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TESTIMONY OF THE HONORABLE JAMES C. GREENWOOD, PRESIDENT & CEO,
BIOTECHNOLOGY INDUSTRY ORGANIZATION
HOUSE COMMITTEE ON ENERGY & COMMERCE, SUBCOMMITTEE ON HEALTH HEARING
"DISCUSSION DRAFT OF THE 'FOOD AND DRUG ADMINISTRATION GLOBALIZATION ACT'
LEGISLATION: DRUG SAFETY PROVISIONS"

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Chairmen Pallone and Dingell, and Ranking Members Deal and Barton, it is my privilege to provide testimony before this Subcommittee today on behalf of the Biotechnology Industry Organization (BIO) on the efforts of BIO's member companies to ensure the safety of the ingredients that they use to manufacture their pharmaceutical and biological products for the American public. We applaud the Subcommittee for convening this hearing, and we are committed to collaborating closely with you and the FDA to better assure the safety, purity, and potency of imported drugs and biologics. We welcome this opportunity to inform you of the steps that our members have been taking to ensure the quality of their products, as part of the successful "closed" regulatory system for imported drugs and drug products.

I want to reiterate the commitment of BIO and its member companies to work with you and this Subcommittee in this endeavor. We do so because the continuing safety of our products is our responsibility to the patients we serve, and it's our top priority.

By way of background, BIO represents more than 1,200 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare,

agricultural, industrial and environmental biotechnology products. BIO and its member companies have worked closely with the Food & Drug Administration (FDA) to ensure that the United States' drug supply is safe, secure, and reliable, and that Americans can be confident that when they use an FDA-approved prescription drug or biologic, the medicine will be safe and effective and work as intended. As you know, FDA's regulatory standards are among the most rigorous in the world and BIO's members will continue to comply with the requirements of the Federal Food, Drug, and Cosmetic Act (the Act) that ensure the safety of prescription drugs.

For example, the Act requires that all new prescription drugs must be approved by FDA as safe and effective for their intended use. FDA approvals are both manufacturer- and product-specific, and include requirements that the sponsor of a new drug application (NDA) or biological license application (BLA) disclose to FDA the manufacturing location and the manufacturing controls that will be used by the manufacturer to ensure the production of a safe prescription drug or biologic. In addition, our members' facilities that manufacture prescription drugs and biologics for the U.S. market must also comply with FDA's Good Manufacturing Practice (GMP) requirements to ensure that the manufacture of their prescription drugs and biologics can be reproduced consistently and in accordance with the agency's quality standards.

Our members are responsible for ensuring the safety of both the domestic- and foreign-manufactured ingredients used for their prescription drugs and biologics. BIO members that are U.S. manufacturers of finished dosages that use imported ingredients test and validate the safety, purity, and consistency of those ingredients that they use in the manufacture of their products. BIO members, like all prescription drug and biologic manufacturers, also are required to disclose the source and specifications of their ingredients in their applications, and their domestic and foreign active ingredient manufacturers must be in compliance with GMPs prior to the approval of our members' NDA or BLA.

In fact, FDA's Drug Master Files (DMFs) were established through FDA regulations to allow producers of active ingredients and other formulation materials to submit this confidential commercial information directly to FDA. In addition to containing information regarding the source and specifications of active ingredients and their manufacturer, FDA's DMFs contain manufacturing information pertinent to the formulation material. The particular DMF is referenced by an applicant for a new drug or biologic and is considered part of the NDA or BLA. Therefore, FDA conducts a pre-approval inspection that includes the inspectional verification of the information submitted to the DMF by the ingredient manufacturer prior to approving an NDA or a BLA submitted by a BIO member. Foreign and domestic ingredient manufacturers may then be subject to a periodic reevaluation for GMP compliance, either during a pre-approval inspection for a different product, or pursuant to a routine post-approval GMP inspection.

BIO recognizes that FDA may inspect both finished prescription drug and ingredient manufacturing facilities that are outside the U.S. less frequently due to the agency's resource constraints. However, irrespective of the frequency of FDA's inspections, BIO members employ processes and procedures to ensure that the prescription drugs that they manufacture are genuine and safe. BIO members realize that it is their responsibility to ensure that the foreign facilities that they use to manufacture finished goods or contract to supply active ingredients meet FDA's GMP requirements. They audit or inspect foreign facilities so that their products meet the requisite quality standards regardless of whether they contract with an outside company or produce the pharmaceuticals or biologics themselves, and they strive to achieve a level of quality assurance that often exceeds FDA's regulatory requirements.

Our members also protect the quality of their products by securing the distribution chains for imported ingredients and strengthening the procedures used to qualify potential suppliers of active ingredients. These steps help ensure the safety, identity, and purity of batches of ingredients that will be used to manufacture

their products.

The Act's provisions create a "closed" regulatory system for imported drug products to help ensure that the domestic drug supply is safe by limiting the drugs and biologics that may be imported into the United States. FDA and industry increasingly face challenges due to globalization of drug development and manufacturing. The changing world has required both FDA and industry to devise and evaluate more complex risk scenarios and apply more sophisticated technologies to screen and evaluate prescription drugs and biologics entering the U.S. to ensure their quality. The "closed" regulatory system of importation has been successful, however, because our industry has implemented rigorous manufacturing and quality control practices. Although the overall quality of drug products in the United States is still very high, the recent FDA announcement regarding the contamination of heparin is a reminder that we need to continue to be vigilant in our efforts to ensure the safety, efficacy, purity, and potency of prescription drugs and biologics and work cooperatively with FDA to achieve this goal.

With that goal in mind, BIO recently met with FDA and Health and Human Services to discuss how we can continue to work together to ensure that Americans can be confident that when they use an FDA approved prescription drug, the medicine will be safe and work as intended. I also sent a letter to BIO's 705 Health Section members asking for their continued commitment to work with FDA to ensure the safety of the prescription drugs that they manufacture, and to ensure that their DMFs are up to date. I know that BIO's member companies are taking this issue very seriously.

On behalf of BIO's member companies, I also want to provide my personal commitment to work with this Subcommittee as it begins to consider legislative options for strengthening the "closed" imported drug

regulatory system. In this regard, I would like to respectfully emphasize several key issues for your consideration.

First, BIO has previously publicly acknowledged that the FDA is woefully underfunded, particularly given the enormous and rightful demands that this Congress and the American public have placed upon this small agency. In fact, BIO led the formation of the Alliance for a Stronger FDA, which successfully advocated for $40 million in additional appropriated funds for FDA's human drug review program last year, and is advocating this year for, among other items, increases in funding for FDA's foreign inspection and import program. While we respect the fact that user fees are and will continue to be part of the solution to the agency's funding crisis – and supported the recent passage of drug safety legislation that dramatically increased such user fees – BIO strongly believes that the imbalance between user fees and appropriated funds within the agency's budget has become too great, hence the need for a much larger appropriation. BIO would urge this Subcommittee to ensure that, if new user fees are created, that the amount and use of any new user fees are set forth clearly in any new legislation, to ensure both transparency and accountability. It also is essential that any new inspection user fees paid by BIO members are not duplicative of existing registration and establishment fees, and are specifically allocated to inspections of their facilities, not used to subsidize the inspections of other regulated parties' establishments. We believe that such fees should be collected fairly from all regulated parties under this proposed legislation, commensurate with the additional inspectional resources needed for purposes of inspecting such parties' establishments.

Second, any new legislation in this area should recognize the significant differences between biologics and small molecule drugs, as well as between and among different types of biologics. This is particularly relevant with respect to the type of testing that may be required to ensure safety and purity. Biologics are

complex products, derived from living organisms. In some cases, the active substance may be poorly characterized; in other cases, it may be characterized, but not easily separable from other components of the product, using current scientific methods. Of course, all biologics, like all other drugs, are regularly tested for purity and to ensure that they continue to meet their approved regulatory standards. But it is important that Congress not seek to create "one-size-fits-all" testing specifications because, frankly, a "one-size-fits-all" approach will not work for all safe, pure and potent biologics. Rather, FDA must have the responsibility and the discretion to ensure appropriate testing based on each particular product.

Third, there currently exists a highly detailed regulatory framework governing approval and post-approval manufacturing of drugs and biologics, including requirements for ensuring the consistent manufacture of a safe and effective product in accord with its FDA approval package. If the Congress is to enact new requirements or programs in this area, it is critical that they build upon and strengthen this established foundation and avoid imposing confusing, duplicative, or vague new mandates.

Fourth, any new legislation should ensure that the FDA has the time, resources, and direction to implement new requirements and programs in a way that will not result in shortages or disruptions to the supply chain of life-saving and life-enhancing medicines. It is important to recognize that the current "closed" regulatory system has been successful overall, and improvements to this system should not occur at the expense of patient access to needed therapies.

Finally, it bears emphasis that this "closed" regulatory system for imported drugs and drug products is an essential element in ensuring drug safety here in the United States. As we seek to strengthen this "closed" system together, we must keep in mind that efforts to broaden permissible importation of drugs will only

undermine such efforts and add to the FDA's already heavy burden.

I want to thank the Subcommittee in advance for the consideration of these views.