Testimony of

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Senator Hatch. Honorable Members of the Senate Judiciary Committee. I am Carole Ben-Maimon, M.D., President and Chief Operating Officer of Barr Research, Inc., the proprietary products research and development division of Barr Pharmaceuticals, Inc., a leading U.S. specialty pharmaceutical company that markets more than 100 generic and proprietary products. I am a physician, board certified in Internal Medicine, and a mother of three. Prior to working at Barr, I was responsible for both generic and proprietary research and development with Teva Pharmaceuticals. I also spent two and one-half years as Chairman of the Generic Pharmaceutical Association.

My experience as a physician, and in both generic and proprietary drug development, has provided me a unique perspective on the pharmaceutical industry, a perspective that truly appreciates the value and contributions made by the passage of the Hatch/Waxman Act and a perspective that makes me an advocate for a legislative process that will permit the timely and efficient introduction of more affordable generic versions of biotechnology pharmaceutical products.

The issue before this committee today is not unlike that of 20 years ago, when Congress was crafting a legislative pathway for the efficient and timely approval of more affordable generic pharmaceutical products. Indeed, many of the arguments made in opposition to Hatch/Waxman 20 years ago are being, and will continue to be, made during this debate regarding generic biotech pharmaceuticals, namely: that "generic companies" lack the scientific sophistication to operate in this complex arena; that it is impossible to adequately characterize the innovator products; and that the safety and efficacy of generic biotech products can not be assured without full-blown clinical trials.

Fortunately for consumers and taxpayers, Senator Hatch and his colleagues had the wisdom and foresight to reject these arguments and approve the Hatch/Waxman Act. As a result, America's generic pharmaceutical industry has been saving consumers tens of billions of dollars on pharmaceutical products each year. It is time for Congress to put these same principles to work in the area of biopharmaceutical products.

To say that generic biotech products cannot be made flies in the face of the facts. The truth is, it is already being done in other parts of the world. Biogenerics are being developed, produced, and sold in countries such as Poland, China, and Lithuania. Given the long lead times for generic biopharmaceutical development, the United States is at substantial risk of losing our preeminence in this global field. The loss of a leadership position threatens that other countries will be dictating the standards for regulatory approval and the quality of these products. In addition, American scientists will lose the opportunity for the high-quality jobs that a robust American generic biopharmaceutical industry could bring to the United States.

Today, we urge Congress to begin the process of creating a regulatory pathway that will enable multiple pharmaceutical companies to develop and manufacture biotech pharmaceutical products in a cost-effective and cost competitive manner while still ensuring appropriate scientific standards for safety and efficacy. We ask Congress to pass legislation that will recognize and apply the current practice of comparability that enables biopharmaceutical manufacturers to change processes or manufacturing locations without conducting new safety and efficacy trials. We seek the establishment of a regulatory process that will enable the use of surrogate markers to ensure the safety and efficacy of generic biotech drugs, just as they do now under the Abbreviated New Drug Application process for traditional generic medicines. An abbreviated generic biotech pharmaceutical development process that accounts for scientific issues but acknowledges advances in scientific knowledge and understanding and thus limits duplication of development and bureaucracy is essential to ultimately limiting the investment required to develop cost-competitive generic biologic drug products. This will ensure that the American consumer reaps the benefits of these cost savings.

We are not asking this Committee or Congress to define the regulatory pathway today. Rather, we are asking Congress to begin the process of negotiating an efficient and cost-effective process for establishing a regulatory pathway that will be based on sound science and seek to re-establish America's position of leadership in this area. As with the approval of all pharmaceutical products, we are urging that this mechanism be reasonable and clearly tied to appropriate science that will establish safe and effective biotech pharmaceuticals.

Reality of Generic Biotech Drugs

As the United States begins the debate regarding the creation of a process for the approval of generic biotech drugs, we are in fact, playing catch-up to the rest of the world. While special interest groups attempt to convince Congress that generic pharmaceutical companies cannot overcome the hurdles to the development of these products, residents of other nations are already enjoying access to more affordable, generic biotech products.

As an employee of Barr, my access to information about the availability of biopharmaceuticals at other drug companies is limited to what is publicly disclosed. But even a cursory examination demonstrates that a number of companies are already supplying generic biopharmaceuticals in other countries. These include Sicor, LG Chemicals, GeneMedix, Cangene, Rhein Biotech, Dr. Reddy's Laboratories, Wochart and Dragon Biotech. They are supplying human growth hormone, interferons, EPO, insulin and other biopharmaceutical products in markets such as Lithuania and other Eastern European markets, Mexico, China, Korea, India, Argentina, Egypt, Peru and Brazil.

The marketing of generic biotech products in other countries clearly demonstrates that the products are comparable and that safety is not an issue. The exposure of thousands of patients, without untoward effects, clearly demonstrates that these products are not only effective, but safe. With the necessary regulatory oversight, safety will be appropriately addressed and thus will not be an issue in the United States either.

There are also a number of biotech products that are already multisource in the United States. Insulin products are one example. These include Humalog, Humulin, and Humulin-L, from Eli

Lilly; and NovoLog, Novolin, and Novolin L, from Aventis. The same is true for Human Growth Hormones, where Nutropin and Nutropin AQ, are made by Genentech Inc.; Humatrope by Eli Lilly, Genotropin by Pfizer; Norditropin by Novo Nordisk; and Serostim and Saizen by Serono Laboratories Inc. Each of these products required full development programs, costing consumers billions of dollars and exposing hundreds of patients to unnecessary clinical trials.

That multiple manufacturers are currently able to develop and produce these products on a large scale provides further confirmation that generic companies can and will develop and manufacture high-quality, equivalent generic biotech pharmaceuticals. Generic companies are no less capable than branded companies of applying state of the art science in manufacturing and product development. However, the regulatory process for generic biotech drugs can and should recognize that the safety and efficacy and many aspects of the safety of these products has already been established and thus significantly less additional testing is appropriate.

The argument that biotech drugs are so complex that they cannot be characterized ignores the fact that there are numerous highly sophisticated analytical methods available to all pharmaceutical companies, including generic companies. These methods permit the characterization of these complex proteins, and more methods are being developed. The argument that generic companies cannot characterize these very complex proteins is, in part, based on the mistaken impression that generic companies do not have the technological expertise or scientific, medical or clinical capabilities to safely develop generic biotech drugs.

Advances over the past 20 years, both in the area of analytical methods and validation techniques have allowed companies to characterize their biologic drug products such that the impact of changes to process and cell lines can be evaluated and biologic drug products can be kept constant.

Generic companies have highly sophisticated R&D organizations and manufacturing capabilities, and most, in fact, already develop and market proprietary products just as brand companies do. While some drug products, both chemical and biotech, might be more complex than others, the vast majority can be a fully characterized with currently available analytical methods. These analytical methods also can help identify and thus control any process-related impurities that are often found with biotechnology products. And continued advances in analytical methods will ultimately enable the characterization of all biotechnology products.

Finally, the argument is made that there is magic to the process of manufacturing biotech drugs. This may have been true when manufacturing processes were not validated and analytical methods were not advanced enough to characterize the final product. This is no longer the case. If it were, many of the products made by the various biotech manufacturers would not be available today. It is only the fact that these manufacturers have been able to utilize comparability protocols that has allowed them to make the necessary changes to processes and even cell lines required to allow them to supply these important drug products. In reality, biotech products can be fully characterized and compared analytically and biotech firms routinely justify process and site changes via comparability protocols.

In the United States, comparability is routinely being used to permit changes in manufacturing. When an innovator biotech company seeks changes in processes supporting the manufacture of

their products, or seeks to change the manufacturing location of a product, comparability is the process by which the amended product is judged to provide the same clinical effect and safety profile. FDA does not require the innovator to conduct full-scale clinical trials to confirm the safety and efficacy of the product.

Utilizing surrogate markers to confirm that the amended drug will provide the same results is the very process that is used today in traditional pharmaceutical manufacturing to ensure the safety and efficacy of a generic drug. Under the current ANDA process, established by Hatch/Waxman Act 20 years ago, the safety of the innovator drug is established by the clinical trials conducted by the innovator prior to the approval of the New Drug Application. The generic applicant does not have to conduct clinical trials to prove safety and efficacy. Instead, the generic manufacturer must prove bioequivalence. Hatch/Waxman relied on the use of surrogate markers - namely plasma levels, the rate and extent of absorption of the drug product into the blood stream, to represent the efficacy and safety measure that is the basis for approval of generic drugs. Such a process, although employing different surrogate markers specific to each individual biologic product, is applicable to the approval of generic biotech products for many reasons. The use of these surrogate markers would allow for a more limited clinical program while still ensuring efficacy and safety.

Application of reasonable surrogates for measuring the efficacy and equivalence of generic drugs can and should be applied to generic biotech products, since it has been proven to be an effective and efficient measure of equivalence and has enabled the approval of safe and effective generic versions of traditional pharmaceutical products.

Compelling Need

America's pharmaceutical biotechnology industry represents one of the most successful and fastest growing segments of U.S. healthcare. Ten years ago, revenues for this industry were approximately $8 billion. According to IMS, the international pharmaceutical data monitoring service, when you compare 2003 to 2002, the pharmaceutical biotech industry enjoyed revenue growth in excess of 22%, compared to 11% for the total market. By 2010, analysts estimate that biotechnology product sales will exceed $60 billion. Generic competition is essential to control costs and continue to stimulate innovation.

More than 150 biotech drugs are on the market, including human insulin, interferons, human growth hormones and monoclonal antibodies. In the past year, more than 30 new drugs were approved, compared to only two in 1982. There are more than 370 biotech drug products and vaccines currently in clinical trials targeting more than 200 diseases including cancer, Alzheimer's disease, heart disease, multiple sclerosis, AIDs and arthritis.

Biologics are a major driver of increasing prescription drug costs. Six biotech pharmaceuticals - Procrit, Epogen, Neuposen, Intron - A, Humulin and Rituxan - generated sales of more than $1 billion. And at least three new blockbusters are expected to join that list. The top three biotech pharmaceuticals: Neupogen, Epogen and Intron A cost patients $23,098, $10,348 and $5,850 respectively, each year. Cerezyme, a drug indicated for the treatment of patients with Gaucher's disease, a rare disease resulting from the genetic deficiency of an enzyme, has annual patient costs of $170,000. Although this drug treats a very limited number of patients, competition

would surely drive these costs down and make this product more affordable for those who need it. As evidenced by these examples alone, generic competition for biotech pharmaceuticals has the potential to offer consumers dramatic and substantial savings, while also lowering America's healthcare bill.

As the number of these products grows, and the lifecycle of these products matures, the patents on these products expire. If Congress does not act now, Americans will continue to be faced with escalating drug prices while others, outside the U.S. reap the benefits of more affordable safe and effective prescription drug products. In addition, without the opportunity to develop and sell generic biotech products in the U.S., it is likely that all development and manufacturing activities will take place outside the U.S. and Americans will not have the opportunity to benefit from those jobs. Given the success of the Hatch/Waxman Act, it is essential that we insure timely competition for these very expensive biotechnology products ensuring cost competition, innovation and a U.S.-based industry.

Creating the Regulatory Pathways to Ensure Generic Competition

As with traditional generic pharmaceuticals before 1984, the obstacle standing between consumers and substantial savings on biotech drugs is the articulation of a regulatory process that will enable safe, effective, FDA-approved generic versions of biotech drugs to reach the marketplace following a well-defined, scientifically-based approval process.

There are three issues here. The first is the lack of a generic approval process under the Public Health Service Act (PHSA). The second involves, what we believe to be, the mis-classification of some products approved under PHSA. It is our scientific contention that many of these products should rightly be reclassified under FFDCA, which would open the door for possible generic drugs under Hatch/Waxman as it exists today. The third issue, or more a correction, is that some products were approved under the FFDCA and these products do have a pathway for approval and should be reviewed through the ANDA process already defined under Hatch/Waxman but are currently not being reviewed as such by FDA.

We urge Congress to create legislation that will clearly define a pathway that enables FDA to review and approve all products on the basis of clinical science, on a case-by-case basis and without placing unnecessary requirements on generic companies which would result in unnecessary testing, increased expense, and limited access.

If generics are compelled to re-create the lengthy and expensive clinical studies required for the approval of the innovator drug, savings from generic biotech drugs will never be realized by American consumers as they currently are in other parts of the world. We urge Congress to ensure that the review process takes full advantage of all clinical data available, just as under the ANDA process, so that the development of generic biotech drugs will not require generic companies to re-create the science already established by the innovator.

Summary

In summary, the economic arguments for creating a process that will ensure timely generic competition for biotech drugs are compelling. We recognize the investment made by biotech

drug developers in intellectual property, and endorse the need to ensure appropriate intellectual property protection and the ability to recoup their investment. As has been proven under the Hatch/Waxman Act, competition fuels innovation, and ensuring timely generic competition will ensure continued innovation in biotech drugs. We must preserve this incentive for innovation, but it is now time to provide the balance of competition to keep America's biotech innovators strong and growing. And we must learn from the lessons of Hatch/Waxman, and address, in advance, intellectual property issues that could, in the future, be used as a barrier to appropriate generic competition.

The pathway created under biotech generic legislation must enable and compel the FDA to review generic biotech applications in a manner that assures safety and efficacy. The standards for generic biotech drugs must be rigorous enough to ensure safety and effectiveness, and support consumer confidence in generic biotech drugs, but must not be permitted to require generic applicants to recreate large clinical studies that simply reinforce the scientific knowledge already available.

The science to create affordable generic biotech drugs exists today. It is being done in other countries. It is being done every time an innovator changes a manufacturing process or location and uses comparability to ensure the biotech drug will provide the same safety and efficacy. America is already losing the race to generic biotech products. But it is not too late. Congress can and must create the regulatory process that will help save consumers additional billions of dollars on prescription drug costs, by enabling the timely, efficient and cost-effective approval of generic versions of biotech drugs.

Thank you.