaining thereto (incl. the provisions securing their claims) are described in §4 of the Articles of Incorporation of Roche Holding Ltd.
- Information on debt instruments which have been issued and on outstanding bonds is provided in the Finance Report, Note 30 to the Roche Group Consolidated Financial Statements ('Debt', page 80).
- Additional information on employee stock options is provided in the Finance Report, Note 14 to the Roche Group Consolidated Financial Statements ('Employee stock options and other equity compensation benefits', page 64).
- Roche has issued no options apart from those which have been awarded to employees or issued in connection with debt instruments.
- Neither the options awarded to employees nor the debt instruments which have been issued have any effect on Roche's share capital.

22) http://www.roche.com/home/company/com_gov/com_gov_arti.htm

Board of Directors and Corporate Executive Committee

- Information on each member of the Board of Directors (including the years in which they were elected and the years in which their terms end) and Corporate Executive Committee is listed on pages 44 to 47. Curricula vitae and other information about Board and Executive Committee members (including information on board memberships) are available on the Internet[23].
- None of the non-executive members of the Board of Directors has been a member of the Corporate Executive Committee of Roche or any of the Group subsidiaries during the three financial years preceding the current reporting period.
- The internal organisation of the Board of Directors and the division of authority and responsibilities between the Board and management are governed by the Bylaws[24].
- The Board of Directors has established a system of controls which is overseen by the Audit and Corporate Governance Committee and consists of the following elements:
  - Reports on financial and operating risks
  - Internal audits
  - Compliance Officer
  - Safety, Health and Environmental protection department
  - Corporate Sustainability Committee
  - Scientific and Ethics Advisory Group (SEAG) for issues relating to genetics and genetic engineering (established 1999).
- Each year several black-out periods are imposed during which all senior employees are prohibited from trading in company stock. The following black-out periods are in effect for 2006:

  1 January to 1 February
  1 April to 26 April
  1 July to 20 July
  1 October to 17 October

  Black-out periods can be changed by the Chairman of the Board of Directors if circumstances warrant.
- The Board of Directors held a total of five meetings in 2005. The Board committees met as follows in 2005:
  - the Presidium of the Board of Directors/ Nomination Committee: five meetings
  - the Audit and Corporate Governance Committee: four meetings
  - the Finance and Investment Committee: three meetings
  - the Remuneration Committee: two meetings
- There are no management contracts which fall within the meaning of Subsection 4.3 of the SWX Directive on Information relating to Corporate Governance.

Participatory rights of shareholders

- The participatory rights of shareholders are defined in Roche's Articles of Incorporation.[25] As Roche shares are issued to bearer, there are no restrictions on admission to Annual General Meetings, with the exception that shares must be deposited within a specified period before the date of a meeting and an admittance card must be issued in the shareholder's name, as provided in §12 of the Articles of Incorporation. Any shareholder can elect to be represented by another shareholder at an Annual General Meeting. The Articles of Incorporation contain no restrictions on the exercise of voting rights, and the only quorum requirements are those stipulated in §16.
- Under §10.2 of the Articles of Incorporation, shareholders representing shares with a nominal value of at least 1 million Swiss francs can request the placement of items on the agenda of an Annual General Meeting. This must be done no later than 60 days before the date of the meeting.

Change of control and defensive measures

- The Articles of Incorporation contain no provisions on the mandatory bid rule. Swiss law applies.
- There are no change-of-control clauses. Those components of remuneration based on Roche NES would be terminated in the event of an acquisition, and vesting period restrictions on pre-existing awards would be removed, so that all such options could be immediately exercised.

23) http://www.roche.com/home/company/com_gov.htm
24) http://www.roche.com/home/company/com_gov/com_gov_bylaws.htm
25) http://www.roche.com/home/company/com_gov/com_gov_arti.htm

Information policy

- As provided by §33 of the Articles of Incorporation[26], corporate notices are published in the Swiss Official Gazette of Commerce *(Schweizerisches Handelsamtsblatt)* and in other daily newspapers designated by the Board of Directors *(Basler Zeitung, Finanz und Wirtschaft, L'Agefi, Le Temps, Neue Zürcher Zeitung)*.

- Roche reports its half-year and full-year results in business reports published in print and online formats and at media events. In addition, first- and third-quarter sales figures are published each year in April and October. Current dates of publications are available in English and German on the Internet[27].
- All relevant information and documents, including all other media releases and presentations to analyst and investor conferences, are available in English and German on the Internet. Further publications can be ordered by e-mail, fax or telephone (basel.webmaster@roche.com; tel. +41 (0)61 688 83 39; fax +41 (0)61 688 43 43).
- The contact address for Investor Relations is: F. Hoffmann-La Roche Ltd, Investor Relations, Corporate Finance, 4070 Basel, Switzerland; tel. +41(0)61 688 88 80, fax +41(0)61 691 00 14. Additional information, including details on specific contact persons, is available on the Internet[28].

Non-applicability / negative disclosure

It is expressly noted that any information not contained or mentioned herein is non-applicable or its omission is to be construed as a negative declaration (according to the requirements of the SWX Corporate Governance Directive, including the Commentary).

Compliance Officer

The Compliance Officer is committed to ensuring that Roche corporate principles are consistently complied with throughout the Roche Group and also serves as a contact person for shareholders, employees, customers, suppliers and the general public on issues relating to the implementation of and compliance with these principles. Employees and other parties who become aware of violations of Roche corporate principles can bring them to the attention of their managers or supervisors or report them to the Compliance Officer (Andreas Greuter, direct phone number: +41(0) 61 688 75 37). Such disclosures will be treated as confidential. Employees who make such disclosures will not be penalised by the company for doing so, but are not immune from prosecution for legal violations. The Compliance Officer submits regular reports to the Audit and Corporate Governance Committee.

26) http://www.roche.com/home/company/com_gov/com_gov_arti.htm
27) http://www.roche.com/home/media/med_events.htm
28) http://www.roche.com/home/investors/inv_contact.htm

Responsible and sustainable management

Sustainability – an integrated approach

Roche strives to create sustainable, value for all major stakeholders. Economic, social and environmental progress are interdependent and influence each other. Only companies that create economic value have the resources to make an active commitment to society and the environment. At the same time, business success is not feasible without an intact environment and a society that embraces both achievement and innovation.

Sustainability is a hallmark of Roche's core business. After all, our corporate strategy as a research-based corporation is by its very nature long-term, given that research and development cycles often last decades. We accept the associated risks in order to develop innovative diagnostic products and medicines that help to save lives or at least alleviate suffering. This is where we see our most important contribution to society. In 2004 Roche was selected for inclusion in the Dow Jones Sustainability World Indexes (DJSI World) and the Dow Jones STOXX Sustainability Indexes (DJSI STOXX) and further improved its position in 2005. Roche also met the FTSE4Good criteria and thus remains a member of the FTSE4Good Index Series. This is a clear sign of recognition of our efforts in this area.

FTSE4Good Index Series

Networked structures on a firm footing

The Corporate Sustainability Committee (CSC) was established in 2002 and the Corporate Sustainability Charter was adopted by Roche's Corporate Executive Committee and Board of Directors in 2005. The Charter describes the mission, context, composition and procedures of the Corporate Sustainability Committee. This committee drafts and coordinates our strategy for sustainable development and reports on efforts and progress in this area; it is also responsible for developing and amending corporate guidelines. The Corporate Sustainability Committee is authorised to appoint cross-divisional, cross-functional expert groups to develop or review position statements and rules. Further information on the Charter can be found at www.roche.com/en/sust-commcharter.pdf.

The Corporate Sustainability Committee reports directly to the Chairman and CEO and submits regular reports to the Board of Directors' Audit and Corporate Governance Committee. Its networked structure and ability to rely, as required, on the expertise of line and functional managers ensures that it is firmly embedded in the organisation and enjoys the support of senior management, thus promoting the integration of sustainable development into all Group operations.

On 15 March 2005 Roche's Corporate Executive Committee appointed the CSC Core Team:

- *Pierre Jaccoud,* Chair; Secretary to the Corporate Executive Committee and Head of the Chairman's Office
- *Peter Bieri,* Head of Corporate Audit

- *Andreas Greuter,* Compliance Officer
- *Peter Heer,* Head of Public Affairs
- *Gottlieb Keller,* Head of Corporate Services and Human Resources
- *Horst Kramer,* Delegate of the Diagnostics Division
- *Karl Mahler,* Head of Corporate Finance Investor Relations
- *Bruno Maier,* Head of Corporate Law and Patents
- *Christopher Murray,* Delegate of the Pharmaceuticals Division
- *Rolf Schläpfer,* Head of Corporate Communications
- *Erwin Schneider,* Head of Corporate Finance Accounting and Controlling
- *Peter Schnurrenberger,* Head of Corporate Safety, Health and Environmental Protection
- *Dianne Young,* Secretary, Corporate Finance Investor Relations

How we deal with risks

As part of the business plan, the most material risks to achieving the company's goals are identified and assessed by the Group Risk Management team.

'An innovation mindset promotes sustainability'

Roche has been working for a number of years with Professor Ulrich Steger, Director of the Forum for Corporate Sustainability Management at the IMD in Lausanne, Switzerland.

Professor Steger, what prompted IMD and Roche to start working together?

In our Forum for Corporate Sustainability Management, of which Roche is a member, we have thoroughly analysed the link between a company's core strategy and sustainability. Roche management wanted to better understand the company-specific drivers behind sustainable development. One key finding: Roche has already closely tied in its business model with sustainability.

Why is this so?

First of all, the history of Roche as a family-owned firm plays an important role. The tradition of commitment to which Roche has pledged itself has been demonstrably present since the company was founded and is very much alive at Roche today. Secondly, Roche stands out from its competitors on account of its level of innovation. The sharp focus on developing novel approaches automatically results in sustainable business practices. Thirdly, management is both professional and thorough in the way it links the business model to sustainability. There are abundant examples of how Roche seeks innovative – and not simply pragmatic – solutions, be it in safety, health and environmental protection, in risk management, in research or in the corporate culture generally.

How does Roche benefit from the co-operation with IMD?

The demands being made on research-based healthcare companies are steadily increasing. Issues such as the cost explosion in healthcare, access to medicines or transparency in clinical trials are some examples of changing dynamics in the healthcare sector. Our co-operation will, we hope, show how the business model can be brought even more closely into line with the demands of business sustainability particularly in areas such as these.

Further information on IMD at: www02.imd.ch

‘To date a total of 259 trials have been registered’

Beat Widler, Head of Global Clinical Quality Assurance, Roche

In 2005 Roche began making information on all clinical trials available publicly. How did this come about?
The debate surrounding clinical trial transparency prompted Roche to create the desired open communication quickly and unbureaucratically. We wanted to reinforce the confidence of the public and patients in clinical trials. We evaluated various internal options and then decided to build up a registry that is managed by an independent company – CenterWatch – and not by Roche itself. At present – i.e. as at the end of 2005 – 259 studies have been entered in the registry, 218 of them ongoing and 41 completed. By autumn 2006 we expect to include a further 170 studies.

Which studies are registered?
All ongoing trials as of Phase II that received initial regulatory approval after October 2002 and that Roche leadmanages. Moreover, all completed studies are registered, regardless of whether the outcome was made public.

What feedback have you received on the project? How is the Internet site with the registered trials accessed?
The feedback – both inside Roche and outside – is positive. We have about 1,600 visitors a week; two thirds of them are private users, for instance patients who would like to find out about clinical trials and their results.

What has been your experience with this project?
I’m pleasantly surprised. I’ve never seen a project implemented so quickly and efficiently. The registry is not only important for patients and the public at large, it also supports a number of efforts being undertaken at Roche to ensure that colleagues in various teams and countries have a faster and clearer overview of our own clinical trials.

The Corporate Sustainability Committee, which is involved in these risk assessment processes, is responsible for assessing the SEE (social, environmental and ethical) risks that it identifies.

Roche is confident that the institutionalisation of sustainable core ethical values throughout the company is a necessary precondition for an effective approach.

For the coming year, the key areas for sustainable development have been defined. These relate primarily to animal experimentations, clinical studies and new technologies such as nanotechnology. Roche undertakes to continually evaluate the associated factors and to define a Roche position with regard to these values.

Roche complies with ethical standards

Roche and its employees are committed to complying with all relevant local, national and international laws and with Roche’s own guidelines, which often go beyond such legislation. These standards are based on the Roche Corporate Principles, which – together with Roche directives, guidelines and regulations – comprise the Roche Code of Conduct. As of 2006, a specially developed, interactive, computer-based learning program covering the

standards will be deployed worldwide at every hierarchical level. Since this is an issue of crucial importance, it is vital that we ensure that all Roche employees actively participate in this programme. Roche companies in the United States, which have their own compliance programmes, are exempted from this programme. (For further information on the Code of Conduct, please go to http://www.roche.com/en/home/company/com_gov/com_gov_cond.htm)

You will find the Roche Corporate Principles on the Internet at www.roche.com/en/home/company/com_gov/com_gov_cond/com_gov_princ.htm.

The Corporate Sustainability Report also addresses societal issues. In this context the enforcement of our policies and procedures addressing fraud and bribery/corruption is tracked. Reported cases of violations are followed up and the necessary measures taken.

Research activities at Roche meet rigorous ethical standards

Innovation is the key to success in all our business endeavours. But research implies responsibility, because groundbreaking science inevitably entails risks as well as opportunities. We have set high ethical standards for our research activities. Roche has issued clear directives governing the ethical considerations to be observed in genetic research, clinical trials, animal experiments, etc. We thereby provide our scientists with decision-making tools that are backed up by targeted continuous training events. Roche was the first company in the industry, back in the 1990s, to set up an external ethics body that advises and supports internal research departments.

Clinical trial protocol registry and clinical trial results database

We believe that Roche has an ethical obligation to ensure that scientifically or clinically relevant data from its clinical trials are made available to the public. In early 2005 Roche was the first company in the industry to set up a clinical trial protocol registry with an independent host. This idea was prompted by two objectives. For one thing, the information is meant to help patients – in consultation with their physicians – to find clinical trials in which they can participate. For another, practising physicians and other healthcare professionals will be able to obtain a balanced overview of clinical trial results. (Further information can be found at www.roche-trials.com)

Ethical responsibility in research and development

In the day-to-day work of developing new medicines and diagnostic tests, ethical issues often arise. Roche has therefore taken a clear position on research in human subjects that is brought to the attention of all employees. (Further information can be found at www.roche.com/pages/downloads/sustain/pdf/poshumsubres.pdf)

A Global Ethics Liaison office was established in 2004 to drive the systematic resolution of such issues; it is open to all Roche employees. In 2005, 37 queries were submitted on issues ranging from trial plan design to data protection and compensation for patients in clinical trials. If the problem cannot be satisfactorily solved together with the Liaison office, the case can be referred to an internal body. Where necessary, an external advisory group may be consulted. (Further information on the Roche Framework for Discussing and Resolving Ethical Issues in Human Subject Research at www.roche.com/sust-resethissclint.pdf)

Responsible animal experiments

At Roche as at all research-based healthcare companies, the appropriate and responsible use of animal experiments is an essential part of biomedical research, and the majority of such experiments are therefore prescribed by the authorities. For the past three years Roche has been gathering data on global research within the company. The aim is to discuss the type and scale of the projects with the research managers and, together with them, to seek ways to optimise the use of animals in research without jeopardising the quality of the work or the safety of patients.

For the past year the data, include not only figures from all research sites but also from contractual partners. More than 95% of all animals used for experiments are rats and mice and about 0.5% are non-human primates. Roche does not simply 'outsource' the most difficult experiments, but conducts these within the company, thus taking full responsibility for them. With the aid of innovative technologies such as biomarkers, the company is endeavouring to further reduce the number of experimental animals used. This is also a cost-effective approach.

We take the public's concern about the use of animals for scientific research very seriously. Roche endeavours to set the highest ethical standards. Thus, by the end of 2006, all Roche research centres are to be accredited by the AAALAC (Association for Assessment and Accreditation of Laboratory Animal Care International). The largest Roche research centres have already been certified. In future, furthermore, all contracts with third parties will include a clause stipulating that the AAALAC requirements must be met and that Roche reserves the right to conduct audits to verify this.

The care and use of animals within the Roche Group will be more intensively coordinated in future. As a first step, Roche has appointed one person to organise the Group's training activities in this area. These efforts are to be backed up by a global network. (Further information can be found at www.roche.com/home/sustainability/sus_res/sus_res_anim.htm)

Genetics and bioethics

In the 1990s Roche – assisted by recognised international experts – drew up the Roche Charter on Genetics, and has since been working together with an independent body, the Science and Ethics Advisory Group (SEAG). Regular meetings are held at which SEAG advises Roche on matters relating to the Charter in particular and to genetics in general. In 2005, for example, SEAG addressed issues relating to ethics, biomarkers and genomics, formulated recommendations on these issues and reviewed the corresponding position papers submitted by Roche. (Further information on SEAG can be found at www.roche.com/en/sci_eth_chart.htm)

Biodiversity and bioprospecting

Roche recognises that the issue of biodiversity and the retention of traditional skills is of growing importance, particularly for low-income countries. Roche supports the principles of the UN Convention on Biological Diversity of 1992. Roche's global position (Global Roche Statement on Biodiversity) can be found at www.roche.com/pages/downloads/sustain/pdf/ropos_biodiv.pdf.

Nanotechnology

Roche tracks all new technologies closely to assess whether they can help improve our products, services or processes. Nanotechnology is one such new technology. We are studying the ethical and social implications of this form of miniaturisation as well as its potential practical applications. An expert group within the Corporate Sustainability Committee at Roche is currently drafting a position paper on nanotechnology which is due to be completed early in 2006.

Stem cell research

Roche is generally interested in relevant scientific developments, for instance in stem cell research and its applications. Currently, however, Roche is not engaged in any activities in the area of therapy using replacement tissue from stem cells, nor does it employ any such methods or technologies. Moreover, Roche has decided not to engage in human cloning for reproductive purposes.

Roche has developed a clear position on stem cell research, related applications and cloning, which can be found at www.roche.com/sust-posstem-cells.pdf.

Marketing

Roche has established and implemented a number of international guidelines on the design and use of advertising material and websites and on the structuring of events. These globally applicable rules ensure that the use of advertising material complies

with all the legally valid regulations. (For further information, see www.roche.com/en/sus_eth_guidel_prom.pdf.) However, Roche goes further than the legal provisions We have, for instance, recognised the Pharmaceutical Research and Manufacturers of America Guidelines on Direct-to-Consumer Advertising. These guidelines will come into force at Roche in 2006 and will be reinforced through training programmes. Moreover, we have implemented the European marketing code of the European Federation of Pharmaceutical Industries' Associations (EFPIA) within Roche. For this purpose, we have drafted a number of internal guidelines that the General Managers of the Roche companies are responsible for implementing. (For further information, see www.roche.com/en/home/sustainability/sus_eth/sus_eth_mark.htm)

Ensuring product safety

Roche products must not only be effective – above all, they must be safe. At Roche a large number of people work in the area of drug safety, where they seek to protect patients from adverse drug reactions. They do this by identifying such effects as early as possible and classifying them in terms of their severity. This is important, as many undesirable effects – headache, for example – may be harmless by comparison with the disease that is being treated (e.g. a life-threatening condition such as cancer). In each case, the benefits of every medicine must be weighed against the risks involved. The employees working in the area of drug safety systematically monitor all Roche products around the world, even after they have been registered. In 2005, staff reviewed and assessed a total of 70,000 reports of adverse drug reactions. Once an undesirable effect is identified, the product information has to be supplemented accordingly in conjunction with the responsible authorities.

Roche is committed to a comprehensive quality management system that ensures the quality, safety and efficacy of its medicines and diagnostic tests. Roche standards are based on the specifications laid down by recognised international bodies and healthcare authorities. Each and every employee is responsible for ensuring that the guidelines are fully complied with in his or her area. Moreover, Roche regularly reviews its quality standards and systems and constantly develops them. This review and development task ranges from conducting internal audits to systematically monitoring product quality, analysing trends and promptly responding to complaints from our customers.

Protection against counterfeits

As counterfeit pharmaceutical or diagnostic products not only violate property rights but also jeopardise the health of patients and can undermine confidence in the health system, Roche combats such forgeries rigorously. In 2005 Roche established a global policy outlining the measures in place to prevent counterfeits. In addition to technical measures relating to design, labelling and packaging, these focus primarily on monitoring the market and agreeing with business partners on clearly defined arrangements and audits. If forgeries are discovered, Roche immediately informs the authorities and – if appropriate – also the general public.

'Suddenly I realised my life was hanging by a thread.'

Predisposition | Early detection | Prevention | **Diagnosis** | Therapy | Monitoring

The tale of a life-saving diagnosis of heart failure

Mohinder Pratap Johar is an easy man to admire. He eats healthily, makes sure he gets enough physical activity and, at 78, still leads a busy life. But things might have turned out quite differently. In 2002 he started feeling tired and short of breath, instead of his usual fit self. His doctor diagnosed high cholesterol and put him on medication, but that didn't seem to help. Fortunately, this was all happening about the time the Elecsys proBNP cardiac test was launched in Mohinder's native India, and he had the test done at the renowned Delhi Heart and Lung Institute.

The results showed an alarming rise in the blood levels of a protein produced by the heart, indicating that Mohinder was suffering from heart failure, a condition in which the heart muscle is no longer pumping efficiently. Further examinations revealed that Mohinder's life was hanging by a thread. Three of the arteries supplying blood to his heart were clogged, putting him at risk for a massive heart attack. He immediately underwent bypass surgery.

In the meantime Mohinder has resumed virtually all of his normal activities. He prefers not to dwell on what might have happened without that heart test.

Diagnosis

Getting a fast, accurate diagnosis can be a matter of life and death. Within minutes Elecsys proBNP can determine whether a person with shortness of breath has heart failure – even in the early stages of the disease, when conventional tests fail. It can thus help prevent disease and promote earlier treatment, and sometimes it can help save lives.

Dialogue with our stakeholders

Listening and learning from our stakeholders

The term 'stakeholder' refers to any individual or group of individuals having an influence on or interest in our company's ability to achieve its objectives. These include in particular – but not only – employees, patients, medical and scientific personnel, investors, the authorities, suppliers and the media. Our relationships with stakeholders are based on the general commitments set out in our Corporate Principles, but are also geared specifically to the concrete needs of both sides.

Our customers

Roche strives to excel in every area, including that of customer relations. We are happy to receive positive feedback from our customers, in particular patients and medical specialists, but we regard even complaints as an important source of information on possible improvements. We aim to respond quickly to the needs of our customers and develop sustainable relationships. We communicate with patients who benefit from our products and services through the following channels: the healthcare professionals who pass on patients' views to us, product-related websites such as www.accu-chek.com or www.bonepain.com and patient organisations.

Holders of shares and non-voting equity securities, and investors

It is in our own interest to cultivate close and transparent relations with our shareholders: holders of shares and non-voting equity securities and financial analysts help decide on the future focus of Roche and expect to be kept up to date. We engage in an ongoing, frequent and substantive dialogue with our shareholders through numerous channels such as management roadshows, broker conferences, visits to Roche, teleconferences and Roche-organised events on topics of key interest. During 2005 management met with over 2,500 investors and analysts to discuss our performance and to gain feedback about their expectations. Roche will continue to ensure that all market players receive regular updates on our business strategy and business performance. Roche is committed to transparent and fair reporting that is available simultaneously to all market players, as outlined in our communication policy. (Further information can be found at www.roche.com/communic_pol_e.pdf). Feedback on our performance is important, and for this reason we participate in a number of investor-relations-targeted external surveys, including the Thomson Extel and Institutional Investor Research Group surveys, as well as additional surveys on our website and in our Annual Report. In the 2005 Thomson Extel Survey, the Roche Investor Relations team in the Pharmaceuticals Division was awarded first place ahead of all our competitors. (Further information on investor relations can be found at www.roche.com/en/home/investors.htm)

Employees and employee organisations

Roche believes that our business depends on the talent and performance of dedicated employees. A crucial factor for success therefore is recruiting, motivating, developing and retaining outstanding people. We make every effort to promote open, two-way communication in the company and to foster cooperation in cross-divisional and cross-border teams. The key elements of our human resource management are set out in the Roche Employment Policy. (Further information at www.roche.com/en/home/sustainability/sus_soc/sus_soc_comm/com_gov_emp.htm)

The Roche Employment Policy states, among other things, that it is the right of every employee to be part of an employee organisation, and Roche is ready to work together in open dialogue with legal employee representatives in all the countries in which it operates. In 2005 there was no major restructuring or reduction in personnel.

Our most important stakeholders and their significance for Roche

Employees	Approximately 25% of sales revenue is used by Roche for compensation of our employees. With over 9.0 billion Swiss francs for salaries, Roche provides 68,218 employees in over 100 countries with attractive jobs.
Holders of shares and non-voting equity securities	The trust that holders of shares and non-voting equity securities have in Roche's strategy and management is important for our success. In 2005, 2.15 billion Swiss francs or 32% of profits were paid out in the form of dividends. 68% of profits are invested in the long-term increase in the company's value.
Patients and the medical and scientific community and its professional associations	Our products are sold in over 150 countries and are instrumental in improving the quality of life and often in prolonging life. Last year we invested 5.705 billion Swiss francs in the research and development of new products and services. More than 130,000 patients who are participating in clinical trials benefit from the latest drug developments.
Public sector	In 2005, Roche paid taxes amounting to 2,224 million Swiss francs; it thus makes a considerable contribution to the financing of state infrastructure and programmes.

In addition to the relationship of trust and cooperation between management and employee representatives at the local level, the Roche Europe Forum – in which employee representatives from different countries meet with members of Roche management – has proved to be a sound basis. The Roche Europe Forum represents approximately 30,000 employees, i.e. about 44% of the workforce. Roche does not keep records on employees' membership of trade unions or on the degree of unionisation at individual affiliates. According to local estimates, about a quarter (25%) of Roche employees are members of a trade union and slightly over 60% are represented by some form of employee organisation.

Authorities and the public sector

Roche strives to maintain relationships with the relevant health authorities and players in the public sector that are long term, strategically driven and transparent. We are active in a political and legal environment that is highly complex and is governed by international and regulatory intricacies. Our goal is to be involved at an early stage in the political processes that are relevant for our business, so that we can intervene proactively. We present our positions transparently. Our primary aim is to ensure that we can continue to develop and provide efficient solutions for health problems by safeguarding an environment that is receptive to research and open to innovation. We therefore consider it to be important to engage in dialogue with political decision-makers and legislators at both the regional and the national level. We also seek contacts with their counterparts on the European and the international stage. Such direct contacts go hand in hand with our efforts within industry organisations.

Society, non-governmental organisations and interest groups

Roche cultivates long-term cooperative relationships with non-governmental organisations (NGOs). The Group plays an active role in these partnerships, primarily by contributing human resources and know-how, and to a lesser extent through funding. The following is a selection from the full list of organisations and initiatives that Roche works with or is involved in:

- National and international business and industry associations
- World Business Council for Sustainable Development (WBCSD): Roche is a founding member of the WBCSD and is involved in various working

groups within the organisation.

- Business Charter for Sustainable Development of the ICC (International Chamber of Commerce): Roche endorsed the charter as a founding signatory in 1992.
- Responsible Care: Roche regards Responsible Care as an important aspect of sustainable development and is dedicated to putting it into practice.
- World Environment Center (WEC): Roche has been an active member since the early 1990s.
- Global Environmental Management Initiative (GEMI)
- Global Business Coalition on HIV/AIDS
- PharmAccess Foundation, CARE-Programm
- European Coalition of Positive People (ECPP)
- Development and disaster relief organisations such as the International Committee of the Red Cross and its national associations.

An extended list of the main stakeholder contacts and organisations of which Roche is a member can be found on the Internet at www.roche.com/en/home/sustainability/sus_soc/sus_soc_coop/sus_soc_coop_int.htm

Suppliers and business partners

Most manufacturers of specific intermediates or products in whose development Roche is involved are already committed to observing the Roche standards. They are also covered by the compliance procedures and are monitored for observance of these regulations. We keep a particularly close watch on our suppliers' approach to workplace safety and occupational hygiene, pollution and waste management. In this way, we aim to ensure that our suppliers and service providers follow not only legal requirements but also our principles of sustainability. Roche recently released a set of guidelines governing its relationships with suppliers and service providers. These guidelines set out in formal terms our ethical requirements for companies from which we purchase products and services. (You will find further information on this subject at www.roche.com/en/sus_eth_guidel_sup.pdf)

How our reporting is viewed by our stakeholders

Our sustainability reports are focused on the information requirements of our stakeholders. It is very important to take their feedback into account when improving and fine-tuning these reports.

The 2004 Roche Sustainability Report received a number of awards and has even been nominated for the 2005 European Sustainability Reporting Award (the award ceremony is scheduled for February 2006). The fact that we successfully completed the assessment process for renewed inclusion in the Dow Jones Sustainability Indexes can also be ascribed in part to the report. In improving certain aspects of the report, we take due account of feedback from our stakeholders. A detailed evaluation was made by a panel featuring a wide range of expertise. It was made up of representatives of NGOs and investors, together with experts in the fields of communication, governance, corporate social responsibility and auditing. The verdict was as follows: 'Overall, the panel felt that Roche had carried out a substantial, detailed and commendable piece of work in the 2004 Sustainability Report. The report demonstrates Roche's real commitment to sustainability, gives evidence of a clear obligation to comply with GRI standards and provides many examples and case studies of good work being carried out by members of the company in many parts of the world.' Detailed examination of the report yielded recommendations for improvements to subsequent reports which included: integration of risk management, detailed objectives and performance figures, greater transparency in the cross-referencing of sustainability with the Roche business model, descriptions of conduct towards stakeholder groups, and improved readability/structure. We are doing our utmost to implement these improvements and are confident that the present report comes even closer to meeting our stakeholders' information requirements.

'The feeling that I had regained control over my disease gave me a huge psychological lift.'

Predisposition › Early detection › Prevention › Diagnosis › **Therapy** › Monitoring

Herceptin – a breakthrough for women with HER2-positive breast cancer

Maggie Duke (57), a specialist in hygienic engineering from Vevey, Switzerland, was diagnosed with breast cancer in 1997 when a small, hard, painful lump was found in her breast. After removal of the lump, Maggie began treatment with chemotherapy, radiotherapy, and hormonal therapy. Unfortunately, within a year the cancer had spread to her bones and liver.

Further tests showed that Maggie had HER2-positive breast cancer, an aggressive type requiring special care. She was then treated with a combination of chemotherapy and Herceptin, a drug designed specifically for HER2-positive cancer.

Within just a few months of beginning treatment with Herceptin, Maggie's outlook improved dramatically, giving her a huge psychological lift and renewed hope of leading a full and active life. Since starting treatment with Herceptin over seven years ago, Maggie has carried on as normal, continuing to work, travel and participate in her much-loved sports. Thanks to the health and energy she has regained, she has even been able to participate in long-distance cycling events to help raise funds for cancer research.

Therapy

In 20% to 30% of all breast cancers, overproduction of the HER2 protein results in fast-growing tumours that respond poorly to chemotherapy alone. Herceptin (trastuzumab) specifically targets HER2, shrinking tumours without harming healthy cells. In both advanced and early disease, Herceptin improves survival while maintaining quality of life for women with HER2-positive breast cancer.

Our commitment to employees

A successful business creates new jobs

As in recent years, Roche has been expanding faster than its competitors. This has led to an increase in headcount in many business areas and regions. In 2005 the Roche Group created a total of 3,624 new jobs, an increase of 5.6%. Headcount increased by 679 in the Diagnostics Division and by 2,941 in the Pharmaceuticals Division, of which Genentech accounted for 1,917. In 2005 Roche spent 9,049 million Swiss francs on employee remuneration, an increase of 801 million Swiss francs (+9.7%) over the previous year. These figures exclude the impact of a one-off gain on the return of part of the Chugai employees' pension fund to the Japanese government.

The largest number of new positions was created in the regions, such as Europe and North America, where sales also grew faster than average. For instance, 2005 saw the founding of new companies in the Eastern European region, leading to an increase in headcount of over 12%. Overall, the increase in the number of new positions was greatest in Research and Development and in Marketing and Sales. The Roche Group hired a total of 8,180 new employees in 2005 in order to fill vacancies as well as to create new jobs. Besides retaining talented and motivated employees, it is also important – in view of our goal of increasing both sales and profit – to take an effective approach to attracting new talent (http://careers.roche.com).

Number of employees and personnel costs by division

	2005	2004	Change	Personnel costs[1] 2005	Personnel costs[1] 2004	Change
Roche Group	68,218	64,594	+3,624	9,049	8,248	+801
Pharmaceuticals	48,049	45,108	+2,941	6,586	5,835	+751
Diagnostics	19,788	19,109	+679	2,329	2,256	+73
Others	381	377	+4	134	157	-23

1 in million francs

Number of employees by region

	2005	2004	Change
Europe	29,934	28,601	+1,333
Switzerland alone	7,860	7,498	+362
North America	21,899	19,715	+2,184
Latin America	4,465	4,971	-506
Asia	10,459	9,885	+574
Japan alone	5,988	5,663	+325
Africa Australia Oceania	1,461	1,422	+39

Employment Policy

The Employment Policy lays down the requirements that human resources management in the Roche Group has to meet and also establishes the rights and obligations of Roche employees with regard to the company. Further information on this topic is available at www.roche.com/en/home/company/com_gov/com_gov_emp.htm.

Roche is a popular employer

The labour market for highly qualified talents in the pharmaceutical industry is extremely competitive. Since 2003, Roche has considerably improved its global presence in this market, becoming more effective in attracting outstanding employees. The approach has been two-pronged: employer branding which underscores the key advantages of Roche as a global employer in our industry, and the introduction of global e-recruiting. In 2004 we launched an Internet-based global recruitment tool which enables candidates to view current vacant positions at a glance, apply for a job online or register in the global or various local talent pools. The tool was used by over 130,000 candidates in 2005 to register or apply for employment. In the past year Roche achieved three demonstrable competitive advantages: recruiting has become faster and more efficient, a better selection from the growing number of well qualified external applicants is possible, and, lastly, transparency for internal applicants. Roche has come considerably closer to achieving its goal of 'one door into Roche' through a unique combination of systems. By the end of 2005, 65% of all known vacancies worldwide were viewable on a website. This percentage will be increased in 2006.

Once again in 2005 Roche companies won a number of prizes or topped the rankings as an attractive employer: e.g. Roche and Genentech in the USA; in Germany (best employer); in Switzerland (best employer for women), in Spain (best employer) and in Australia. Roche was also voted the 'highest climber' in popularity as an employer in Europe. We record employee satisfaction by conducting surveys and through two indirect indicators: illness rate and departures not initiated by Roche. A global illness rate of 3.7% is a clear indication that our employees enjoy good working conditions and feel comfortable working at Roche.
The total attrition rate of permanent staff was 6.7% in 2005. The number of regretted losses was only 2.2% (1,533 employees). The proportion of departures of qualified staff was highest in Sales (6.3%) and Administration (4.3%). We are pleased that the lowest numbers of departures of qualified staff in 2005 were in Research (1.7%), Production (2.7%) and Marketing (3.1%).

This demonstrates overall that Roche can count on a stable pool of motivated employees. The risk of not achieving the projected results in business-critical areas as a result of significant numbers of regretted losses can still be regarded as minimal.

	2005	2004
Fluctuation	6.7%	6.1%
	4,556 employees	
'Regretted losses', i.e. fluctuation not initiated by Roche	2.2%	2.9%
	1,533 employees	

Performance culture at Roche

Since 2002 performance management has been emphasised as a key management instrument for generating sustainable added value at Roche. The link between corporate goals and the day-to-day business carried out by management and employees is forged using goal-setting management. In this process, the performance of management staff is measured in terms of their contribution to sustainable value creation within the company. All senior managers at Roche share a common goal: sustainably increasing enterprise value, as measured against OPAC (operating profit after cost of capital).

One door into Roche – Roche vacancies at a glance

At the beginning of 2004 Roche launched a global career Internet site http://careers.roche.com that shows all vacancies within the Group at a glance. To date, over 30 countries have been linked up to this site, which meant that by the end of 2005 more than 65% of vacancies at Roche could be viewed online. The site contains information about Roche and the individual country affiliates as well about as the vacant positions. Anyone interested in applying for a job at Roche can have their personal data and CV registered in the Roche talent pool. As soon as a vacancy comes up, Roche contacts all those potential candidates whose profile matches the requirements for the job in question. Roche employees can also apply for job openings in this way. Roche's career Internet site is a unique instrument in the industry that supports the Group's growth-driven corporate strategy.

In 2005 the target group of this standardised performance management, which had originally been senior management (approx. 1,000 managers), was extended to include a larger population in specific critical segments. In 2004 and 2005 Roche refined a Group-wide standardised database and an integrated system. This provides goal-setting agreements with greater transparency, thus facilitating comparison and control. It also provides a broader factual basis for decisions regarding development, promotions and transfers.

In 94% of the affiliates, various goal-setting models for performance management or regular feedback on performance are in place. Altogether, 85% of the workforce have defined goals or set objectives, or regularly receive feedback on their performance.

Talent management and development at Roche

Business success at Roche, today and in the future, depends on the efforts of a large number of motivated and highly qualified employees and managers. What characterises performance culture at Roche is a high degree of individual responsibility. Regular feedback and development reviews are the cornerstones of performance management and career development. Staff are promoted to higher management positions on the basis of their leadership qualities and actual performance.

The succession management process for global key positions is well established and is reviewed at regular intervals. Succession planning was carried out in 2005, as it is every year, for the Group's 1,000 top managers at Group and Divisional level. The talent situation at Roche is very encouraging on the whole. In the Group, we have an average of 2.5 succession candidates for each key position (compared with 2.6 in 2004), which is in the best-practice range of 2.5–3.0 candidates per position. We are confident that our focus on performance management not only produces a sufficient number of internal candidates but ensures that they are of a very high standard. The risk of gaps in key positions causing a negative impact on business as a result of people leaving is therefore negligible. In 2005 there were only very few cases of vacancies among the top 1,000 positions not being filled within a short time. The processes of global succession planning and talent identification have been taken over and adapted in many countries. In 2005, 69% of Roche affiliates had a systematic succession planning

Training and management development

	2005	2004
Total hours invested in training/staff development	2.14 million	1.85 million
Training time per employee	3.3 days (26.7 hours)	2.9 days (23 hours)

process in place. 83% of our affiliates have put programmes into place for the systematic identification and development of talents.

Employee development at Roche takes many forms. The primary tool in this process is the development plan. In 2005 a training or development plan that described concrete development prospects or steps was agreed with 62% of all Roche employees. In addition to continuing education, the plan calls for strategic postings of talented employees abroad and a growing number of project assignments and job rotation.

In an effort to deal efficiently with peaks in the work volume, we have employed 3,006 employees on a temporary basis (as per end-2005) compared with 3,745 as per end-2004. In addition, we are currently training 959 apprentices and offering them the prospect of a career with a future.

In 2005 Roche introduced the Leadership Charter, a competence model for managers in the company, which was adapted by both Divisions. This model is based on the essential competencies that managers at Roche should possess. This gives Roche managers a consistent view of what is expected from them in terms of management competencies. Another achievement in 2005 was the new Executive Development Programme for senior management at Roche which will begin in 2006. The target group for this programme are the top 350 managers in the company.

Compensation and benefits

The remuneration policy adopted in 2004 is designed to support value creation and reinforce Roche's culture of performance and innovation, while delivering remuneration to meet employees'

'30% of Roche employees are already participating in Roche Connect'

Lisa Teverson, Group Head of Compensation & Benefits

What exactly is Roche Connect and how does the programme function?
Roche Connect is a share purchase programme that gives Roche employees the option to acquire Roche non-voting equity securities (known as Genussscheine in Switzerland) at a discount. They thus have the chance to participate in the company's growth. The programme started in 2002, and is now offered to employees in 41 countries worldwide. This is a great success given the short time span since the programme was launched.

Who can participate in the programme?
As soon as Roche Connect is launched in a country, all permanent employees there can participate. Worldwide, 30 percent of the employees to whom it has been offered have already decided to take part. The programme was, however, not developed for temporary employees since shares are generally considered to be a long-term investment.

What are the next steps for Roche Connect?
We have now implemented the programme in the countries where this is relatively easy. We cannot currently offer the plan in countries like the USA or China as the legal requirements are much more complicated. We will continue to check feasibility, especially in China, and we hope we will soon be able to include employees from these countries in Roche Connect. But to achieve that goal we still have a lot of work to do.

needs both now and in the future. The first awards were made under Roche Long Term, the new incentive programme for executives and key managers which was approved at the end of 2004. Participants receive either stock-settled stock appreciation rights or options to acquire Genussscheine, depending depending on tax efficiency. This marks a notable change, particularly in the USA, where incentives were traditionally based on American Depositary Receipts instead of the Genussscheine. The incentives for entitled participants worldwide are all based on the growth in the value of the Genussscheine. Thus, everyone involved has an immediate financial interest in increasing our company's value.

Following on from the two awards won in 2004 for Roche Connect, the employee stock ('Genussscheine') purchase plan, Roche has again received external recognition for its employee equity programmes. The Global Equity Organization (GEO) – a leading international organisation promoting share ownership for employees – awarded Roche their 2005 award for the most creative and innovative design for companies with more than 30,000 employees. This time the award was received for the new Roche Long Term incentive programme. In making the award the judges praised the way that Roche had identified and addressed differences in prior incentive plans, and in the changing competitive, accounting and tax environments, to arrive at the new global programme. With the launch of the plan in Argentina in 2005, a further country was included into Roche Connect, bringing the total number of countries where the plan is offered to 41. Membership of the plan also continued to grow significantly, reaching over 11,600 (+22% vs. 2004:) 9,067). This is a further indication that Roche employees identify with their company.

A number of new benefit plans and changes to existing plans were approved during the past year, including some changes to the pension plan for employees in Switzerland.

Promoting diversity in the workplace

Roche places a high value on diversity and seeks to benefit from it by integrating differences in perspective into the Group's activities. Roche employs people from over 190 countries. 60% of our affiliates are headed by general managers from the local country and the trend is rising. The affiliates' management teams, too, boast a consistently high proportion of staff from the local region. Talent pools worldwide feature a growing percentage of personnel from a variety of countries and continents. The 336 employees at our Corporate Center come from 23 countries.

Roche aims to be an attractive employer for both women and men and for this reason promotes diversity in its staff. 2005 was the fourth year in a row in which Roche recruited more women than men. Women account for 43% of the entire workforce. By contrast, only about 30% of the 4,556 employees who left Roche in 2005 were women. 32% of managers at Roche are female. Among our identified global key positions (mainly global senior and middle management) 19% of all incumbents are female.

Respect for the work/life balance is also a key concern at Roche. This follows different paths depending on the country, but is based on a straightforward principle: For instance, Roche supports its employees to enable them to deliver optimal performance in accordance with their family obligations. There are a variety of working arrangements at Roche: special working-time (e.g. part-time employment, flexitime, sabbaticals, parental leave for men and women), childcare facilities or other arrangements that help to reconcile the needs of

	2005	2004
Women as a percentage of the total workforce	43%	42%
Percentage of women in management positions	32%	31%
Number of women in the top 80 positions	7	5
Percentage of women among candidates for top management positions	16%	12%

career and family. All these measures comply with local legislation and in many cases go far beyond the legal requirements. Roche offers the option of part-time employment wherever the requirements of the job permit. Approximately 6 % of our current employees work on a part-time basis (over 10 % of them are men).

Respecting human rights

Roche supports and respects human rights as defined by the United Nations and applies these principles consistently. The Compliance Officer monitors this policy throughout the Roche Group, and serves as a contact person for all employees. Further information on this topic can be found at www.roche.com/en/home/sus/sus_soc_comm_hum.htm

Two violations of employment policy principles were reported to the Roche Executive Committee or the Compliance Officer in 2005. As soon as these violations became known, measures were taken to deal with them appropriately.

Our commitment to society

In brief

As a research-based company, Roche operates according to a business model that focuses on creating sustainable added value for the principal stakeholders rather than maximising short-term gains. Involvement of society as a whole is a key prerequisite for this long-term orientation and for our success as a business. We regard our specific aptitude in finding innovative and efficient solutions to unmet medical needs as our principal contribution to society. We also contribute substan-

Roche and the International Committee of the Red Cross develop partnership

Gilles Carbonnier, Head Private Sector Relations at the ICRC, Geneva, Switzerland

Roche and the International Committee of the Red Cross (ICRC) initiated a new partnership on 7 October 2005. What does this involve?
Roche is one of seven Swiss companies with which the ICRC is developing a long-term strategic partnership to tackle various social issues around the globe. Over the next six years, Roche will support the ICRC both financially and through the provision of materials (e.g. drugs) and services. Even before this agreement, though, Roche and the ICRC co-operated on various projects, such as providing assistance to the victims of the tsunami catastrophe in December 2004. On that occasion Roche sent the ICRC antibiotics and other medicines to treat 80,000 people.

In what other areas do Roche and the ICRC work together?
For instance, in exchanging ideas. The ICRC can benefit substantially from the knowledge of Roche employees in dealing with medicines. That is why, in late April 2005, the ICRC's leading pharmacists came to Basel, where they were able to see how drugs are manufactured under sterile conditions. This is important for the ICRC because we purchase drugs the world over, and because we want to be certain that what we buy is of good quality and does not include any counterfeits that may be deleterious to health.

Are Roche and the ICRC working together to combat AIDS?
This is another area where co-operation makes sense. It's not only a question of protecting the victims of wars and natural catastrophes against AIDS but also of ensuring the safety of our own people. The ICRC has some 13,000 employees working in over 60 countries, a large part of them in Africa. Roche has helped us, for instance, by putting us in touch with the main players in the fight against AIDS in West Africa.

How will this partnership develop going forward?
In the near future we will be examining ways of reinforcing our links. Some possible areas are personnel management, risk management and logistics. There's still a lot of potential in the co-operation between Roche and the ICRC.

tially by creating value for our main stakeholder groups and seeking to maintain or enhance an operating environment that is conducive to innovation.

In addition, Roche maintains and supports a number of activities that are closely bound up with our specialist skills and our particular business model. In the societal context, too, we attach importance to cooperating with reliable partners that focus on a limited number of sustainable and effective projects. Roche's position on social responsibility is currently undergoing a review process due for release in 2006.

Ensuring access to healthcare worldwide

Roche's most important contribution to society lies in the research, development and production of innovative and cost-effective solutions for unmet medical needs. Accordingly, Roche focuses on areas where the company can create genuine sustainable added value as a result of its special expertise, its role in the healthcare system and the corporate culture that it has nurtured. By developing and maintaining innovative solutions in collaboration with competent local partners, it is often possible to provide more lasting assistance designed to deal with the causes of disease and based on very simple methods. This applies especially to programmes to benefit those groups in the Least Developed Countries defined by the United Nations as being the poorest. That is where the need is greatest and where, in many cases, access even to fundamentals such as food, drinking water and the most basic medical care cannot be guaranteed. The fight against HIV/AIDS is one example of a programme in which medicines are the focal point of sustainable development. The distribution of the two HIV protease inhibitors Invirase and Viracept may be regarded as exemplary for Roche's policy. Roche offers the medicines at no-profit prices from Roche Basel to the least developed countries and to sub-Saharan Africa. The price reductions on HIV protease inhibitors from Roche apply to 93% of all people with HIV/AIDS in the world.

Strategies implemented by Roche to improve global access to healthcare include:

- Developing a clear patent and pricing policy aimed at facilitating access to HIV medication for the poorest people in the world, who make up around 69% of all people worldwide living with HIV/AIDS.
- Working in partnership with committed governments, non-governmental organisations and other parties sharing similar goals.
- Undertaking research and development to develop new anti-HIV/AIDS medicines and to improve existing ones.
- Promoting education, training and knowledge-sharing.
- Donating technical expertise in the area of industrial development of medicines and, in particular, of antimalarials in order to support the development and distribution of a new drug to combat malaria.

You can find more detailed information in the brochure 'Committed to Making a Difference' published in 2005; see also p. 30. (Further information can be found at www.roche.com/comm_diff_rep.pdf as well as www.roche.com/en/home/sustainability/sus_med.htm and www.roche-hiv.com)

In its AmpliCare programme, Roche Diagnostics supplies sub-Saharan Africa (including South Africa) as well as countries classified by the UN as 'least developed' countries with HIV-B load tests at the lowest possible prices.

The AmpliCare programme works together with all the laboratories and clinics to provide a tailored solution, determining those products that are both affordable and suited to the region in question. We are not dealing here with pharmaceutical prices but with costs that reflect a range of outlays, including tests, instruments, consumables, training and logis-

tics. The services we offer thus vary according to the customers' differing needs. Depending on individual requirements, these costs may be up to 70 percent below the standard price. Through the AmpliCare Initiative, we are cooperating with the US-based William J. Clinton Presidential Foundation.

For details, please see the brochure 'Commitment and Care across the Globe' (further information is also available at www.roche.com/pages/downloads/sustain/pdf/rochehivbro_e.pdf)

Tradition of commitment – sponsorship and donations

Owing to our areas of expertise and our corporate culture, we are mainly involved in:

- humanitarian and social projects focused on the developing world
- promoting science, medicine and the professional development of young scientists in these areas
- contemporary art and culture, as well as
- local community and environmental projects.

Since it is difficult to ascertain the sustainability of monetary or product donations and other donations in kind, Roche has decided not to publish any detailed figures on the monetary value of its activities. In 2005, 63% of all Roche donations went to humanitarian and social projects, and 28% of donated funds supported the advancement of science and education. Nearly 5% of donations went to projects in contemporary culture and the arts and about 3% to community and environmental projects. In 2005 about one-quarter of donations were made in kind and about three-quarters were in the form of financial support. Roche only makes political donations in clearly defined exceptional cases and in line with prevailing legal and ethical standards. Such donations are made only to political organisations that support conditions that favour innovation and not to individuals. Political donations account for 2% of all donations and sponsorship expenditure. In 2005 Roche began collecting data on the impact of all its monetary or product donations. We now have the first results: Over one million patients benefited directly from donations in 2005, especially of a humanitarian or social nature. Roche has agreed to donate over 5 million packs of Tamiflu to the World Health Organisation (WHO) (for details see p. 23). Last year Roche maintained contacts with more than

2,500 NGOs – impressive proof of our policy of only working with reliable partners to fulfil our commitments to society. Over 600,000 people enjoyed support from Roche in 2005 through its donations to promote science and education, community and environmental projects, and culture.

In providing disaster relief, Roche supplies know-how and, where appropriate, its own products and services to competent, locally rooted aid organisations in order to alleviate acute emergencies. The decision to undertake this kind of action lies with the local affiliate. Both at the beginning of 2005 following the tsunami disaster in Asia and after the earthquake in Pakistan in October 2005, Roche assessed the situation together with the relevant General Managers – who were in touch with local authorities and aid organisations – and organised emergency assistance in conjunction with the international relief bodies. In the countries affected by the tsunami, Roche supplied medicines for the treatment of some 80,000 people. (You can find further information on the Roche Drug Donations Policy at www.roche.com/pages/downloads/sustain/pdf/drug_don_pol.pdf.)

Not least because of the founder's family, Roche has had a long and intensive relationship with contemporary art and culture, in particular music but also – as demonstrated by the Tinguely Museum, which was donated and is maintained by Roche – the visual arts and architecture. The Roche'n'Jazz project is an example of a new kind of activity. Set up in 2005, its aim is to enable Roche companies to stage a

		Support in 2005
Roche Research Foundation www.research-foundation.org	Founded by Roche in 1971, the RRF provides support for young scientists conducting basic research in biology and medicine	Support totalling 2.17 million Swiss francs paid to 77 projects (out of 344 applications). After the Swiss National Science Foundation, the RRF is thus the country's most important institution supporting young scientists.
Roche Organ Transplantation Research Foundation www.rotrf.org	Roche is donating 50 million Swiss francs within a ten-year period to this independent research foundation. With this money, the foundation supports innovative research projects in the field of organ transplantation.	Ten projects from Europe, South America, the United States and Australia, which the foundation supported with grants totalling 2 million Swiss francs.
Roche Foundation for Anemia Research www.rofar.org	Founded by Roche in 2004 to undertake research on new approaches to the treatment of anemia.	Total of 1.5 million Swiss francs paid to seven projects in Switzerland, Germany, the UK and the USA (out of 70 applications).
Genentech Foundation for Biomedical Sciences www.gene.com/gene/about/community/gfbs	Support for educational and community-based organisations in the San Francisco Bay Area (USA)	Total of 1.2 million US dollars donated to 26 projects.

Global Roche Employee AIDS Walk

The Global Roche Employee AIDS Walk is a sponsored walk involving Roche employees all over the world. The principle is simple but effective: employees can register for the Walk and then encourage colleagues, friends and family members to sponsor them. Roche then doubles the sum collected by the employees. The money donated is used to support AIDS orphans in Malawi, Africa, where about half a million children have lost one or both parents to AIDS.

About 40 million people around the world are infected with HIV, and 25 million of these live in sub-Saharan Africa. In Malawi itself, approximately 15% of all adults are infected with HIV. Malawi is classified as one of the Least Developed Countries, but is a peaceful and politically stable country. This stability means that the projects put forward by Roche employees can be planned for the long term, as long-term planning is essential for bringing about a sustainable improvement in the orphans' situation. The donations are invested directly in the projects without being held up by bureaucracy. They are managed by a partner organisation of Roche – the European Coalition of Positive People (ECPP). Thanks to these Roche donations, this organisation has been able to build orphanages in which some 3,000 children not only receive food and clothing but can benefit from school education.

The first AIDS Walk took place in 2003 at the Roche sites in Basel (Switzerland) and Nutley and Palo Alto (USA). In the first year, 1,300 employees took part in the event. Between them they 'walked up' a total of 330,000 Swiss francs for AIDS orphans in Malawi. By 2005, already 90 sites were participating, and the number of those taking part increased tenfold: This time about 12,000 employees joined in, donating approximately 1,000,000 Swiss francs for the children in Malawi.

In April 2005, seven of the most successful Roche fundraisers travelled to Malawi to see at first hand how the donations were being put to use. On their return, they were convinced that the donations were being used to directly benefit the orphans. As one participant said: 'Our donations are helping to provide hope and a future for these children.'

series of concerts in partnership with local jazz clubs. The series is intended primarily for Roche employees and their families, but is open to any interested members of the public as well. It is also designed to promote local jazz performers and composers. (www.roche-n-jazz.net)

As of 2006, contributions by employees – augmented by Roche contributions in some cases – will be co-ordinated by the Roche Employee Action and Charity Trust (Re&Act), founded in 2005. The Trust, headquartered in Basel, will in future co-ordinate emergency measures, longer-term reconstruction programmes and the distribution of funds collected by the AIDS Walk.


Predisposition
Early detection
Prevention
Diagnosis
Therapy
Monitoring

Avastin – opening a new era in cancer therapy

Hamish Hutchinson (58) was diagnosed with advanced bowel cancer in January 2005, after first noticing abdominal discomfort around Christmas. Exploratory surgery established the extent of the cancer, and the affected part of Hamish's colon was successfully removed, together with surrounding tissue containing a secondary tumour.

Hamish started chemotherapy in February 2005 and had one session before Avastin was added to his treatment regimen. In August, after 11 cycles of chemotherapy plus Avastin, a CT scan showed that he was clear of the cancer and treatment was stopped. Hamish now feels well enough to live a normal life and has returned to work as an anesthesiologist at the hospitals in Tunbridge Wells, UK.

Being told he had advanced cancer came as a huge shock to Hamish and his family: 'My first reaction was total disbelief.' The support of his wife, Helen – who has had cancer herself – and their two daughters, Pollyanna and Victoria, played a big role in his recovery. 'Thanks to them,' says Hamish, 'I never gave up.'

Therapy

Avastin (bevacizumab) is opening a new era in cancer therapy, offering patients better outcomes and greater hope than standard chemotherapy alone for the treatment of metastatic colorectal cancer. Avastin, the first anti-angiogenic drug with demonstrated anticancer benefit, inhibits the growth of the network of blood vessels that supply nutrients and oxygen to cancerous tissues, thus shutting off the blood supply that is essential for the growth of cancers and their spread to other parts of the body.

Safety, health and environmental protection

Corporate policy in the field of safety, health and environmental protection

Roche gears its corporate policy in the field of safety, health and environmental protection (SHE) to ISO 14 000 'Environmental Management Systems'. This policy is based on its own experience going back many years and on the commitment to sustainable development it has entered into in the context of the Charter of the International Chamber of Commerce (ICC), the World Business Council for Sustainable Development (WBCSD) and the chemical industry's Responsible Care Programme. The Roche Guidelines for the Assurance of Safety, Health and Environmental Protection apply throughout the Group. Each division has an eco-delegate who supports the organisation with concrete SHE projects. (Further information can be found at www.roche.com/ en/home/sustainability/sus_env/sus_env_pol.htm).

Thanks to the professionalism and hard work of the staff involved, no Roche company was fined any significant amount for infringements of safety, health or environmental regulations. As this can evidently be accomplished without resorting to rigid management systems that consume considerable resources, there is no intention to attain ISO

SHE key figures[1]

	2005	2004
Investments in SHE (in millions of CHF)	240	160
Operating costs for SHE (in millions of CHF)	356	323
Occupational accidents	563	493
Work-related fatalities	0	0
Work-related accidents per million working hours	4.66	4.78
Workdays lost due to work-related accidents	6,629	5,051
Total number of workdays	15,083,631	12,871,583
Occupational illnesses	333	208
Occupational illnesses per million working hours	2.76	2.03
Workdays lost due to occupational illnesses	1,416	996
Occupational accidents (contractor firms)	133	129
Work-related accidents per million working hours (contractor firms)	11.6	13.9
Number of transport accidents (road)	2	1
Transport accidents per metric ton transported (road)	2.7×10^{-5}	6.0×10^{-6}
Total energy consumption (TJ/year)	12,515	11,899
CO_2 (t/year)	1,059,304	1,013,860
NO_x (t/year)	363	442
SO_2 (t/year)	151	261
VOCs (t/year)	604	1,010
Particulate matter (t/year)	50	63
Water consumption (in million cubic meters per year)	3.9	4.3
TOC (t/year)	1,830	1,344
Heavy metals (t/year)	1.463	2.231
Chemical waste (t/year)	38,380	42,722
Full-time SHE personnel	559	532
Total number of employees	68,218	64,594

1 Based on the CEFIC Health, Safety and Environment Reporting Guidelines (November 1998)

and/or EMAS certification centrally. Nevertheless, approximately nine local manufacturing companies (representing 30% of total production volume and 70% of chemical production volume) have decided at their own discretion to adopt such an approach, based on existing corporate policies.

Auditing

Safety, health and environmental protection audits ('SHE audits') are a key element in the Roche SHE management system. Corporate Safety, Health and Environmental Protection CSE has been carrying out systematic Group-wide SHE audits at company sites since 1980 – to date, nearly 800 have been completed. In the year under review, a total of 24 production facilities, distribution centres, research sites and office buildings were audited in 15 countries. Once again, the results were good.

The audits focused primarily on the safe and environmentally responsible behaviour of employees in

Energy consumption reduced by 30 percent

In Palo Alto, California, Keith Sonberg and his team are busy translating the Roche energy conservation policy into action. The result: lower energy consumption and lower costs.

Keith Sonberg's team are proud award-winners in ECOmpetition04 – a Roche competition for sustainability-related ideas. They won the award for their project that reduced energy consumption for laboratory fume hoods. The savings come to 2,500 US dollars a year for each fume hood. 'I think the competition is a laudable idea', says Sonberg. 'It clearly shows that Roche management is aware of sustainability and environmental issues'. In addition to the fume hood project, Sonberg and his team in Palo Alto have developed and implemented a comprehensive sustainability programme, ranging from energy-saving light bulbs, to Green Engineering, to employee training.

The results are impressive: In the past three years, energy consumption at the Palo Alto site has been reduced by 30 percent and water consumption by 25 percent. The recycling rate for construction waste is as high as 90 percent. As Sonberg says with some pride: 'Roche is now listed right up there on the Dow Jones Sustainability Index. Our goal is to remain environmentally friendly, economically effective and socially accountable in future too'.

Rudolf Schwob from Roche Corporate Safety, Health and Environmental Protection explains the criteria by which the projects were awarded competition prizes. 'What counted was that the projects had an impact not only on the environment but also on the budget. It was also important that projects could be implemented at other Roche sites as well'.

All Roche employees were given the chance to participate in the competition by submitting projects that improve sustainability in their working environment. The third time ECOmpetition was held – in 2004, following competitions in 1994 and 1999 – a total of 131 projects were submitted, of which 18 were selected by a jury as prize-winners.

the workplace, as well as on the technical safety of processes and plants. The risk of dust explosions in production formulation as well as hazards in the handling of biologically active compounds and potentially contaminated diagnostic instruments have become increasingly important aspects of risk assessment.

Systematic audits of strategically important suppliers manufacturing chemical intermediates, finished products or exclusive equipment parts were also performed again. 18 of these audits were completed in the past year.

Scope of reporting

This year SHE reporting covers the Roche Group with the Pharmaceuticals and Diagnostics Divisions as well as Chugai and Genentech. As the scope of the reporting is the same as for the previous year, the key figures are directly comparable even in absolute terms. Owing to the different system boundaries, this is not possible for earlier years. The bulk of the data was collected in November on the basis of ten months and then extrapolated for the entire year. For SHE costs, as well as for accidents and incidents, the full-year data for 2005 have been collected. For details on safety, health and environmental protection, please see www.roche.com/en/home/sustainability/sus_env/sus_env_care.htm.

Results in brief

The Group's SHE performance in 2005 is being published as part of the Sustainability Report for the third year in succession. For more than ten years previously, it was published in a separate SHE Report. The Group's performance can be described as good on the whole. The trend for achieving the goals set in 2003 for energy consumption and greenhouse gas and VOC emissions is pointing in the right direction. New targets are intended to spur the Roche Group on to further improve its SHE performance.

In 2005 there were no reports throughout the entire Group of significant damage that affected either individuals or the environment. The number of occupational accidents was kept at a low level. The number of occupational illnesses per million working hours increased as well as the number of working days lost as a result of occupational illnesses. In line with the growth of the company in terms of headcount and number of sites as well as production volume, energy consumption has increased in absolute figures, but efficiency has improved in relation to sales revenue or number of employees. The same is true for the volume of greenhouse gas emissions. Other emissions in air and water have declined, as has the volume of chemical waste.

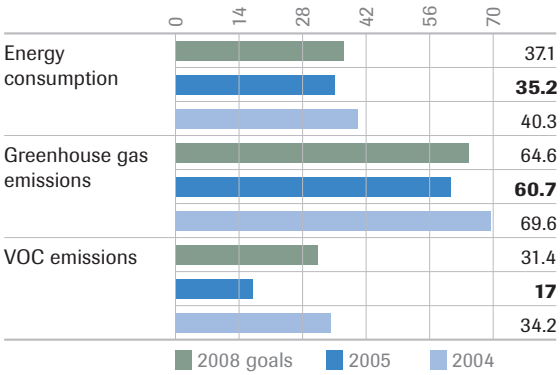
Goals and progress in safety, health and environmental protection

In 2003 Roche set itself a target of reducing the Group's greenhouse gas emissions – i.e. CO_2 from energy generation and halogenated hydrocarbons from air conditioning equipment and chillers – by 10 percent within five years.

Over the same period, energy consumption and emissions of volatile organic compounds (VOC) were to be reduced by the same percentage. Absolute values are based on Group sales in order to allow for the changes in the corporate structure and to enable comparisons to be made from the same baseline.

Owing to various measures to reduce emissions and the positive trend of Group sales revenue, the targets set for 2008 have already been reached. Roche is determined to make further efforts to confirm and improve these good results.

SH&E goals



For the purposes of the graph, values normalised to sales were given a multiplier factor (energy consumption x100, greenhouse gas emissions x2, VOC emissions x1000)

In 2004 additional SHE objectives were defined within the framework of a medium to long-term programme.

- a 20% reduction in the Roche Accident Rate (RAR) by 2010
- a 10% reduction in absences overall by 2015 (the relevant indicator will be recorded this year for the first time)
- a 10% improvement in the ecobalance by 2015 (this indicator will also be recorded this year for the first time)
- a further 10% reduction in consumption per employee by 2010 in line with the energy-saving goal
- annual target: no relevant fines in the SHE area

Eco-efficiency and expenditure for safety, health and environmental protection

Eco-efficiency

Eco-efficiency is an important element in promoting sustainable development. Eco-efficient production processes conserve resources such as raw materials and energy and reduce the impact on the environment by decreasing emissions and waste volumes. There is also a positive financial impact.

Roche quantifies eco-efficiency by calculating the Eco-Efficiency Rate (EER). The EER is an indicator of the ecological effect of expenditure in the environmental area. It is determined by means of readily measurable parameters (such as quantities of substances emitted or waste produced) as well as by financial figures such as sales and spending earmarked for environmental protection. The higher the EER, the greater the degree of eco-efficiency. For further details see www.roche.com/en/home/sustainability/sus_env/sus_env_care.htm.

Expenditure for SHE 2005[1]

	Roche Group
Investments for Safety and Health	120
for Environmental Protection	120
for SHE	240
Operating costs for SHE	356
Total expenditure for SHE	596

1 In millions of CHF

Ecobalance

To achieve the target of a 10% improvement in the Group's ecobalance, a criterion must be established that can be compared over a number of years. For

Eco-Efficiency Rate (EER) (including Chugai and Genentech as of 2004)

	2005	2004	2003	2002	2001
Sales[1]	35,511	29,561	22,428	21,438	22,757
Environmental expenditure[1]	242	192	172	144	130
Environmental damage[2]	6.02	8.40	4.38	6.37	7.38
EER	24.39	18.34	29.28	23.28	23.72

1 In millions of CHF 2 In millions of environmental damage units

Key figures for eco-efficiency (including Chugai and Genentech as of 2004 and including other sources such as CO_2 emissions from external energy generation – hence not comparable with previous years)

Key figures	Unit	2005	2004	1992	Δ% 92/05
Energy	TJ/1 million sales	0.352	0.403	0.649	-45.8
CO_2	t/1 million sales	29.83	34.35	26.755	11.4
VOC	t/1 million sales	0.017	0.034	0.207	-91.8
Water	m^3/1 million sales	109.8	145.65	1,776	-93.8
TOC	t/1 million sales	0.051	0.045	0.199	-74.2
Chemical waste	t/1 million sales	1.08	1.45	1.72	-37.2

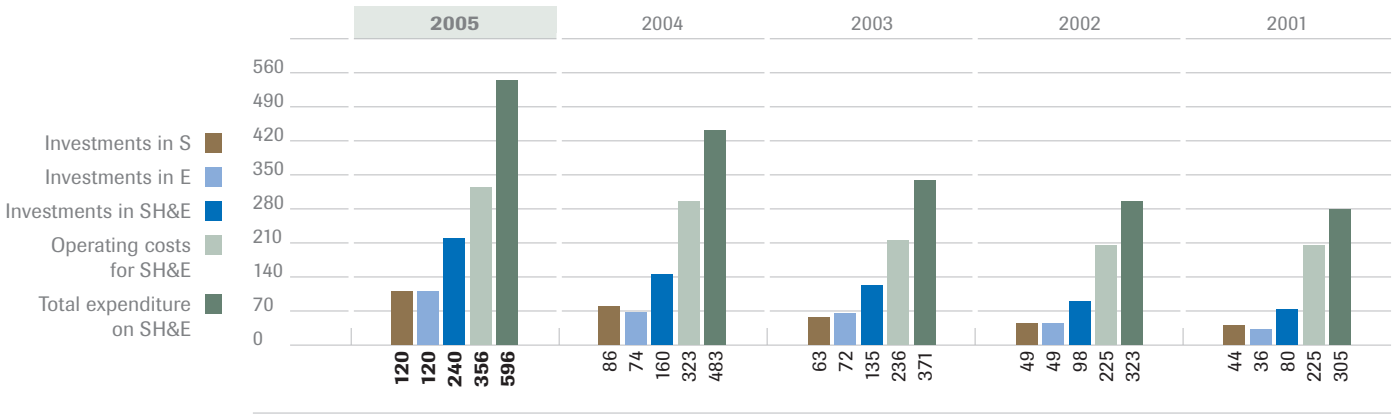
this purpose, Roche employs a method of the Swiss Agency for the Environment (BAFU) in which environmental impact points are given to ecologically relevant parameters such as emissions, waste or energy consumption. The points are added up and expressed as a function of the number of employees. For the past year the ratio was 6.58, a figure which serves as the baseline for measuring any improvements.

Investment and operating costs

SHE expenditure in the Roche Group totalled 596 million Swiss francs in 2005. This amount comprises investments that were made in various areas as well as to operating costs. The calculation of SHE investments takes account of the full value of construction projects solely for the purpose of SHE, e.g. fire extinguisher systems, wastewater treatment or waste incineration plants. A portion of the investment was calculated for SHE arising out of other projects such as new production facilities or plants. In 2005 investments amounted to 120 million Swiss francs for environmental protection and to 120 million Swiss francs for safety and health.

SHE operating costs for the year under review amounted to 356 million Swiss francs. This inclu-

SH&E expenditure (in millions of CHF)



des current spending for services and personnel costs in the area of SHE. In 2005 the total number of employees working full-time in SHE in the Roche Group was 559. SHE expenses expressed as a proportion of total sales were 1.68% in 2005 (2004 1.62%).

Safety and health protection

Roche believes it is very important that employees can work in as healthy and safe a working environment as possible. Safety and health committees that focus on technical activities (production, laboratories, workshops) have been introduced at virtually all Roche subsidiaries. They cover all employees at a given site.

We are increasingly using the workplace as a way of reaching employees not only in order to help prevent potential work-related problems, but also to enhance staff health in general. Initiatives include offering preventive medicine measures as part of health monitoring programmes, motivating staff to increase their level of physical activity and providing information on healthy nutrition. In 2005 Roche began collecting data on general absences. The aim is to discover something about the causes of such absences and to seek possible improvements.

Accident statistics 2005

	Roche Group
No. of employees in Roche Group	68,218
No. of employees recorded for statistics	65,949
No. of workdays	15,083,631
No. of lost workdays recorded	6,629
No. of occupational accidents recorded	563
Occupational accidents/1,000 employees	8.54
Accidents/million working hours (CEFIC)	4.66
RAR (Roche Accident Rate)[1]	0.099

1 See Glossary/Explanatory notes at www.roche.com/en/home/sustainability/sus_env/sus_env_care.htm

Working with highly active substances

Recent pharmaceutical research has produced medicines with even more specifically targeted biological action. They fit precisely particular receptors without influencing other targets. Because of their targeted action, they are often effective even in minuscule quantities. If this is the case, they are called highly active compounds.

Such substances, however, are potent not only in patients. In manufacturing, it is essential to ensure that employees are not overexposed to these substances, and care must be taken not to contaminate other products. Highly active substances can only be processed in contained systems.

Within Roche, the Industrial Hygiene Committee – consisting of specialists in occupational toxicity, industrial hygiene and occupational medicine – prepares assessments of the hazards posed by each substance and defines exposure limits, which serve as a tool to derive the appropriate protective measures for each workplace. Special emphasis is placed on a technical approach (i.e. contained systems).

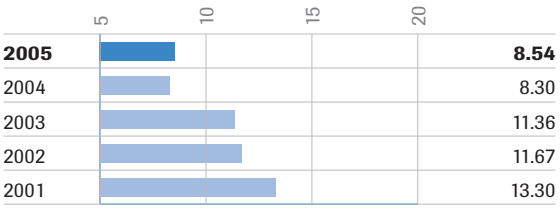
In 2005 Roche decided to build a completely new plant meeting the necessary technical standards for the manufacture of drugs containing highly active substances. It chose to erect this new plant at Toluca in Mexico.

Occupational accidents

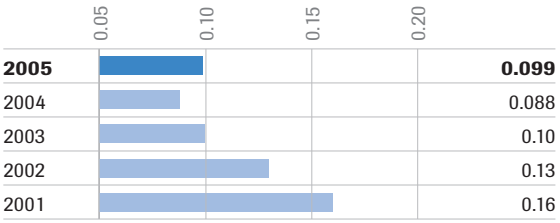
The figures for occupational accidents at Roche deteriorated slightly, though at a low level, in the year under review. The number of accidents involving Roche employees rose by 14.2% in 2005, the severity of accidents, i.e. the number of working days lost per accident as a result of accidents, increased by 12%, the Roche Accident Rate (RAR) rose by 12.5%.

In addition to Roche employees, a total of 133 employees from contractor firms were involved in accidents, i.e. 3.1% more than the previous year. The figure parallels the number of contractors, who in the past year worked mainly in the construction sector.

Accidents per 1,000 employees in the Roche Group



Roche Accident Rate (RAR)



Occupational illnesses

The total number of occupational illnesses reported increased by 60%, 42% more working days were lost as a result of illness in the year under review. The types of illnesses reported over the last few years have remained unchanged. Locomotor disorders continue to be the most common. Most of these are back problems and especially inflammation of the upper extremities caused by repetitive movements. Illnesses relating to the use of chemicals are limited to allergies; there were, however, no cases of intoxication.

Occupational illnesses 2005

	Roche Group
No. of recognised cases of occupational illnesses	333
Lost working days	1,416

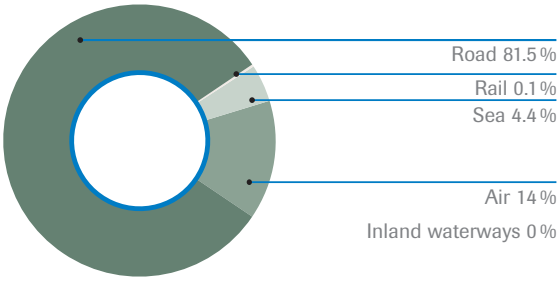
Incidents

In 2005 no incident or accident with a significant impact on people or the environment was reported anywhere in the Roche Group. Owing to the small number of minor incidents, statistical analysis of such events is virtually impossible. Nevertheless, human error has been identified as the main cause.

Transport

As in previous years, road transport accounted for the bulk of all goods moved (81.6%), followed by air transport (14%). Only two incidents were reported in 2005: A lorry loaded with pharmaceutical active substance was stolen, and the cargo of another lorry was destroyed as a result of an accident.

Various transport modes in 2005 shown as a percentage

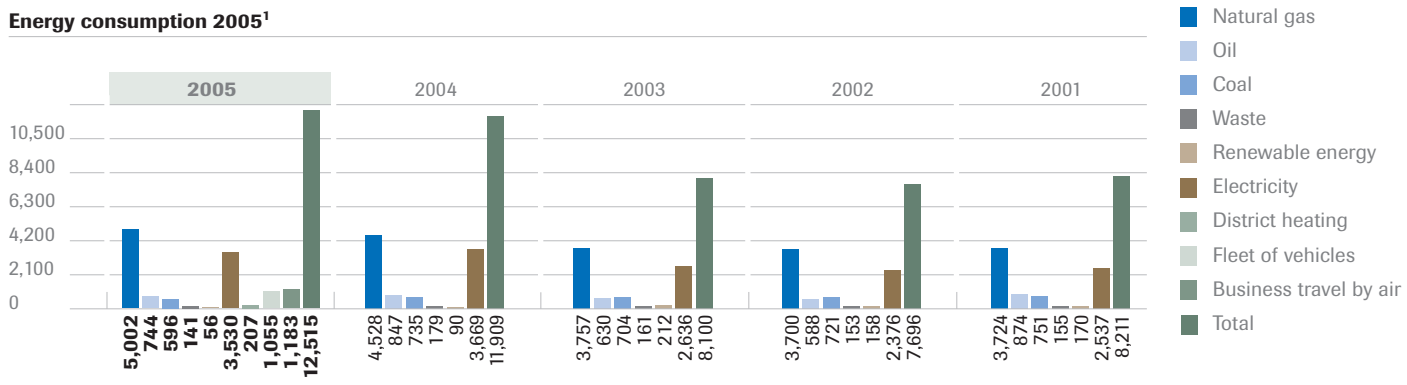


Environmental protection

Energy consumption

Sustainable development also implies responsible use of the resource energy. Roche has therefore set itself two goals for reducing energy consumption in the company: Alongside the corporate target of reducing energy consumption by 10% in relation to sales within five years (by 2008), an additional longer-term goal has been formulated: to reduce consumption by a further 10% in relation to headcount for the period 2005–2010. There is a close correlation between energy consumption and CO_2 emissions. A decrease in energy consumption will therefore lead to a reduction in the release of greenhouse gases into the atmosphere.
In the year under review, the Roche Group needed 12,515 terajoules of energy from various sources to run its operations. This figure includes the energy required to run the Group companies and the fleet of vehicles as well as the energy consumed for business travel. In absolute terms, consumption has thus risen by 5.2% year-on-year; however, use per employee has actually fallen by 0.4%.

Energy consumption 2005[1]



[1] Figures in TJ = 10^{12} Joules

Greenhouse gases

Roche supports the efforts of the international community, as laid down in the Kyoto Protocol, to adopt a worldwide approach to controlling global warming and the greenhouse gases which are responsible for it. The Group-wide target of a 10% decrease in these emissions in relation to sales by 2008 through its own measures has already been reached. Trading of emissions certificates is currently not an option for us and is unlikely to become so in the foreseeable future.
Greenhouse gas emissions are measured in accordance with the Greenhouse Gas Protocol, which serves as the GRI standard. This requires us to account for direct emissions (power generation from fossil fuels, waste incineration, fleet of vehicles, business travel, wastewater treatment) as well as those from imported energy (electricity).

Greenhouse gas emissions at Roche mostly consist of CO_2 from power generation. Direct emissions from the combustion of fossil fuels account for about half of CO_2 output. Approximately 45% of all emissions comes from the CO_2 resulting from imported energy, in particular electricity. Roche was responsible for CO_2 emissions that amounted to 1,059,304 metric tons in 2005.

Halogenated hydrocarbons play a smaller role in greenhouse gas emissions. They are used in cooling and air conditioning installations as well as in fire extinguishing equipment. In 2005 these emissions amounted to 7.2 metric tons. The global warming potential of halogenated hydrocarbons is converted into CO_2 equivalents, using the conversion factors

Specific contribution to the anthropogenic greenhouse effect, Roche Group

	2005	2004	2003	2002	2001
CO_2 emissions from combustion (t)	1,059,304	1,014,000	334,000	326,000	348,000
CO_2 equivalents from halogenated hydrocarbon emissions[1] (t)	19,141	13,567	27,497	40,289	23,281
CO_2 equivalents total	1,078,445	1,027,567	361,497	366,289	371,281
Sales (in Swiss francs millions)	35,511	29,522	28,960	26,545	25,761
CO_2 equivalents (t)/1 million francs of sales	30.37	34.80	12.48	13.80	14.41

[1] Mean global warming potential of halogenated hydrocarbons based on recalculation using conversion factor from IPCC

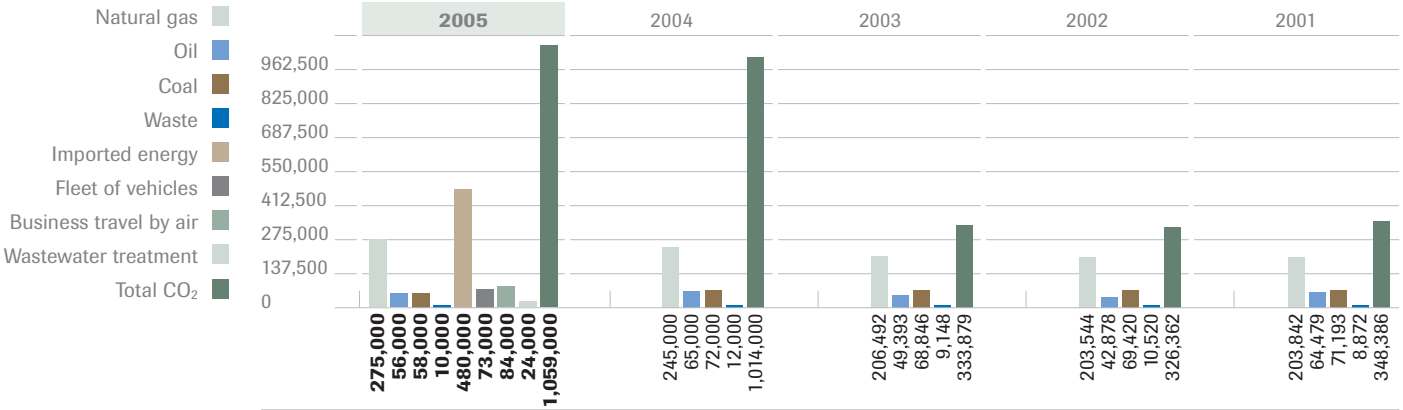
stipulated by the Intergovernmental Panel on Climate Change (IPCC), and added to the total quantity of CO_2 emissions.

The Roche climate strategy prescribes measures to lower emissions in both areas: the close link between power generation and CO_2 output means that energy saving measures will automatically lead to a reduction in CO_2 emissions. Corporate guidelines exist in relation to the use of halogenated hydrocarbons in cooling systems, outlining their gradual phasing-out from use by 2015. The 5.4% fall in the inventory of these compounds compared with the previous year illustrates the progress made in implementing these guidelines.

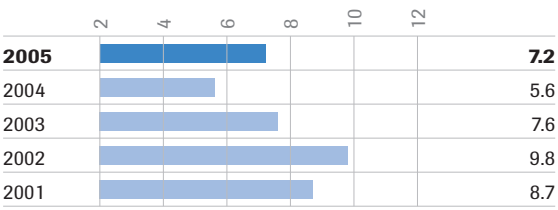
Greenhouse effect – Roche's contribution

To calculate Roche's exact contribution to the greenhouse effect – expressed in CO_2 equivalents per million francs of sales – greenhouse gas emissions and sales serve as benchmarks. In 2005 this results in a value of 30.37, representing an improvement of 12.7% over 2004.

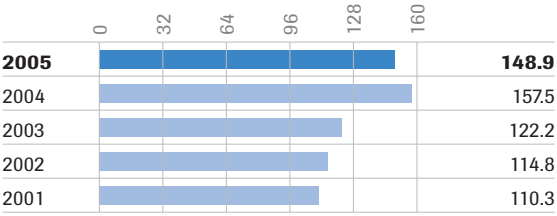
CO_2 emissions (t/year)



Halogenated hydrocarbon emissions (t)



Halogenated hydrocarbon inventory (t)



Waste

In 2005 the volume of waste from chemical production amounted to 38,380 metric tons, of which 37,116 metric tons were incinerated. The rest, including inert substances such as the incineration residues slag and ash, but also sewage sludge, was deposited in landfills. As waste or by-products, 5,674 metric tons of residual substances were recycled. The total of general waste came to 17,604 metric tons in 2005, of which 1,732 metric tons were construction waste, the majority of which was deposited in landfills. A total of 12,597 metric tons of general waste was deposited in landfills.

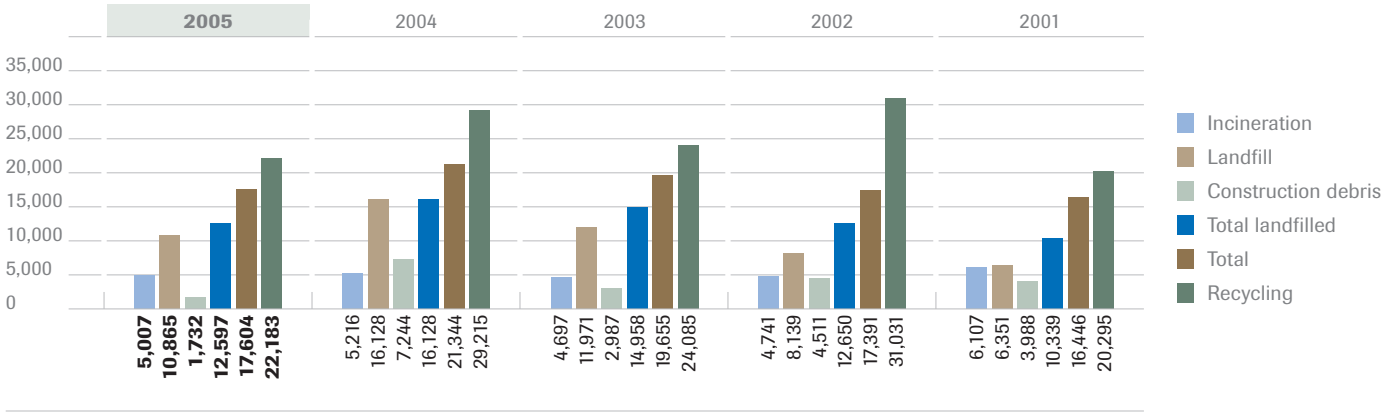
General waste in 2005 (in metric tons per year)

	Roche Group
Incineration	5,007
Landfill	12,597
of which construction waste	1,732
Total	17,604
Recycling	22,183

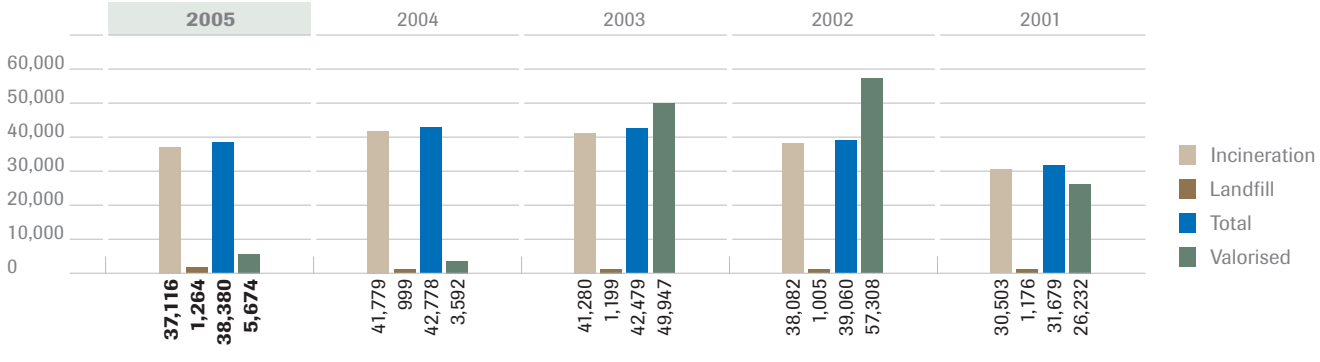
Chemical waste in 2005 (in metric tons per year)

	Roche Group
Incineration	37,116
Landfill	1,264
Total	38,380
Valorisation	5,674

General waste (figures in t/year)



Chemical waste (figures in t/year)



Contaminated sites are the responsibility of the originator

Industrial activities can leave traces in the subsoil at the sites in question. The substances used at installations where chemicals are manufactured or processed often leave residues in the soil. In addition, by its very nature the synthesis of pharmaceutical substances results not only in the desired substance, but also in by-products which ultimately have to be disposed of as chemical waste. In the past, a lack of know-how and the appropriate technical resources meant that landfill dumping was the disposal method of choice. This approach was governed by legislation, as a result of which various local authorities have made suitable plots of land available for a charge, often for joint use by a number of companies.

Improved knowledge of geological characteristics and negative experiences with leaking earth formations have led to the discontinuation of landfills for the disposal of chemical waste. Contaminated sites are subject to increased monitoring and thorough examination in order to evaluate the associated risks and initiate the steps required for containment or remediation of the site in question.

Since Roche has always been a pharmaceutical company with relatively low volumes of chemical production, our total quantities of chemical waste and share of deposits in common landfill sites are as a rule small.

As soon as a contaminated site is brought to our attention, we authorise the studies required to evaluate the associated risks. Depending on the outcome, steps for containment or, if necessary, remediation of the site are subsequently taken. This process is conducted in close collaboration with the competent authorities and in compliance with current legislation.

Where we have been solely responsible for a contaminated site or a landfill, we have promptly conducted an investigation and taken all the necessary remediation measures. Thus, for example, a number of contaminated sites, originating with companies prior to their acquisition by Roche, have been remediated. Conversely, Roche continues to assume responsibility and the costs of any necessary remediation of contaminated sites or landfills arising in connection with the Vitamins Division, which has been sold, and to bear the costs relating to such actions. Sizeable reserves have been set aside for this purpose.

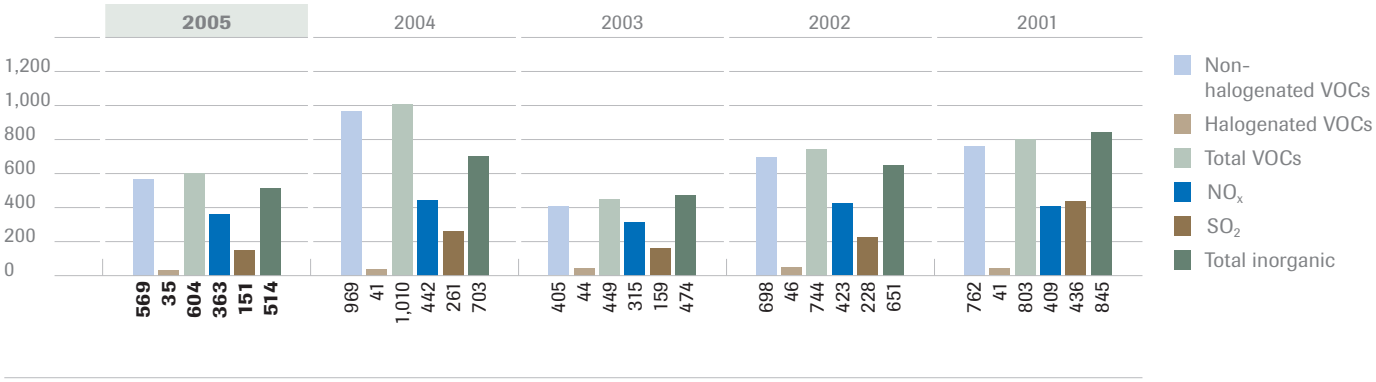
In the case of landfill sites shared with other companies, collaboration is sought with all parties concerned in order to come up with solutions that are acceptable to all.

We accept responsibility for all waste deposited by Roche at its sites or in landfills, even if the method of disposal was widespread at the time and based on the relevant legal requirements.

Air emissions

In 2005 Roche was responsible for 514 metric tons of inorganic emissions in the form of sulphur dioxide (SO_2) and nitrogen oxides (NO_x). These substances were the result of incineration processes in energy generation. Air emissions of soot particulates and dust came to 50 metric tons. Emissions of volatile organic compounds (VOCs) came to 604 metric tons, of which 6% contain halogens.

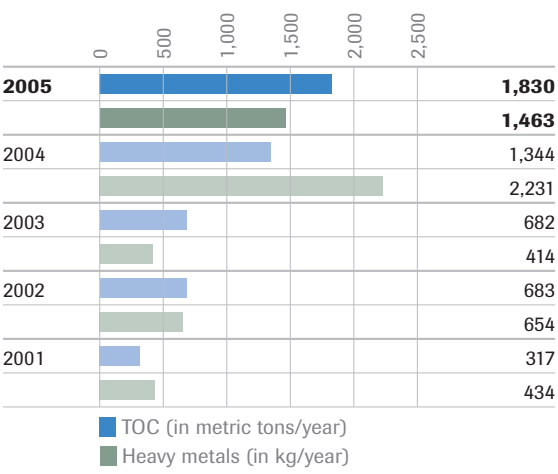
Atmospheric emissions in 2005 (in metric tons per year)



Wastewater

The organic carbon load is measured as total organic carbon (TOC) after wastewater treatment. A total of 1,830 metric tons was discharged in 2004. In addition, heavy metal discharges in wastewater amounted to 1,463 metric tons.

Emissions into water 2005



Water consumption

Reporting on water consumption at Roche is based on the GRI Water Protocol. In 2004, 3.9 million metric tons of water were consumed, i. e. went into a product or were vaporised in cooling or air conditioning systems. 7.1 million metric tons of wastewater from chemical production were purified in wastewater treatment plants; 9.8 million metric tons represented water from cooling systems that could be returned to receiving waters after thorough analysis without further purification.

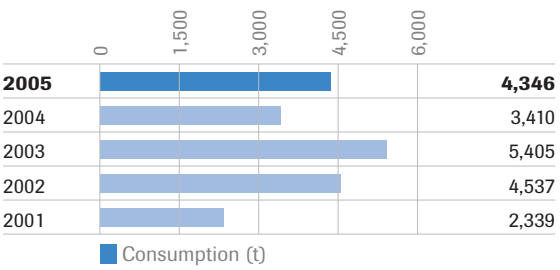
Water consumption (in million cubic metres per year)

	Roche Group
Withdrawal from various sources	20.8
Purified in treatment plants	7.1
Returned to receiving waters	9.8
Used	3.9

Special chemicals

In the year under review, a total of 4,346 metric tons of halogenated solvents were used by Roche production facilities and laboratories. Methylene chloride accounted for the greater part of this total, at around 98 %. Production of the active substance used in the AIDS drug Fuzeon accounted for more than half the total used. The higher consumption reported in 2005 reflects the increase in production volume. Chloroform is used in small quantities only in laboratories.

Halogenated solvents (in metric tons per year)



In compliance with a Group Directive, all Roche affiliates supply figures regarding quantities and use of substances that, as precursor substances for chemical weapons, drugs or narcotics, are subject to international regulation. The quantities reported have remained at a consistently low level for a number of years. These compounds were used for the manufacture of Roche products. No such substances were sold to third parties.

'I've got my independence back.'

Predisposition | Early detecion | Prevention | Diagnosis | Therapy | **Monitoring**




Self-monitoring lets patients get on with their lives

At age 19 Alexander Bäcker very nearly died. During a school trip the young German collapsed and had to be rushed to hospital, where doctors discovered that he had meningitis and a cerebral hemorrhage. Alexander survived, but his speech was severely impaired. And the episode also left him requiring life-long treatment with blood-thinning anticoagulants, which meant that he had to report regularly to a doctor to have his therapy monitored.

Alexander quickly overcame his speech impairment. He trained as a social care provider and now works predominantly with people with disabilities. Two years ago he regained even more of his old independence thanks to a device that's scarcely bigger than a cell phone. With his CoaguChek S, Alexander is now able to monitor his anticoagulant therapy himself, eliminating the need for weekly trips to the doctor.

Last year Alexander, who is now 28, went on a nine-month, round-the-world trip that took him to the United States, Australia, New Zealand and Japan. Travelling with him were his girlfriend and the companion that made the trip possible in the first place, his CoaguChek.

Monitoring

Patients on anticoagulants have to monitor their coagulation status closely so that they can keep the dose at the right level. There was a time when this required a trip to the hospital or a doctor's office. Now devices like CoaguChek S are giving patients their independence back by enabling them to monitor their treatment themselves.

Assurance

Independent Assurance Report on the Roche Group Sustainability Reporting 2005

To the Roche Corporate Sustainability Committee

We have been engaged to provide assurance on the Sustainability Reporting of Roche and its consolidated subsidiaries excluding Chugai and Genentech (the 'Group'), all for the year ended December 31, 2005. We have performed evidence-gathering procedures on (hereafter jointly referred as the 'subject matter'):

- The SHE key figures of the table entitled 'most important SHE key figures' on page 86;
- Some selected social dimension information ('social data'); and
- The management and reporting for the preparation of the report and figures.

We have evaluated the subject matter against the following criteria (the 'evaluation criteria') described on page 58:

- The Roche Group internal sustainability reporting guidelines with respect to the Responsible Care Health, Safety and Environmental reporting guidelines published by the European Chemical Industry Council CEFIC and the 'Sustainability Reporting Guidelines 2002' published by the Global Reporting Initiative (GRI);
- The procedures by which the SHE data and the social data are prepared, collated and aggregated internally; and
- The control environment over the accuracy and completeness of the SHE data and the social data.

Our statement should be read in conjunction with the inherent limitations of accuracy and completeness for sustainability data, as well as in connection with the Roche Group internal reporting guidelines explained on page 88 and the 'scope of reporting' on page 88.

Roche Group is responsible for both, the subject matter and the evaluation criteria.

Our responsibility is to report on the internal reporting processes, data, and key figures for Social Dimension and SHE based on our evidence-gathering procedures in accordance with International Framework Standards for Assurance Engagements, approved December 2003 by the International Auditing and Assurance Standards Board (IAASB).

We planned and performed our evidence-gathering procedures to obtain a basis for our conclusions in accordance to the International Standard on Assurance Engagements (ISAE) 3000 'Assurance Engagements other than Audits or Reviews of Historical Information', approved December 2003 by the IAASB.

The scope of our evidence-gathering procedures was to:

- Assess how Roche staff apply the Group internal sustainability reporting guidelines at the site level using a sample of five production sites covering the Pharmaceutical and Diagnostics divisions;
- Test the effectiveness of the internal sustainability reporting system used to collect SHE data and the social data from Group sites;
- Observe compliance with the Group internal sustainability reporting guidelines at selected sites; and
- Perform specific procedures to check, on a sample basis, the SHE data and the social data.

Our evidence-gathering procedures included the following work:

- Visiting selected sites in Austria, South Africa, Turkey and the US
- Interviewing the responsible staff for data collection and sustainability reporting on the sites we visited and on Group level;
- Assessing the data consolidation process on Group level;
- Reading and performing tests of the relevant documentation on a sample basis, including Group policies, management and reporting structures, documentation and systems used to collect, analyze and aggregate reported SHE data and social data; and
- Performing tests on a sample basis on evidence supporting selected SHE data and social data with regard to the reported data aggregation from the selected sites to Group level. However, we have not performed site visits at Chugai and Genentech.

In our opinion
- the Roche Group internal sustainability reporting guidelines are applied properly at the selected sites;
- the internal SHE reporting system to collect the SHE data is functioning as designed; and
- the social dimension reporting provides an appropriate basis for the disclosure of social dimension information, in all material respects, based on the evaluation criteria.

Based on our work described in this report, nothing has come to our attention that causes us not to believe that the procedures by which the SHE data and social dimension information was prepared, collated and aggregated and the control environment at the selected sites are based on established and accepted measurement and analytical methods and give a fair picture of the SHE and social dimension performance, in all material respects, based on the evaluation criteria.

PricewaterhouseCoopers AG

Dr Thomas Scheiwiller
Zurich, 16 January, 2006

Jürg Hutter

Track record 2005/Outlook 2006

Objectives	Goals	Targets 2006 & onwards	Achievements 2005
General			
Remain top tier regarding transparency on sustainability related activities	• Increase internal and external awareness, and improve position in external investigations	• Remain in top quartile of indexes & ratings within healthcare sector • Revised website based on stakeholder feedback • Expansion of communication activities sustainability both internally and externally	• Renewed inclusion in FTSE4Good and DJSI • New website to be launched in the first quarter of 2006 • Sustainability topics integrated into overall communication strategy • Sustainability included as topic at key internal corporate events
Establish the Roche Business Case for Sustainability	• Identification of drivers of business case, and monitoring and measuring against appropriate KPIs	• Establish and implement process • Document the business case • Define a set of relevant key performance indicators (KPIs)	• Workshop held with members from all corporate and divisional functions to identify key areas • Integrated Operations section of Annual Report with Sustainability Report to form single Business Review 2005
Ethics, Governance and Responsible Management			
Strengthen business ethics awareness	• Increase awareness and adherence to Roche's Corporate Principles and Roche's directives, guidelines, and regulations (which together form Roche's Code of Conduct)	• High participation rate in new e-learning tool on Roche's Code of Conduct • No incidents	• Publication on Roche Intranet and Internet sites of the Roche Corporate Principles together with Roche's directives, guidelines, policies and regulations which form Roche's Code of Conduct • Development new e-learning tool
Ensure highest standards in relation to Human Subject Research and create more transparency with regards to clinical trials	• Independent external body to review escalated ethical issues: Clinical Research Ethical Advisory Group (CREAG) • Recognised as having leading Clinical Trial Protocol Registry and Results Database	• Discussion of controversial political and ethical topics • Inclusion of all data from phase II-IV trials on products marketed since 1 October 2002	• Establishment of a Clinical Research Ethical Advisory Group (CREAG) • Established Clinical Trial Protocol Registry and Results Database (259 trials registered)
Continue implementation new Supply Chain policy	• All future and retrospective contracts aligned with the supply chain policy	• 100% of all contracts incorporate new policy	• 100% all new contracts have incorporate Roche supplier policy
Coordinate Social, Environmental & Ethical (SEE) risk identification and management	• Alignment of the SEE Risk assessment with the Group Risk Report process • Rigorous SHE management system with focus on risk assessment, risk reduction measures and audits	• Establishment of clear procedure for assessing SEE risks	• Responsibilities for assessment of SEE risks defined & allocated

Objectives	Goals	Targets 2006 & onwards	Achievements 2005
Ensure appropriate and responsible use of animal resources	• Global coordinator system introduced/implemented in all sites • AAALAC accreditation of all Roche Research Sites conducting animals tests	• Continuation of audits • Documentation and adjustment of processes • Proof of accreditation on Sustainability website	• Revised animal welfare paper • Global coordinator for animal welfare identified at all sites
Contribution to Society			
Develop new health solutions for unsolved health problems with high medical need	• Produce medically differentiated products which are either first in class or best in class	• Number of new innovative products launched	Key innovative launches • Avastin • Herceptin • Tarceva • Bonviva/Boniva • AmpliChip CYP450
Improve access to healthcare in developed and least developed countries	• Recognised in top quartile of companies ensuring access to healthcare • Improve transparency of Roche activities in this area	• Monitor pricing • Improved website & documents/brochures • Rating • Activities	• Clinical trial policies in Least Developed Countries and Sub-Saharan Africa • Further reduction in pricing • Tiered pricing for Tamiflu
Corporate policy/position on Corporate Responsibility (CSR)/ philanthropy	• Formal CSR policy	• Internally and externally established CSR policy • Continuously updated reports on CSR activities on Sustainability website • Updating of internal action plan • Regular and transparent reporting	Review process initiated
Stakeholder Dialogue			
Improve systematic stakeholder dialogue	• Identification of key stakeholders with established communication channels • Provide consistent and timely communication with all stakeholders	• Good results in external ratings • Establishment of an agenda and defining of responsibilities • Continuous reporting on dialogue on website	• Published list of memberships and key partners on the web • Stakeholder survey performed • Conditions created for collecting data on NGO contacts
Valuing Employees			
Keep and improve our position as employer of choice within the healthcare industry	• Recognised as a top tier employer in the industry • Maintain high level of relationship within the company as part of the Corporate Culture	• Good results in peer review and relevant awards • Low rate of regretted losses	Numerous awards such as Science, Fortune

Objectives	Goals	Targets 2006 & onwards	Achievements 2005
Safety, Health and Environmental Protection			
• Reduce accident rate	• 0.099 to 0.079 • 20% reduction in 2010 vs. 2005	Roche Accident Rate (RAR)	RAR 2005: 0.099
• Reduce absence rate (incl. illness and home accidents)	• 68.9 to 55.12 • 10% reduction in 2015 vs. 2005	h/employee	68.9
• Reduce energy consumption	• 184 to 166 • 10% reduction in 2010 vs. 2005	GJ/employee	184
• Improve total ecobalance	• 6.58 to 5.93 • 10% improvement in 2015 vs. 2005	Points/employee	6.58
• No relevant SHE fines	0	No fines of more than CHF 100,000	No relevant fines
• Reduce GHG emissions	• 35.9 to 32.3 • 10% reduction in 2008 vs. 2003	CO_2 equivalents/sales	29.38
• Reduce VOC emissions	• 0.035 to 0.032 • 10% reduction in 2008 vs. 2003	Tonnes of VOC/sales	0.017
Develop strategy or position on key topics related to SHE matters	• Have public position on key topics of public interest		Position on contaminated sites, other issues

The key performance indicators

Economic and business performance	2005	2004
Sales (continuing operations) (in CHF millions)	35,511	29,522
EBITDA (continuing operations) (in CHF millions)	11,404	9,047
Operating profit (before exceptional items) (in CHF millions)	9,025	6,766
Net income (in CHF millions)	6,730	7,063
Core earnings per share diluted (CHF)	7.68	5.72
Research and development (in CHF millions)	5,705	5,154
Research and development as % of sales	16.1	17.4
Contacts with stakeholders		
Dividends distributed (in CHF millions)	2,156	1,725
Taxes paid (in CHF millions)	2,224	1,865
Personnel costs (in CHF millions)	9,049	8,354
Patients participating in clinical trials	130,000	(not available)
Patients benefiting from donations	over 1,000,000	(not available)
Commitment to employees		
Newly created positions	3,624	2,387
Number of employees	68,218	64,594
of whom women (as a %)	43	42
Percentage of women in management positions (as a %)	32	31
Fluctuation (as a %)	6.7	6.1
Number of training hours per employee	26.7	23
Percentage of country affiliates with local general manager (as a %)	60	56
Safety, health and environmental protection		
Investments in SHE (in millions of Swiss francs)	240	160
Operating costs for SHE (in millions of francs)	356	323
Work-related accidents per million working hours	4.66	4.78
Workdays lost due to work-related accidents	6,629	5,051
Occupational illnesses per million working hours	2.76	2.03
Workdays lost due to occupational illnesses	1,416	996
Work-related accidents per million working hours (contractor firms)	133	129
Total energy consumption (TJ/year)	12,515	11,899
CO_2 (t/year)	1,059,304	1,013,860
NO_x (t/year)	363	442
SO_2 (t/year)	151	261
VOCs (t/year)	604	1,010
Particulate matter (t/year)	50	63
Water consumption (in million cubic meters per year)	3.9	4.3
TOC (t/year)	1,830	1,344
Heavy metals (t/year)	1.463	2.231
Chemical waste (t/year)	38,380	42,722

GRI reference list

Vision and Strategy	1	2	3	4	5	6	7	Page in report/remarks
1.1 Statement of the organisation's vision and strategy regarding its contribution to sustainable development.	■							Pages 48
1.2 Statement from the CEO.	■							Page 4
Profile								
Organisational Profile								
2.1 Name of reporting organisation.	■					■		Page 3
2.2 Major products and/or services.	■					■		Pages 24, 25, 38, 40
2.3 Operational structure of the organisation.	■					■		Page 58
2.4 Description of major divisions, operating companies, subsidiaries and joint ventures						■		
2.5 Countries in which the organisation's operations are located.	■					■		Page 115
2.6 Nature of ownership; legal form.						■		
2.7 Nature of markets served.	■					■		Pages 26, 33
2.8 Scale of the reporting organisation:								
• number of employees;	■					■		Page 72
• products produced/services offered (quantity or volume);						■		
• net sales;	■					■		Page 2
• total capitalisation broken down in terms of debt and equity.						■		
In addition to the above, reporting organisations are encouraged to provide additional information, such as:								
• value added;						■		
• total assets; and						■		
• breakdowns of any or all of the following:								
• sales/revenues by countries/regions that make up 5 percent or more of total revenues;						■		According to region, no further detail
• major products and/or identified services;	■							Only products with highest sales, Pages 24, 25, 34, 35, 40
• costs by country/region; and						■		
• employees by country/region.	■					■		Page 72
2.9 List of stakeholders, key attributes of each, and relationship to the reporting organisation.					■			
Report Scope								
2.10 Contact person(s) for the report, including e-mail and web addresses.	■							Page 114
2.11 Reporting period (e.g., fiscal/calendar year) for information provided.						■		
2.12 Date of most recent previous report (if any).	■							Page 88
2.13 Boundaries of report and any specific limitations on the scope.	■							Page 88
2.14 Significant changes in size, structure, ownership, or products/services that have occurred since the previous report.	■					■		Page 88
2.15 Basis for reporting on joint ventures, partially owned subsidiaries, leased facilities, outsourced operations, and other situations that can significantly affect comparability from period to period and/or between reporting organisations.						■		Based on CEFIC; all required parameters are shown
2.16 Explanation of the nature and effect of any re-statements of information provided in earlier reports, and the reasons for such restatement.	■							Page 88
Report Profile								
2.17 Decisions not to apply GRI principles or protocols in the preparation of the report.			■					
2.18 Criteria/definitions used in any accounting for economic, environmental, and social costs and benefits.			■					
2.19 Significant changes from previous years in the measurement methods applied to key economic, environmental, and social information.	■		■					Page 88
2.20 Policies and internal practices to enhance and provide assurance about the accuracy, completeness, and reliability that can be placed on the Sustainability Report.	■							Page 58
2.21 Policy and current practice with regard to providing independent assurance for the full report.	■							Page 102
2.22 Means by which report users can obtain additional information and reports about economic, environmental, and social aspects of the organisation's activities, including facility-specific information (if available).	■							Page 117

Governance structures and management systems	1	2	3	4	5	6	7	Page in report/remarks
Structure and Governance								
3.1 Governance structure of the organisation.	■					■		Pages 48–57
3.2 Percentage of the board of directors that are independent, non-executive directors.	■					■		Page 44
3.3 Process for determining the expertise board members need to guide the strategic direction of the organisation, including issues related to environmental and social risks and opportunities.	■					■		Page 48
3.4 Board-level processes for overseeing the organisation's identification and management of economic, environmental, and social risks and opportunities.	■							Pages 48, 59
3.5 Linkage between executive compensation and achievement of the organisation's financial and non-financial goals (e.g., environmental performance, labour practices).	■					■		Page 49
3.6 Organisational structure and key individuals responsible for oversight, implementation, and audit of economic, environmental, social, and related policies.	■					■		Page 57
3.7 Mission and values statements, internally developed codes of conduct or principles, and polices relevant to economic, environmental, and social performance and the status of implementation.	■							Pages 58–60
3.8 Mechanisms for shareholders to provide recommendations or direction to the board of directors.	■					■		Page 55
Stakeholder Engagement								
3.9 Basis for identification and selection of major stakeholders.	■							Page 66
3.10 Approaches to stakeholder consultation reported in terms of frequency of consultations by type and by stakeholder group.		■						
3.11 Type of information generated by stakeholder consultations.		■						
3.12 Use of information resulting from stakeholder engagements.	■							Page 66
Overarching Policies and Management Systems								
3.13 Explanation of whether and how the precautionary approach or principle is addressed by the organisation.		■						
3.14 Externally developed, voluntary economic, environmental, and social charters, sets of principles, or other initiatives to which the organisation subscribes or which it endorses.	■							Pages 63, 67, 68, 86
3.15 Principal memberships in industry and business associations, and/or national/international advocacy organisations.	■							Page 67
3.16 Policies and/or systems for managing upstream and downstream impacts, including:								
• supply chain management as it pertains to outsourcing and supplier environmental and social performance; and	■							Page 68
• product and service stewardship initiatives.	■							Page 53
3.17 Reporting organisation's approach to managing indirect economic, environmental, and social impacts resulting from its activities.	■							Page 58
3.18 Major decisions during the reporting period regarding the location of, or changes in, operations.						■		
3.19 Programmes and procedures pertaining to economic, environmental, and social performance. Include discussion of:								
• priority and target setting;	■							Page 104
• major programmes to improve performance;	■							Page 104
• internal communication and training;	■							Page 104
• performance monitoring;	■							Page 104
• internal and external auditing; and	■							Pages 87, 102
• senior management review.	■							Page 58
3.20 Status of certification pertaining to economic, environmental, and social management systems.	■							Page 102

GRI Content Index								
4.1 A table identifying location of each element of the GRI Report Content, by section and indicator.	■							Page 108

Economic performance indicators	1	2	3	4	5	6	7	Page in report/remarks
Customers								
EC1: Net sales	■					■		Page 2
EC2: Geographic breakdown of markets	■					■		Pages 19, 33
Suppliers								
EC3: Cost of all goods, materials, and services purchased						■		
EC4: Percentage of contracts that were paid in accordance with agreed terms.					■			In principal each contract is carried out according to the agreed terms.
Employees								
EC5: Total payroll and benefits	■					■		Page 72
Capital providers								
EC6: Distributions to providers of capital						■		
EC7: Increase/decrease in retained earnings at end of period						■		
Public sector								
EC8: Total sum of taxes of all types broken down by country	■					■		Page 67. Total income taxes are shown (not broken down by country)
EC9: Subsidies received					■			
EC10: Donations				■				Roche does not currently issue any global figures as they have only limited significance.

Environmental performance indicators								
Material								
EN1: Total materials used other than water, by type				■				The production of individual pharmaceutical substances takes place using completely different syntheses in many different places and at different times. This figure does not have any continuity and as such does not value in the estimation of environmental performance..
EN2: Percentage of materials used that are wastes				■				See remarks for EN1.
Energy								
EN3: Direct energy use	■							Page 93
EN4: Indirect energy use	■							Page 93
EN17: Initiatives to increase energy efficiency	■							Pages 87, 89, 94
EN19: Other indirect energy use	■							Page 93
Water								
EN5: Total water use	■							Page 98
Biodiversity								
EN6: Biodiversity-rich habitats			■					Not relevant to Roche business
EN7: Impacts on biodiversity				■				Eco-toxicological material data for intermediate and end products are being prepared but are not published in this report.
Emissions, Effluents, and Waste								
EN8: Greenhouse gas emissions	■							Pages 93, 94
EN9: Use and emissions of ozone-depleting substances	■							Page 97
EN10: NO_x, SO_2 and other significant air emissions by typen	■							Page 97
EN11: Total amount of waste	■							Page 95
EN12: Significant discharges to water by type	■							Page 97
EN13: Significant spills of chemicals, oils, and fuels	■							Page 98
Products and services								
EN14: Significant environmental impacts				■				Environmental risk assessments of principal products and services were prepared for all active substances but are not published in this report.
EN15: Recyclable products	■							Page 95. Valorised by-products, recycled solvents.
Compliance								
EN16: Fines for non-compliance	■							Page 86
EN35: Total environmental expenditures by type	■							Page 89

Social performance indicators								
Employment								
LA1: Workforce	■							Page 72
LA2. Net employment creation and average turnover	■							Pages 72, 73
Labour/Management relations								
LA3: Percentage of employees represented	■							Page 66
LA4: Policy and procedures involving information, consultation, and negotiation with employees over changes	■							Page 66

Health and safety	1	2	3	4	5	6	7	Page in report/remarks
LA5: Occupational accidents and diseases	■							Page 92
LA6: Health and safety committees	■							Page 91
LA7: Key figures on injury, lost day, and absentee rates and work-related fatalities	■							Pages 86, 91, 92
LA8: Description of policies or programmes on HIV/AIDS				■				See www.roche.com/home/sustainability/sus_soc/sus_soc_comm.htm
Training and further education								
LA9: Average hours of training per year per employee	■							Page 74
Diversity and opportunity								
LA10: Equal opportunity policies and programmes	■							Page 76
LA11: Composition of senior management and corporate governance bodies (including the Board of Directors)	■					■		Pages 18, 32, 47
LA12: Employee benefits		■		■		■		Locally arranged according to performance of each local business.
Human rights								
Strategy and management								
HR1: Prevention of discrimination in business activities and procedures to deal with human rights	■						■	Page 77
HR2: Human rights and investment and procurement decisions	■						■	Page 77
HR3: Human rights and the supply chain	■						■	Pages 68, 77
Non-discrimination								
HR4: Prevention of discrimination in business activities	■						■	Page 77
Freedom of Association and Collective Bargaining								
HR5: Principles of freedom of association policy	■						■	Page 66
Child labour								
HR6: Principles regarding exclusion of child labour	■						■	Page 77
Forced and compulsory labour								
HR7: Guidelines to prevention of forced and compulsory labour	■						■	Page 77
Social								
Guidelines on communities/companies								
SO1: Description of policies to manage impacts on communities areas affected by activities, as well as description of procedures/programmes to address this issue, including monitoring systems and results of monitoring.					■			No general guidelines. Defined locally. 40% of local companies have their own guidelines.
SO4: Awards received relevant to social, ethical, and environmental performance				■				
Bribery and corruption								
SO2: Guidelines to addressing bribery and corruption	■							Page 61
Political support								
SO3: Guidelines to managing political lobbying and contribution						■		No general guidelines. Directed by local arrangements.
Competition and pricing								
SO6: Court decisions pertaining to anti-trust and monopoly regulations						■		
SO7: Guidelines to prevention of anti-competitive behaviour	■							Page 61
Product responsibility								
Consumer health and safety								
PR1: Guidelines to preservation of customer health and safety	■							Page 63 These principles are covered in the pharmaceutical industry to a great extent by national and international laws and guidelines.
Products and services								
PR2: Guidelines to product information and labelling	■							Page 63 These principles are covered in the pharmaceutical industry to a great extent by national and international laws and guidelines.
Respect for privacy								
PR3: Guidelines to consumer privacy	■							Page 63 These principles are covered in the pharmaceutical industry to a great extent by national and international laws and guidelines.

1 Indicator and detailed data in report
2 Indicator is covered in report but detailed data is not fully available
3 Indicator does not apply to Roche
4 Data submitted but not published in this report
5 Data not available
6 To be found in the Finance Report
7 No material violations

Sales

Manufacturing

Overview

Switzerland	■	■	■	■	Czech Republic	■	
Argentina	■				Denmark	■	
Australia	■	■			Dominican Republic	■	
Austria	■	■			Ecuador	■	
Bangladesh	■	■			El Salvador	■	
Belgium	■				Estonia	■	
Bermuda	■			■	Finland	■	
Brazil	■	■			France	■	■
Canada	■				Germany	■	■	■	■	
Chile	■				Great Britain	■	
China	■	■		■	Greece	■	
Colombia	■				Guatemala	■	
Costa Rica	■			■	Guernsey				■	

Roche – a Global Market Presence

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Research and development

Services, financing

Toll manufacturing by third parties

Honduras	
Hungary	
India	
Indonesia	
Ireland	
Italy	
Japan	
Latvia	
Lithuania	
Luxembourg	
Malaysia	
Mexico	
Morocco	
The Netherlands	
New Zealand	
Nicaragua	
Norway	
Pakistan	
Panama	
Peru	
Philippines	
Poland	
Portugal	
Romania	
Russia	
Serbia and Montenegro	
Singapore	
Slovenia	
South Africa	
South Korea	
Spain	
Sweden	
Taiwan	
Thailand	
Turkey	
Uruguay	
USA	
Venezuela	

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This Annual Report contains certain forward-looking statements. These forward-looking statements may be identified by words such as 'believes', 'expects', 'anticipates', 'projects', 'intends', 'should', 'seeks', 'estimates', 'future' or similar expressions or by discussion of, among other things, strategy, goals, plans or intentions. Various factors may cause actual results to differ materially in the future from those reflected in forward-looking statements contained in this Annual Report, among others: (1) pricing and product initiatives of competitors; (2) legislative and regulatory developments and economic conditions; (3) delay or inability in obtaining regulatory approvals or bringing products to market; (4) fluctuations in currency exchange rates and general financial market conditions; (5) uncertainties in the discovery, development or marketing of new products or new uses of existing products, including without limitation negative results of clinical trials or research projects, unexpected side-effects of pipeline or marketed products; (6) increased government pricing pressures; (7) interruptions in production; (8) loss of or inability to obtain adequate protection for intellectual property rights; (9) litigation; (10) loss of key executives or other employees; and (11) adverse publicity and news coverage.

The statement regarding earnings per share growth is not a profit forecast and should not be interpreted to mean that Roche's earnings or earnings per share for 2006 or any subsequent period will necessarily match or exceed the historical published earnings or earnings per share of Roche.

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