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CHAIRMAN AND CHIEF EXECUTIVE OFFICER, ALKERMES.
HOUSE COMMITTEE ON ENERGY & COMMERCE, SUBCOMMITTEE ON HEALTH
HEARING ON "REAUTHORIZATION OF PDUFA: WHAT IT MEANS FOR JOBS, INNOVATION, AND PATIENTS"

FEBRUARY 1, 2012

Chairmen Upton and Pitts, and Ranking Members Waxman and Pallone, it is my privilege to provide testimony before this Subcommittee today. My name is Richard Pops and I am Chairman and CEO of Alkermes. I am here testifying on behalf of the Biotechnology Industry Organization where I serve on BIO's Health Section Governing Board and coordinated BIO's strategic engagement in the Prescription Drug User Fee Act (PDUFA V) technical discussions with FDA. BIO represents over 1,100 members involved in the research and development of innovative healthcare, agricultural, industrial, and environmental technologies. As an entrepreneur with more than twenty years experience managing biotechnology companies and successfully developing novel therapies for patients, I would like to speak to the positive impact that the PDUFA program has had on patients and medical innovation, and highlight the challenges we seek to address under PDUFA V.

In short, BIO supports quick enactment of the PDUFA V recommendations as we believe they can enhance the drug development and review process through increased transparency and scientific dialogue, advance regulatory science, and strengthen post-market surveillance. Most importantly, from the standpoint of young, innovative companies, our hope is that PDUFA V will provide patients and doctors with earlier access to breakthrough therapies.

I. BIOMEDICAL INNOVATION REQUIRES A RELIABLE, PREDICTABLE, SCIENCE-BASED REGULATORY ENVIRONMENT

At Alkermes, we have a steadfast commitment to develop innovative medicines based on our imaginative science and proven technologies. We are inspired by real patient needs as we develop products to help patients and physicians better manage diseases. We are in an exciting phase of growth, with our diversified portfolio of commercial products that address central nervous system (CNS) disorders such as addiction, schizophrenia and depression, and an exciting late-stage pipeline. We began as a raw start up in rented labs next to MIT, and today Alkermes employs 1,200 individuals in Massachusetts, Georgia, Ohio and world-wide.

The U.S. biotechnology industry is poised to be a major driver in an innovation-driven economy. Biotechnology offers real solutions to our most pressing health care needs: curing disease, reducing costs, increasing quality, and ensuring that people enjoy not only longer lives, but better and more productive lives. A key to Alkermes' success and the future of the U.S. biotechnology industry is a reliable, predictable, and science-based regulatory environment, and the PDUFA program represents an important element of our nation's overall innovation eco-system. A fundamental part of biotechnology companies' ability to innovate and raise private investment is having an FDA with the resources and infrastructure required to review and approve innovative products effectively, consistently, and in a timely manner based on the best available science. Since 1992 Congress, FDA, and the biopharmaceutical industry have supported a carefully structured user fee program to help fund FDA's human drug review activities. This program has contributed to the approval of more than 1,200 new medicines and, initially, reduced review times for the newest, most innovative drugs by more than a year. In the past year alone, biopharmaceutical companies have successfully brought to market remarkable therapies to treat

hepatitis C, melanoma, lung cancer, lupus, and rare genetic disorders. Last week, after a decade of development, FDA approved an exciting new diabetes drug, which only needs to be administered once a week, developed by us and our partners. These advancements in patient care represent the leading edge of the next generation of biotechnology innovations.

But the pace of biotech innovation—and, more specifically, the pace at which new pharmaceutical treatments reach patients who need them—is not keeping up with our nation's healthcare needs. Developing innovative treatments and cures is a time- and capital-intensive endeavor, and the average time between treatment discovery and availability to sick and suffering patients is between 10 to 15 years. That is much too long. Additionally, new scientific and regulatory complexities in the FDA's drug review process have stressed our ability to speed safe and effective new treatments to patients. Unpredictability and inconsistency in the review process, suboptimal communication with sponsors, and decreased FDA performance not only hinders patient access to new treatments, but also negatively affects the ability of biotechnology companies to raise funding to support clinical development and ongoing innovation. This undermines economic growth in the biotechnology sector as well as biomedical research into key public health priorities.

II. PDUFA V: GETTING BACK TO BASICS FOR PATIENTS

Just as we have witnessed a revolution in genomics and our understanding of the molecular and biological basis of disease, we also must pursue new regulatory paradigms and modern approaches to how we assess the safety and effectiveness of novel therapies. When we began the process of organizing for our discussions of PDUFA V, we in the industry started with a simple

set of principles that could provide the foundation for our discussions with FDA and other stakeholders. These were that a *science-based, transparent,* and *well-managed* review process that appropriately *balances benefits and risks* can enhance public trust and increase patient access to new medicines.

With these principles in mind, industry and FDA agreed upon a set of enhancements under PDUFA V that seek to reinforce FDA's review performance and get back-to-basics for patients. These proposals also have been informed by an unprecedented level of public input through workshops, meetings, and stakeholder outreach, which further strengthened the technical agreement. These enhancements include:

- **New Molecular Entity (NME) Review Program:** Historically, nearly 80% of all NME applications submitted to FDA are ultimately approved, but fewer than half are approved on the first submission.[i] Sponsors and FDA can and must do better for patients. By strengthening scientific dialogue and transparency between FDA and Sponsors under the proposed review program for novel drugs and biologics, we can minimize the potential review issues that can delay patient access to needed treatments. Increased FDA-Sponsor scientific dialogue and transparency, such as a mid-cycle communication, exchange of discipline review letters and advisory committee information, and a significant new late-cycle meeting, will help to identify and resolve issues earlier in the review. This represents a significant paradigm shift in FDA's review process while maintaining FDA's high standards for safety and efficacy. An additional two-month validation period during the review period will help to ensure FDA has all the information it needs at the

beginning of the process to perform a complete review. Finally, a robust third-party evaluation will provide data on whether we have been successful in this program of leading to fewer review cycles, shorter approval times, and earlier patient access to needed treatment.

- **Enhanced Communication during Drug Development**: To help advance American innovation and promote the development of the next generation of modern medicines, FDA has also committed to a philosophy under PDUFA V that timely, interactive communication with biotechnology and life science companies during drug development is a core Agency activity.

  FDA's recent report on driving biomedical innovation highlights that "the private sector is the engine of innovation, and much of this innovation begins with small business."[ii] Indeed, many small biotechnology companies operate on the cutting edge of biomedical science to develop new therapies for devastating diseases. Yet we must acknowledge that the scientific method does not operate in a vacuum, and it is critical to promote interactive, scientist-to-scientist communication between FDA and Sponsors. In the course of drug development, Sponsors sometimes have simple or clarifying questions, the responses to which could have a significant impact on the development program, but which are not extensive enough to warrant formal meetings. To obtain timely responses to such questions, Sponsors currently often have to engage in a lengthy exchange of multiple formal letters with FDA, which is an inefficient and cumbersome use of both FDA's and the Sponsor's time. For small biotechnology companies reliant on limited

venture capital, these delays can create significant impediments to development programs.

Additionally, independent reports commissioned by FDA have also demonstrated that enhanced communication during drug development ultimately results in higher quality applications, which can improve efficiency for FDA reviewers.[iii]

BIO fully supports the PDUFA V proposal to promote innovation through enhanced communication between FDA and Sponsors during drug development, which will establish best practices for this type of interactive dialogue, train staff on communication practices, and provide the Agency with additional staff capacity to respond to sponsor inquiries in a timely manner.

- **Modernizing Regulatory Science:** Additionally, the PDUFA V agreement makes new resources available to modernize regulatory science, for example, in the areas of personalized medicine and rare disease drug research. Modern approaches to drug development and evaluation, such as through the application of new tools for rare disease drug development, flexibility with regard to creative study designs and new endpoints, greater utilization of biomarkers and patient reported outcome tools will introduce new efficiencies in the drug development enterprise and provide FDA with additional tools to evaluate the benefits and risks of pharmaceutical products. These proposals will also integrate more structured and systematic approaches to assessing benefits and risks of

therapies, and allow FDA to conduct outreach to patients and hold workshops to understand better patient perspectives on disease severity and unmet medical need.

- **Robust Drug Safety and Post-Market Surveillance Capacity:** PDUFA V continues industry's commitment to a lifecycle approach to product evaluation by strengthening FDA's post-market surveillance and benefit/risk management capacity. Earlier discussion of risk management strategies, standardized approaches to REMS, and further validation of the Sentinel Network will promote patient confidence in drug and biologics.

Under the PDUFA V agreement, industry has reinforced its commitment to a well-funded drug and biologics program that supports sound, science-based regulation consistent with FDA's public health mission. However, user fees are intended to support limited FDA activities around the drug review process and were never intended to supplant a sound base of appropriations. User fees currently account for nearly two-thirds of the cost of human drug review. We urge Congress to support FDA's mission and fund the Agency at the Administration's FY12 requested levels.

Additionally, it is critical for PDUFA to be reauthorized well in advance of PDUFA IV's expiration in September 2012, to avoid a reduction in force at the FDA. Even the threat of a downsizing at the FDA would be devastating to the Agency's public health mission and its ability to review new drugs and biologics.

BIO looks forward to working with Congress and FDA to fully implement these enhancements under PDUFA V.

III. PEDIATRIC DRUG DEVELOPMENT

The Best Pharmaceuticals for Children Act (BPCA) and Pediatric Research Equity Act (PREA) have been remarkably successful in ensuring that the medications used in children are tested and labeled appropriately for their use. BPCA and PREA have generated a wealth of pediatric drug information for physicians and parents, contributing to improved health outcomes for pediatric patients. Working in tandem, BPCA and PREA have resulted in nearly 425 pediatric labeling changes since 1998, according to the FDA. Congress should recognize the success of these programs and:

1. Reauthorize the existing framework and incentive for ongoing pediatric research, and
2. Make the programs permanent by eliminating their sunset provisions.

The five year sunset periods for BPCA and PREA result in an uncertain regulatory environment for pediatric drug development. Since the average pediatric clinical research program spans 6 years, most clinical programs will span two reauthorization periods in which the ground-rules for pediatric research are subject to change. This uncertainty makes it difficult for companies to invest in infrastructure to support development of products for children, and practically impossible for the FDA to issue guidance to promote understanding of the current regulatory framework.

Since their enactment, BPCA and PREA, working together, have been widely acknowledged as effective in promoting pediatric drug research. There is no logical reason to continue to allow such important legislation to sunset, as the ambiguity associated with this situation has the potential for limiting or endangering the pediatric research infrastructure that companies have been endeavoring to build and expand.

IV. REFORM OF ADVISORY COMMITTEE CONFLICT OF INTEREST POLICIES

As a pre-eminent science-based regulatory agency, it is critical that FDA have access to the most knowledgeable and most qualified scientific minds to help inform key public health decisions and evaluate the safety and effectiveness of innovative new cures and treatments for patients. BIO thanks Representative Burgess for his work on this issue and for introducing legislation that will enhance FDA's ability to empanel highly-qualified external scientific advisors, while maintaining the highest levels of integrity for these proceedings.

In recent years, arbitrary limits and unnecessarily restrictive interpretations of conflict of interest rules have created barriers that have prevented FDA from consistently recruiting highly qualified scientific advisors. Consequently, advisory committee vacancies are at an all-time high, the quality of the scientific discourse on such panels has suffered, and FDA has at times had to rely on scientific advice from panel members lacking relevant expertise, particularly with respect to rare diseases and cutting-edge technologies where the pool of available experts can be quite small.

BIO believes that FDA should have greater flexibility and discretion to select the most appropriate advisors, consistent with the rules that apply to other federal agencies. Such changes will help to ensure that FDA decisions are informed by the best available scientific experts and in the best interest of patients.

V. FDA MISSION STATEMENT

FDA's mission, as amended by the Food and Drug Administration Modernization Act of 1997 and set forth in section 903 of the Federal Food, Drug, and Cosmetic Act (FFDCA), is to promote and protect the public health. However, the FDA mission statement does not reflect the Agency's critical role in incorporating modern scientific advances into review practices to ensure that innovative treatments and therapies are made available to the patients who need them.

The pathway for such long-sought health technology advances as personalized medicine, health applications of nanotechnology, and other cutting-edge developments to reach patients and to improve healthcare in the United States goes through FDA. The Agency has a critical role in facilitating healthcare innovation, but this fact is not formally and forcefully recognized in FDA's legislative mandate. BIO applauds Congressman Mike Rogers for introducing legislation and advancing a dialogue on updating the FDA's mission for the 21st century.

VI. SUPPLY CHAIN INTEGRITY & ADOPTION OF A NATIONAL PHARMACEUTICAL TRACEABILTY SYSTEM

Due to the nature of the United States' closed and highly regulated pharmaceutical supply chain, American patients have high confidence in the integrity of the drugs and biologics they are prescribed. BIO member companies believe the quality and safety of their products is their responsibility to the patients they serve, and is their first priority. BIO supports the initiatives that FDA has already implemented to expand the Agency's global presence through foreign offices; expand the foreign inspectorate and part of a risk-based inspectional strategy; and modernize registration and facility tracking systems and information technology infrastructure.

This Committee has also been examining granting the Agency several new regulatory authorities to further secure the supply chain and BIO looks forward to working with the Committee to further strengthen FDA's import programs and oversight. BIO is supportive of well crafted proposals to increase penalties for criminal counterfeiters and adulterers, provide FDA with authority to detain or destroy known counterfeits at our ports, modernize FDA's facility registration and tracking systems, and better leverage the resources of established international regulatory authorities through joint inspections.

In addition to enhancing oversight over the "upstream" supply chain for pharmaceutical ingredients, it is critical to make enhancements to the "downstream" domestic supply chain for finished pharmaceutical products. BIO supports the establishment of strong, uniform, national standards for serialization and tracing systems, rather than relying on the emerging patchwork of individual state mandates. In this case, BIO believes that the Congress should enact laws governing drug product serialization and traceability systems that regulators can leverage to hold supply chain members accountable for ensuring that legitimate product reaches the patient. A national system using existing and proven technologies would best protect supply chain integrity and patient safety.

Specifically, this approach would standardize efforts nationwide and provide immediate measures to increase supply chain security. Such an approach would enable the identification and adoption of a consensus and technology neutral standard for a traceability system achieved through a progressive process where each system advancement is predicated upon clearly defined triggers and benefits analysis. Such a system should be sufficiently flexible to allow the

end-state to reflect the realization of the project's goal—facilitating the identification of and preventing the introduction of counterfeit, diverted, substandard, adulterated, misbranded or expired drugs from the supply chain and improving the efficiency and effectiveness of recalls.

VII. CONCLUSION

Thank you for the opportunity to offer BIO's support for the PDUFA V recommendations. We believe that these are common sense recommendations that will help advance innovative new cures for patients. We call on Congress to fully support FDA's appropriated budget and to pass PDUFA V as expeditiously as possible. I would be pleased to answer any questions from the committee.

REFERENCES

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[ii] FDA, *Driving Biomedical Innovation: Initiatives for Improving Products for Patients*, October 2011, http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM274464.pdf

[iii] Booz Allen Hamilton, *Independent Evaluation of FDA's First Cycle Review Performance –- Final Report* July 2008, http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm127117.htm