

**STATEMENT OF
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SANDOZ
ON BEHALF OF
THE NOVARTIS GROUP OF COMPANIES**

BEFORE THE SENATE HELP COMMITTEE HEARING

“FOLLOW-ON BIOLOGICS”

**SD-430 DIRKSEN SENATE OFFICE BUILDING
THURSDAY, MARCH 8, 2007, 10:00 A.M.**

Good morning, I am Dr. Ajaz S. Hussain, Vice President & Global Head of Biopharmaceutical Development at Sandoz. I want to thank Chairman Kennedy, Senator Enzi and the other distinguished members of the Senate H.E.L.P Committee for giving me the opportunity to represent the Novartis Group of companies (“Novartis”) at this hearing. As a former research scientist, as a regulator with ten years of experience at the FDA - where I was Deputy Director of the Office of Pharmaceutical Sciences until October 2005 - and as an American who has at various points in my life also been a patient, I believe in the “Gold Standard” of the FDA approval process and want to see only safe and effective medicines made available to patients. I believe that this is as achievable for follow-on biologics as it is for all other drugs, generic and innovator, including biologics.

Novartis is a world leader in the research and development of products to protect and improve health and well-being both by developing innovator drugs and biologics, and also by making generics available once patents have expired. Novartis is unique among pharmaceutical companies because it has made large investments in both branded and generic drugs. Given this, our position on follow-on biologics is not based on the commercial interests of one particular product. Instead, Novartis strongly supports a balanced position, which advocates that the same standard of high quality and science be applied to all medicines, and that there be respect for legitimate intellectual property, while recognizing the role that both generic drugs and follow-on biologics can play in the health care system. Novartis’ success as a global leader of the

innovator biopharmaceutical industry is demonstrated by the approval and launch of fifteen (15) new molecular entities in the US since 2000 – more than any other company. Novartis’ global research base, the Novartis Institutes for Biomedical Research, is located in Boston, Massachusetts where thirteen hundred (1,300) researchers work towards developing the next generation of therapies. We also are relocating our Novartis Vaccines and Diagnostics Division Global Leadership to Commonwealth of Massachusetts in the third quarter of this year, and will be bringing together hundreds of additional researchers to develop the next generation of vaccines¹. We are committed to a future of innovation and new medicines, but we also believe in free markets and competition, and we are not afraid of them.

In the debate so far, you have been hearing essentially two opposite ends of the spectrum on the issue of follow-on biologics. At one end of the spectrum, some have argued that follow-on biologics are impossible and inherently dangerous, while others suggest that this is just a re-run of the 1984 debate when generic drugs were said to be impossible too and that everything we need to develop such products can already be done today. And the former, those adverse to follow-on biologics, do not accept that interchangeable products can ever be produced by other than the original manufacturer. In such a polarized context, Novartis appreciates this opportunity to share an alternative perspective; one that we believe encompasses a viable and responsible solution compatible with the current state of the science.

In considering this public health issue, we start from the premise that follow-on biologics are essential to the future economics of health care both in order to stimulate innovation, and, as important, to ensure that patients have access to the medicines they need at affordable prices. That a fair solution can enable both the innovator industry and the generic industry to prosper such that patients can benefit across the board, is a concept too often lost in this debate as both extremes try to pursue their respective “wish lists.” For its part, Novartis believes that a balanced solution is possible, one that will provide greater access to safe and effective medicines through the availability of competitively-priced biologics when patents expire. Toward this end,

¹ Note that the Novartis Corporate Headquarters are in New York, and Novartis has facilities in Arkansas, California, Colorado, Georgia, Massachusetts, Michigan, Nebraska, New Jersey, New York, North Carolina, Wisconsin with total US employees numbering 29,000

Novartis believes it is time for an explicit regulatory pathway that encourages the development and approval of follow-on biologics, including interchangeable products.

We define follow-on biologics broadly to include comparable versions of already-approved biologics and also improved versions of current therapies that depend on the same mechanism of action, are used in the same indications as the originator product, and are developed based upon an extensive and sound set of data generated by the subsequent sponsor, which includes stand-alone product and process development and the demonstration of comparability with the reference product on all relevant levels, that is, chemical, preclinical, and clinical (including immunological) and appropriately qualifying differences.

The success of the biopharmaceutical industry deserves comparable regulatory progress

The biopharmaceutical industry has made phenomenal progress since the first biotechnology-based medicine was licensed in the U.S. in 1982. Technologies to make and characterize protein products and other complex biologics have progressed rapidly in the last two decades, and the use of comparability to facilitate manufacturing changes has become established by innovator companies and regulators around the world since FDA led and then first formalized the concept in the US in 1996 with the Comparability Guidance. Comparability allows for flexibility in the development of products that is essential to their optimal manufacture and iterative improvement. It is a science-based regulatory success story, with very few exceptions.

Significant and continual advancements in scientific disciplines such as analytical characterization, product and process design, process control, and clinical assessment based on underlying mechanisms of action provide a sound scientific basis to utilize the fundamental principles and procedures of comparability evaluation for follow-on biologics. We are confident that this science based approach will enable the industry to progress to the greater availability of affordable biologics to which we all aspire.

In supporting a new regulatory pathway based on comparability such as that described in the “Access to Life-Saving Medicines Act”, Novartis is merely recognizing the next logical step in the evolution of the biopharmaceutical industry. The biotech industry is a success story with multiple blockbuster products and well-capitalized companies, as well as those small and emerging companies that hopefully will contribute to its future. Its very success, creativity, and growth, since insulin was approved as the first biotechnology product back in 1982, is what makes this next step possible. With key patents expired and expiring, the time is appropriate to enable greater access to these medicines.

In proposing that the development and approval of follow-on biologics be enabled, Novartis is drawing on its own decades of experience as well as its current capabilities and portfolio across the full breadth of the biotechnology and pharmaceutical industry. While care must be taken and standards maintained, the dramatic progress in biotechnology has already enabled development of the first follow-on biologic products. Indeed, some would say the entire industry is already a follow-on industry because most of the first-generation biotechnology products themselves were follow-ons to their naturally-sourced counterparts. We believe that this great success achieved by the biopharmaceutical industry working with the FDA regulatory experts should be the bridge to an even greater future. We envision the advancement of public health through the increased therapeutic options that become available and are accessible when follow-on biologics are approved through the appropriate application of the new regulatory pathway. Just as we trust the FDA to judge the appropriateness of comparability for innovators, so we can trust them to apply the same principles carefully and responsibly to all other sponsors.

Interchangeability is an important public health need

A regulatory pathway that encourages the integration of appropriate public prior knowledge, as well as one that enables a subsequent sponsor to submit data comparing their candidate to a previously approved product, are natural progressions in enabling the safest and most effective products to be made available to patients. Moreover, just as comparability for innovators’ products pre- and post- any manufacturing change has presumed interchangeability to their final product, so the potential for interchangeability of a product from a subsequent

sponsor, who has demonstrated comparability to an existing product, must be a legitimate consideration if not a foregone conclusion.

The industry and FDA accept that batch-to-batch variation is inevitable for biologics, and, as long as manufacturers ensure that subsequent batches stay within the same “goal posts” of that accepted variation, then the product is made available to patients. Comparability principles ensure that, for biologics, the same rules apply for after-approval manufacturing changes, and they can likewise be imposed on follow-on biologics. In none of these cases is “sameness” a useful or scientifically-valid concept, any more than it has been at any time for any biologic. To argue otherwise (for example insisting on “sameness” requirements that are not the current regulatory standard) creates hurdles to follow-on biologics that are greater than those required for innovator products and counter-intuitive. Similarly, an unintended consequence of such protectionism disguised as “sameness” raises the hurdles for innovator products, and makes products for unmet medical needs increasingly unavailable to patients. What we need are consistent and appropriate regulatory standards applied to all biologics independent of their sponsor.

In addition, a regulatory pathway that allows any sponsor to further innovate and develop a new second-generation product that is expressly different from but related to the first-generation product, and that represents an improvement in the medical options for patients, can be enabled by a pathway based on principles of comparability. This element encourages second-generation biologics but is precluded in the European approach and yet may represent an significant opportunities in the “Access to Life-Saving Medicines Act”.

Biotechnology Medicines Have The Confidence Of The Public

It is essential that the high standards for safety and efficacy that patients expect and that the biopharmaceutical industry has provided in collaboration with FDA are maintained through appropriate and consistent regulatory requirements for *all* biologics. These standards have been achieved through the application of rigorous, science-based regulatory requirements by experts for over a century under the PHS Act. The current statute reinforces the requirements for safety,

purity and potency. However, just as we trust the FDA to assess the unknown (new) biologic about which we necessarily have the least experience, (namely the innovator products), using these criteria, so too we can entrust the Agency to evaluate follow-on biologics which refer to products for which we now have decades of experience. We believe Congress should confer on FDA the flexibility to accommodate progress in science, and help enable the regulatory requirements to evolve appropriately as well. As such, FDA can, through public notice-and-comment rulemaking, and guidance as appropriate, implement a comparability-based pathway for follow-on biologics without requiring arbitrary, unnecessary or unethical duplication of pre-approval studies or clinical trials, and by allowing appropriate extrapolation between indications based on mechanism of action. We can also allow FDA to use their experience with comparability to evaluate a follow-on biologic sponsor's data, and judge the appropriateness of the products being designated as interchangeable -- all while recognizing that FDA does not regulate the practice of medicine. The EU may have chosen to defer to member states on interchangeability (the EMEA has not rejected interchangeability for biosimilars as some have misrepresented), but the history of generic drugs in the US makes it much more fitting that FDA recommend the designation -- they have the skill and the public health responsibility that make this appropriate. It should also be noted that, throughout this process, no access to the innovator's data is required -- the approval of the follow-on biologic can rest solely and surely on the shoulders of the subsequent sponsor's comparative data which it obtains by running side-by-side studies of the innovator reference product and its own follow-on biologic.

Protection of Intellectual Property Is The Lifeblood Of Innovation

Strong intellectual property protection, including patents, trade secrets, and confidential information, is essential to promoting innovation that results in new therapies to meet patient needs. However, Novartis believes that, by having a regulatory pathway that allows more rapid and efficient realization of this innovation through greater use of comparability and prior knowledge for second-generation products as well, these IP rights are enhanced not undermined by a follow-on biologics pathway. Moreover, with each follow-on sponsor developing its own independent data package, and not relying on the innovator's data, we believe these property rights are respected even for those products on which the patents have expired and competition

appears imminent. Historically, the biotech industry has established robust patent estates. However, when these patents expire (including patents claiming those PHS Act products for which up to five years of patent-term restoration already has been granted under existing Hatch Waxman), increased competition and access to safe and effective medicines should proceed in the free market. Litigation over patents will still occur, but those litigation proceedings should, and in fact do not need to be coupled to the regulatory approval process. Nonetheless, Novartis is prepared to work with the Committee and its staff to develop appropriate legislative provisions that would apply at the conclusion of the FDA approval process. Such a process for follow-on biologics could include a 45-day notification of an issued approval, during which time the innovator would be alerted to an approval referencing its product, and the innovator could institute litigation if it believed that its patent or other intellectual property rights have been violated.

Novartis believes that, if follow-on biologics are to become available to patients in a timely manner, it is essential to “decouple” patent litigation from the approval of new products using a comparability-based regulatory pathway. The complexity of biotechnology product patent estates is such that we do not believe waiting for resolution of biotech patent litigation in the Courts will be other than a barrier to the timely availability of follow-on biologics. Consequently, we believe companies should be able to decide how best to approach the market if they believe there are not outstanding patents, or that any patents still in force are invalid or not infringed just as they can for any PHS Act biologic today.

In legislating this “decoupling”, it may be appropriate for Congress to consider other mechanisms by which to make the exclusive marketing window more predictable for innovators. Novartis supports a non-patent research incentive such as may be achieved through modelling on EU data exclusivity provisions, more appropriately called market-exclusivity provisions, for innovator biologics approved after enactment of any new legislation, as a way to enhance regulatory certainty for all sponsors (which would be independent of the patent estates). Such an approach would prevent diversion of excess resources being used by either innovators or the sponsors of follow-on biologics on slow and expensive patent litigation, and enable those resources to be dedicated to the development and new and more efficient manufacturing of

biologics. However, beyond harmonizing this one discrete component of the EU system, in general, the EU approaches on follow-on biologics *per se*, their so-called “biosimilars”, suit an EU environment of 27 distinct countries with different legislative and regulatory histories as well as very different health care and reimbursement systems. The U.S. needs a solution that suits U.S. needs and statutory environment as it has been evolving here for over two hundred years following adoption of the U.S. Constitution.

The Development Of New Regulatory Requirements Must Be Transparent And The Rules Fair

For any new regulatory pathway, the FDA will need to go through a process of developing regulations. While promulgation of regulations need not be blocking applications in the meantime, their development can be expected to facilitate the choices for those sponsors and patients who can afford to wait a little longer. The FDA has a mission to enhance the public health, and follow-on biologics will be part of that as a result of enhanced patient access and competition. Novartis supports such an open process, while not accepting that it should ever serve to block follow-on biologics while the regulatory implementation process proceeds. Unlike the EU, the U.S. has a long established and very accessible public participatory process, in which submissions to dockets are available to the public. It will be through this notice-and-comment rule-making, as well as the development of guidance, to which the experienced innovator industry and others will be able to contribute and ensure that only safe and effective follow-on biologics are approved.

In Conclusion

Novartis envisions a win:win public health and public policy solution whereby a follow-on biologics industry is enabled, patients get greater access to high-quality and improved biotechnology products at competitive prices, and that provides innovators relief from outdated requirements and a less burdensome pathway to improve existing products. As recognized by the FDA leadership, it is not appropriate to use outdated regulatory requirements just because those parameters were considered historically useful. In this and other important regards, the opportunities to innovators through the creation of a new regulatory pathway based on comparability such as, for example, in the “Access to Life-Saving Medicines Act”, should be at

least as great as any available to generics, especially with respect to second-generation products. We do not believe that this is a zero-sum game. PhRMA's own numbers say 418 biotechnology medicines are in development, and yet, only 4 recombinant PHS Act applications were approved in 2006. It is time for all of us to work with FDA to improve the review for all biologics such that every patient can get access to safe and effective medicines that will compete in the market place and be more affordable, while also encouraging the development of the new therapies which are so desperately needed.