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Biotechnology Innovation Organization

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Energy and Commerce Committee, Subcommittee on Health

Hearing on "Examining FDA's Generic Drug and Biosimilar User Fee Programs"

Mr. Chairman, Ranking Member Green, and Members of the Subcommittee,

What an honor it is to speak to you today on behalf of the Biotechnology Innovation Organization (BIO) about the Biosimilars User Fee Act reauthorization. This Committee planted the seed that has grown into multiple user fee programs that provide FDA with a significant portion of the resources it needs to ensure that patients have timely access to safe and effective new drugs and biologics, generic drugs, biosimilars, and medical devices. This Committee also tilled the ground and successfully produced, with an overwhelming bipartisan House vote, the legislation that established an FDA pathway for the approval of biosimilars – the Biologics Price Competition and Innovation Act (BPCIA). BIO was an early and strong supporter of this legislation to create a facilitated and balanced pathway for greater competition in the biologics marketplace.

I am Kay Holcombe, the Senior Vice President for Science Policy at BIO. BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers, and related organizations across the United States and in more than 30 other nations. While our membership includes most of the large biopharmaceutical companies, the vast majority of our members are small biotechnology companies working on the most cutting-edge R&D. They have small staffs, no marketed products, and no profits, and they are heavily reliant on private capital to fund their work. They take enormous risks every day to develop the next generation of biomedical breakthroughs for the millions of patients suffering from diseases for which there are no effective cures or treatments today. BIO is proud of their innovative spirit and their dedication to alleviating human suffering.

You asked for our views on two proposals the Committee is considering: the Biosimilars User Fee Act and H.R. 749, the Lower Drug Costs through Competition Act. In summary, BIO strongly supports the reauthorization of BsUFA, as we supported the initial enactment of the BPCIA and the initial BsUFA program. We also want to express support for competition in the prescription drug marketplace not only between innovator biologics and biosimilars, but also between innovator drugs and generic drugs – which is the subject of H.R. 749. We believe that, in both cases, our shared ultimate goal is achieved – to provide patients with greater access to therapies that save and improve their lives.

As BIO's lead negotiator for the BsUFA process, I want to focus my comments today principally on this reauthorization. As BIO considered this approaching reauthorization in consultation with our members and other stakeholders, we coalesced around two over-arching goals. First, we want to ensure that FDA will have the resources over the next five years of the BsUFA program to accomplish the fundamental objectives of the program, including clarifying further and enhancing the processes and tools the agency uses to regulate biosimilars. Second, we want to improve the transparency, financial accountability, and sustainability of the BsUFA program. We believe the BsUFA reauthorization proposal meets these two goals.

What Has Been Accomplished during BsUFA I?

To inform our thinking, we looked at what FDA has accomplished in the first four years of the program, including reviewing the third-party assessment of the costs and workload associated with activities related to the development of policies and procedures to implement the new biosimilars program and to the review of biosimilar applications.

FDA has issued five final Guidance documents to assist sponsors and other stakeholders to understand some of the agency's thinking about how the new biosimilars pathway would work and about its expectations regarding the kinds of studies and data that would be required for biosimilars approval. FDA also issued final Guidance on naming for biosimilars and innovator biological products. This was a particularly important document that needed to take an approach that would provide clarity for prescribers and patients and assist pharmacovigilance, but not suggest, by virtue of a naming convention, that some products may raise safety or efficacy issues that do not exist.

FDA also has issued an additional five Guidance documents that remain in draft, including the recent draft Guidance regarding FDA's views on determining interchangeability. BIO has urged FDA to lay out its thinking on interchangeability, so we are pleased that a draft is available for public comment. We hope the agency will finalize this draft as quickly as possible after the public comment period ends. Many stakeholders believe it is crucial for FDA to explicate its expectations for the data needed to determine that a biosimilar product is interchangeable with its reference biological product, which the statute defines as a biosimilar that can be substituted for, or switched with, the reference product with no adverse impact on any given patient's clinical outcome. Such a determination, many believe, may serve to encourage greater prescribing and use of biosimilars as the availability of biosimilar products increases, provided the determination is sufficiently rigorous.

Beyond issuing these Guidance documents, FDA has committed substantial time and resources to make the pathway to approval for biosimilars viable and credible. Because of both the complexity of the products and the novelty of this category of "highly similar" or "interchangeable" products, we recognize that these early years necessarily have been a time of learning and building within the agency. And although four new biosimilars approved since enactment of the BPCIA and the initiation of BsUFA

may seem like a small number, we are confident that the program – and the availability of biosimilars – will grow as the agency builds expertise and capacity.

In fact, as FDA has reported in its annual BsUFA Performance reports and as an independent contractor also has documented, the number of meetings between FDA and sponsors planning or executing biosimilars development programs has increased substantially since the program began. As of October 2016, based on meetings between FDA and sponsors, there are 66 biosimilar development programs under way, to develop biosimilars to 20 different reference biological products. Of course we do not know what percentage of those programs will result in applications, or which applications will be approved. But the numbers certainly demonstrate the upward trend for which supporters of biosimilars have hoped.

What Can Be Accomplished during BsUFA II?

BIO worked with FDA and other industry organizations representing biosimilars developers and innovators, with input from many other stakeholders such as patient organizations and healthcare providers, to develop detailed proposals for continued progress and enhancements during BsUFA II. These proposals are encapsulated both in the legislative language proposed to this Committee and in the Biosimilar Biological Product Authorization Performance Goals and Procedures for Fiscal Years 2018 through 2022, referred to as the Goals Letter. The Goals Letter is of particular interest because it defines the commitments FDA is able to make as a result of receiving the Congressionally-authorized BsUFA fees. Among those commitments are several I want to highlight.

Review Timelines

First, FDA agrees to meet defined timelines for its reviews and decisions regarding biosimilars applications. Specifically, for 90% of original applications, a decision will be made within 10 months of the date on which the application is officially accepted for review by the agency. How well FDA does in meeting this timeframe, like others for re-submitted applications and supplements, will be reported annually and publicly by the agency.

Meeting Management

FDA-sponsor meetings before an application is submitted have been a key part of BsUFA and an essential component of a concerted effort to stand up this new program. These are formal opportunities for sponsors to discuss their development plans and approaches with the agency reviewers and receive technical assistance regarding ways to proceed that will give the development program the highest chance of success. Under BsUFA I, there was agreement that user fees would be associated with these meetings; that agreement will continue under BsUFA II. It is a long-term goal we share with FDA that these Biosimilar Product Development meeting fees eventually will be phased out, based on the agency's ability to meet its annual target revenue for the BsUFA program, and to meet its performance goals with fees assessed on biosimilars applications and products – as is the case, for

example, in the PDUFA program. This will require a more significant increase in applications and products than is expected over the next five years.

Some enhancements to the formal meeting processes also are among the performance goals for BsUFA II. These have the purpose of ensuring that requirements for both FDA and sponsors, in terms of response times, meeting times, and documentation, are reasonable to allow for the best and most productive meetings and the most timely and useful advice for sponsors.

New Review Program

A new approach to the review of biosimilars applications will be implemented during BsUFA II, which is modeled after the so-called "new NME" program under PDUFA. The anticipated advantage of this program is an increase in the number of first-cycle approvals – saving time and money for sponsors and, importantly, making approved products available to patients as efficiently as possible. The Program provides applicants with new opportunities, during the course of the review, to receive updates from FDA about how the review is proceeding. If there are questions or concerns, the applicant will have a chance and the time to respond – avoiding a scenario of last-minute problems that cannot be resolved adequately in the time remaining before the BsUFA deadline.

Based on an independent third-party review of the PDUFA "new NME" program, the program has been highly successful in the view of both the FDA and sponsors. Importantly, this approach has achieved its intent to increase the number of first-cycle approvals. In short, this means there is a higher chance that an application entering FDA in month one will exit, approved, in month 12. In addition, this approach greatly reduces the chance that the 12-month timeline will be extended, or that the application will need to be submitted for a second review cycle, thus delaying its approval and availability to patients for as long as another full review cycle.

The hope, in establishing this type of program under BsUFA II, is that results will mirror those that have been seen for new drug and new biological license applications. In other words, more and more productive communication between FDA and sponsors will lead to less overall time to product approval.

Under the program, the applicant is encouraged to meet with the FDA review team to discuss the content of the planned application in advance of the submission. Once the complete application (as agreed at the pre-submission meeting) is accepted for review by the agency (60 days), the 10-month count-down begins. At approximately mid-cycle, FDA will arrange a mid-cycle meeting with the applicant – in most cases by telephone – during which appropriate review team members will update the status of the application and identify any concerns or questions, discuss the review team's thinking about possible post-market requirements, and provide the applicant with upcoming milestone dates such as advisory committee meetings. If an advisory committee is planned, it will be scheduled at least two months before the end of the 10-month review time.

A second, late-cycle meeting will be held no later than 12 days before any planned advisory committee meeting. At this meeting – usually a face-to-face meeting – FDA will discuss with the applicant any major deficiencies in the application, the agency's views on the submitted data and any additional data

that may be needed, manufacturing issues, inspectional findings, any proposed post-market requirements, and any issues FDA plans to raise with the advisory committee. This timeframe will provide the applicant more than two months before the BsUFA goal date to work with FDA to resolve outstanding issues – a meaningfully longer time than frequently was the case previously. And if there is no advisory committee planned, the late-cycle meeting will occur no later than three months before the BsUFA goal date.

The establishment of this new review approach is significant for several reasons. First, it provides clear, guaranteed, important opportunities for applicants to know what is happening with their reviews – in a timely way that allows them to have meaningful input and an opportunity to address problems and concerns. Second, it provides timeframes for various steps in the review process that are publicly reportable through FDA's BsUFA annual Performance Reports. While we are hopeful that this type of program will be as relevant and helpful as it has been in the innovator context, it is critical that, given the inherent differences in the biosimilars development and approval processes, an independent third-party evaluation of this new biosimilars review program be undertaken. Under the Goals Letter, the evaluator will look not only at how the program is working and whether it is achieving its aim of more first-cycle approvals, but also at the question of whether and to what extent the earlier Biosimilar Product Development meetings, for which applicants also pay user fees, could have or should have identified issues that subsequently may be raised at a mid-cycle or late-cycle meeting during the review. Under the Goals Letter, the third-party evaluator will submit both an interim and a final assessment of the program, by the end of 2020 and by June 2022 respectively. These reports will be published for public comment, and public meetings will be held on each.

Guidance

Stakeholders across the spectrum agree that timely and substantive guidance, particularly in this new program area and for this new approval pathway, is essential to the success of the program. The lack of Guidance leads to uncertainty and missteps that limit or delay the availability of new safe and effective products for patients. Guidance that remains in draft for lengthy periods of time has the same effect. Thus, it is important that goals be set under BsUFA II not only for the issuance of new Guidance that explains FDA's perspectives in general, as well as with respect to specific biosimilars products or types of products, but also for the finalization of Guidance already issued in draft. Those goals are laid out clearly in the Goals Letter. While meeting these goals – a key publicly reportable user fee commitment – FDA also needs to ensure that the public has ample opportunity to comment on draft Guidance and that such public comment is taken into account in the finalization of any Guidance.

In addition, the Goals Letter provides FDA's commitment to revise and update the Good Review Management Practices Guidance and general guidance relating to processes, procedures, and timelines for meetings between FDA and sponsors, both of which apply to NDAs and BLAs, to include and reference biosimilars specifically.

Finally, the Goals Letter includes FDA's commitment to continuing to clarify the biosimilars review pathway and provide information important to sponsors both of biosimilars and innovator biological

products. This includes, for example, revision or re-issuance of Guidance relating to the so-called "transition" products; harmonization of varying definitions of "biological product;" and updating of the "Purple Book" with information including the date of first licensure of potential reference biological products.

Financial Transparency and Accountability and Program Viability through Enhanced Resource Management, Capacity Planning, and Time Reporting

BsUFA will benefit from the modernized time reporting and new capacity planning efforts being undertaken across the Centers for Biologics (CBER) and Drugs (CDER). By statute, FDA staff who review biosimilars applications are the same as those who review applications for approval of new drugs and new biological products. Therefore, modernized time reporting will be as useful for determining resource needs for BsUFA as for PDUFA. Modernized time reporting will provide data that are much more accurate than currently available about the time and resources actually spent and required to complete the various tasks associated with application review. Having this information will allow FDA, for both the BsUFA and the PDUFA programs, to plan in advance for the capacity necessary to meet the needs of future years. By the second quarter of 2018, FDA will publish an implementation plan for establishing and utilizing a capacity planning function and modernized time reporting, which will include biosimilars review activities specifically.

Further, an independent third party will evaluate various options and make recommendations regarding the best ways for FDA to assess its resource needs on an ongoing and forward-looking basis, for all CDER and CBER review-related activities. The specific tasks associated with the review of biosimilars applications will be built into this assessment. As with all other BsUFA and PDUFA reports and assessments by FDA or by independent contractors, this evaluation will be public, and public comment will be invited and taken into account.

These activities are critically important to those who pay user fees. They assure that fee payers and other stakeholders can be confident that there is a sound basis on which target revenues and fee amounts are calculated. It has been especially difficult to predict the amount of funding needed for BsUFA, because this is a new-to-the-U.S. industry without a history of development times or application submissions. This will change with time, but until then, the perspectives of experienced independent experts will be essential.

FDA also will include BsUFA resource management in the scope of work for the contractor that will evaluate PDUFA resource management. This evaluation will include an assessment of how the BsUFA program is administered, how the user fee funds are allocated and used, and what changes might be made to improve the governance of the program.

FDA will publish a five-year financial plan by the second quarter of 2018 and update the plan annually. The plan and updates will be made public, and FDA will convene annual public meetings to take comments on the plan and on how FDA is executing it.

Hiring

As this Committee is very aware, FDA has had significant problems hiring the experts it needs to do its work. This matter was discussed in depth during the development of the BsUFA reauthorization proposals, as it was during PDUFA discussions. In both contexts, FDA committed to making changes internally to makes its processes better.

BIO, as part of the FDA-regulated industry, supports a strong, capable, and skilled FDA that can make timely and science-based decisions in the interest of patients and the public health. Achieving this hinges on the agency's ability to attract, hire, and retain highly educated scientists, physicians, statisticians, and others. We are especially appreciative of this Committee's efforts, working with the Senate HELP Committee and many other Members of the House and Senate, to include changes in the 21st Century Cures Act that will greatly benefit FDA's hiring capabilities. These changes will provide FDA with some key authorities that it needs to attract the highly educated, experienced, and talented individuals we all want to see working on our applications for approval.

But FDA itself needs to improve, and that process is under way already. Numerous changes have been made and more are expected. Both the BsUFA II and the PDUFA VI agreements include a commitment that FDA will contract with third parties to help implement its new and expedited Human Resources processes and to evaluate on an ongoing basis the progress the agency is making. Because all the reviewers in the BsUFA program also are PDUFA reviewers, it is crucially important to the success of the biosimilars program for FDA to meet the significant hiring goals under PDUFA. Even more important is for the agency to put in place sustainable and durable processes and procedures, so that this hiring is not merely a five-year surge, but is a lasting approach that keeps FDA staffed at the level it requires to do its job.

Importantly, all of the activities that will be and already are being undertaken to improve the hiring situation will be public. We all will be able to see the assessment of the third-party evaluator, consider any recommendations, and provide comments to FDA. We also will be able to see the numbers. We do not want FDA to fall behind its hiring goals, because we know that the user fee commitments we rely on cannot be met unless the people are there to meet them. Annual hiring goals are included in the BsUFA and PDUFA agreements, and the public will be able to see in the annual Performance Reports whether these goals are being met. We want to see what is happening so we can work with this Committee and FDA to help stop any downward trend. We believe we share this goal with stakeholders across the spectrum. And we know, because of what this Committee did in 21st Century Cures, that we share it with all of you as well.

In discussing FDA hiring, I also want to reiterate BIO's longstanding views on the potential negative consequences that arise from the sequester of agency funds or hiring freezes that can result in FDA's inability to fill vacancies and make new hires that are necessary for meeting its commitments under the prescription drug and biosimilars user fee programs – or, in general, for carrying out its crucial public health responsibilities. User fees paid by biosimilars applicants, as well as user fees paid by applicants for new drug and new biological product approvals, support a significant number of FDA personnel. In

particular, they support the staff identified to carry out the program performance goals. If FDA is unable to make these hires, user fees cannot be spent. This is a situation that is not good for fee payers, for FDA, or for patients who are waiting for approved therapies.

H.R. 749: The Lower Drug Costs through Competition Act

Before I conclude, I will briefly address the second topic of this hearing, the Lower Drug Costs through Competition Act.

BIO supports competition in the prescription drug marketplace. Indeed, the United States has a robustly competitive market for drugs, where innovators compete vigorously with one another to produce safer and more effective medicines within the same class, and then compete on price as part of negotiations with powerful, sophisticated, and aggressive commercial middlemen such as insurance companies and pharmacy benefit managers who control patient access to these innovative products. While there are pockets of exceptions to this competitive environment, the reality is that the average innovator drug has a short period of time on the market without competition from other similar products, and roughly 90% of all prescriptions filled in America are for cheaper generic copies of once-branded drugs.

Still, BIO recognizes that more can be done to promote generic entry, particularly where an older, off-patent drug has lost regulatory exclusivity yet nonetheless lacks meaningful competition for various reasons. We all want to see FDA approve generic drugs as efficiently as possible and for the backlog of generic drug applications to be reduced quickly.[1] Unwarranted delay in access to such medicines is not good for patients. More choice and competition is good for patients, and whatever reasonable steps can be taken to help FDA enhance its generic drug processes should be considered seriously.

BIO does not have a position on the question of timelines for generic drug review or awarding certain generic drug applicants with priority review vouchers, as H.R. 749 contemplates. We defer to the Association for Accessible Medicines, which represents generic drug manufacturers, for analysis of those provisions. However, BIO does support as a matter of policy efforts to lower drug prices through the promotion of more robust competition in the drug marketplace, including the timely entry of generics and biosimilars once patents and exclusivities for innovator drugs have expired.

Thank you for the opportunity to testify today on behalf of BIO. I am happy to answer any questions you may have.

[1] We note that there have been numerous statements in the press about an unacceptable number of drugs in an FDA backlog. The number 4,000 has been mentioned. In some cases, there has been an implication that innovator drugs and biologics may be in this large backlog. That is not the case. In fact, for new drugs and biologics, FDA is meeting its performance goals under PDUFA. This large backlog is of generic drugs.