Biotechnology Industry Organization

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Committee on Energy & Commerce Subcommittee on Commerce, Manufacturing, and Trade Hearing "The U.S. - E.U. Free Trade Agreement: Tipping Over the Regulatory Barriers"

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Comments Submitted by:

Biotechnology Industry Organization (BIO)

Introduction

The Biotechnology Industry Organization (BIO) appreciates the opportunity to submit its perspective on non-tariff measures affecting the industry that should be addressed in the negotiation of a Transatlantic Trade and Investment Partnership (TTIP) agreement. BIO applauds the U.S. and EU governments for their courage and ambition in launching an initiative that holds tremendous promise for the long-term competitiveness of the Transatlantic economy, and which can contribute specifically to shared U.S. and EU leadership with regard to innovative technologies.

BIO represents more than 1,100 companies, academic centers and research institutions involved in the research and development of innovative biotechnology products and services. Our members are primarily small- and medium-sized enterprises working to develop and commercialize cutting-edge products in the areas of healthcare, agriculture, energy, and the environment. Since its inception roughly 30 years ago, the biotechnology industry has spurred the creation of hundreds of thousands of jobs in the United States and Europe, and millions more through indirect employment.

To fully appreciate the biotechnology perspective on TTIP, it is necessary to understand the nature of the biotechnology enterprise and the elements that enable biotechnology innovation. Biotechnology research and development is capital intensive. It is generally acknowledged that it takes more than a decade and costs on average $1.2 billion to bring a biotechnology therapy to market[1]. The history of the industry is replete with anecdotes of

[1] Grabowski, Henry. "Follow-on Biologics: Data Exclusivity and the Balance Between Innovation and Competition" *Nature* 7 June 2008 Pg. 482

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meticulous, lengthy and expensive experiments that have failed. It is estimated that only one in 10,000 experimental compounds make it to market as successful medicines[2].

Yet because of its tremendous potential, the U.S. and most major European economies have invested significant capital resources in this industry. As such, U.S.- and EU-based innovators boast a tremendous number of scientific discoveries, many of which have the potential to yield the next cure for cancer, Alzheimer's, diabetes or other diseases. A concerted effort through the TTIP to unleash the potential of biotechnology in the Transatlantic economy and beyond will go a long way to bringing innovative products to consumers, create jobs, and improve economic prospects on both sides of the Atlantic.

The TTIP represents an important opportunity to advance progress in these areas. BIO has submitted detailed public comments to the U.S. Trade Representative, outlining its chief objectives for the agreement. Aside from the vital area of intellectual property rights, these objectives all fall broadly within the category of non-tariff barriers to trade, and fall into three categories: 1) regulatory issues connected to the approval of new medicines; 2) transparency and accountability of governmental systems to reimburse and price medicines, and 3) the regulatory process for agricultural biotechnology products.

1) **The Regulatory Process for Approval of New Medicines**

General Perspective

The prospect of significantly deeper regulatory cooperation and convergence related to bio-pharmaceuticals represents one of the most promising aspects of the TTIP. Such convergence will enhance Transatlantic innovative leadership in a sector that benefits the well-being of people in the U.S., the EU, and around the world. BIO requests that USTR pursue a distinct and targeted set of sectoral outcomes on bio-pharmaceuticals as part of the TTIP negotiations on regulatory convergence and cooperation.

Objectives with especially promising prospects for advancing innovation include:

- Mutual Recognition of Inspection Findings: The FDA and EMA have pursued pilot programs on coordination of inspections to assess compliance with Good Manufacturing Practices (GMP) and Good Clinical Practices (GCP). The agencies have a confidentiality agreement governing this cooperation. Based on this progress, TTIP should aim to produce agreement for mutual recognition of FDA and EMA GMP and GCP inspections. Under such an arrangement, regulatory authorities could

[2] Ernst & Young report, Beyond Borders 2009f

also work to identify systematically high-risk sites and to coordinate inspection schedules.

- Parallel Scientific Advice Mechanisms: TTIP should aim to build on an existing FDA and EMA program to provide parallel scientific advice in order to remove remaining limitations on use of this program. Specifically, the EMA and FDA should amend the current program policy to expand its applicability to all medicines, and grant sponsors the right to receive parallel scientific advice upon request.
- Parallel Evaluation on Quality by Design (QbD) Applications: TTIP should aim to achieve formal adoption of current "pilot" efforts between FDA and EMA to conduct parallel assessment of QbD applications. This will enable parallel evaluation of relevant development and manufacturing quality components submitted to both agencies.
- Data Field Requirements for Clinical Trial Disclosure: FDA and EMA could establish a harmonized list of clinical trial result data fields and agree on which of these data fields may be disclosed to the public.
- Collaboration in Developing Therapeutic Area Guidelines: FDA and EMA should establish a procedure for collaboration in developing scientific and other regulatory guidelines for specific therapeutic areas, in order to eliminate unnecessarily divergent requirements that are burdensome for innovators and delay the delivery of new treatments to market.
- Verification of Falsified Medicines: A TTIP bio-pharmaceutical work program could develop common national/regional coding systems for purposes of supply chain monitoring in connection with the control of falsified medicines. Work would focus on use of common standards for unique identifiers, developed using non-proprietary, harmonized international standards.

A number of additional components of regulatory cooperation can be built upon ongoing FDA-EMA collaboration under the auspices of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). These include:

- Pediatric Medicines: The FDA and EMA should work within the ICH framework to reduce divergences and achieve greater regulatory convergence in the scope, content, and timing of submission of pediatric investigation plans (PIP), so that companies are required to prepare only a single plan for submission in both territories. Such convergence could promote increased research efficiencies and result in more rapid completion of pediatric trials.
- Safety Reporting Requirements: Existing disparities between EU and U.S. safety reporting requirements should be targeted for intensified convergence work within the ICH. Specifically, the agencies should add an ICH "cluster" on pharmacovigilance issues to their existing slate of ICH priorities.

- Duplicative Testing Requirements: Existing ICH documents describe considerations for accepting foreign clinical trial data to support approval of the tested medicine in the EU or U.S. In practice, however, regulators from countries other than the U.S. and EU may require unnecessarily onerous bridging studies before a sponsor may gain approval of a medicine based on foreign test results. Additional work within the ICH could be useful in reducing the requirements of these bridging studies. FDA and EMA should also provide harmonized advice on the design of multi-regional clinical trials to support approval in both regions.
- Benefit-Risk Assessment: EMA and FDA should develop a harmonized structural framework and methodology for benefit-risk assessment, while retaining authority to make different risk-benefit judgments under their individual approval processes.
- Submissions Requiring Manufacturing Changes: EMA and FDA have similar requirements for submissions regarding manufacturing changes, but the details of these requirements can diverge. The agencies should work together to develop a harmonized approach to post-approval variation submissions for manufacturing changes.

Establishment of a "Working Group on Biopharmaceuticals" to oversee implementation of all aspects of regulatory cooperation foreseen under provisions of the TTIP.

Non-Disclosure of Data – An Issue Requiring Priority Attention

In addition to the regulatory objectives outlined above, BIO requests USTR to address, as a matter of priority, the need to ensure the non-disclosure of all personal data and other confidential commercial information (CCI) submitted to the EMA in connection with the marketing approval process. BIO is deeply concerned about recent indications by the EMA that it may disclose such information, including patient-level data, if requested by a third party, and its proposal to disclose such information proactively. This is inconsistent with the treatment of such information by the U.S. FDA, which appropriately applies a presumption that new drug applications and, indeed, marketing applications for all regulated products constitute confidential information that are generally not considered available for public release.

2) Market Access for Bio-Pharmaceuticals

General Perspective

Both the United States and the EU have recognized, in past free trade agreements, the particular challenges confronting market access for pharmaceuticals and medical devices. The product-specific chapters negotiated in respective U.S. and EU FTAs with Korea, for example, address the circumstances surrounding regulatory determinations on pricing and reimbursement of drugs and devices. The FTA chapters sought to surround these

determinations with rules and disciplines that ensure procedural fairness, transparency, non-discrimination, and improved patient access to innovative medical products.

The experience of BIO members in the EU market has reinforced that addressing these issues in the TTIP will be critical to advancing meaningful improvements in market access for our industry's bio-pharmaceutical products. BIO recognizes the significant fiscal challenges faced by all governments, and stands ready to be a productive partner in finding solutions.

A bio-pharmaceutical market access component of the TTIP should address the following major issues. Implementation of these provisions should be overseen on an ongoing basis by a specialized committee or working group.

A. General Provisions/Principles

- Recognize the economic and social value of promoting the development of, and facilitating access to, pharmaceutical products and medical devices for U.S. and EU citizens;
- Ensure sound incentives that promote near-term access to pharmaceutical products and medical devices and foster an innovative environment capable of sustaining research and development investment and advancing medical science;
- Recognize that bio-pharmaceuticals have a role in reducing the need for other more costly medical expenditures and improving the lives of patients;
- Respect the right of physicians and other health care providers to prescribe the appropriate medicines for their patients based on clinical need;
- Recognize the value of ethical interactions between bio-pharmaceutical representatives and health care professionals; and
- Agree that any reimbursement controls/determinations should apply only to products dispensed and reimbursed in that Party.
- Identify specific international organizations/workstreams to foster further cooperation among the Parties to improve patient access to safe and effective medicines.

B. Access to Innovation

Beyond the general principles reflected above, the TTIP should reflect a common understanding that innovative medicines should be priced and reimbursed at levels that appropriately reward and recognize their value. The agreement should:

- Provide that during the patent term or term of regulatory exclusivity of a bio-pharmaceutical product, the government price for that product should be based on the value of that product and never be set by reference to prices for generic products. Stipulate that, in the framework of pricing and reimbursement decisions, the parties

should not reassess the elements on which the market authorization for a product is based, which can include the quality, safety, efficacy or bioequivalence of the medicinal product based on specific national regulatory policies.

- Clarify that the negative impacts – to patient access and innovation – of a government entity establishing prices for bio-pharmaceuticals under patents or regulatory exclusivity mechanisms based on prices of the same product in other countries, are significantly exacerbated if the reference countries are dissimilar in terms of their socio-economic level, populations, disease burdens and health care systems. Government prices for patented bio-pharmaceuticals or bio-pharmaceuticals covered by regulatory mechanisms should be prohibited from being set by reference to prices for the same product in countries in economic or political crisis (for example, countries receiving aid from the International Monetary Fund or countries identified by the U.S. State Department as terrorist or unstable states); and
- Provide that a manufacturer should be permitted to apply for an increased amount of reimbursement and/or government price based on evidence of the safety and efficacy of its patented bio-pharmaceutical or bio-pharmaceutical protected by regulatory exclusivity mechanisms.
- Emphasize that a manufacturer should be permitted to apply for reimbursement for additional medical indications based solely on evidence of safety and efficacy.

C. Transparency

A transparent, timely and predictable pricing and reimbursement process that provides applicants with meaningful due process is essential to ensure patient access to innovative medicines. USTR should pursue the following provisions within the TTIP:

- Clarify that all provisions in a TTIP bio-pharmaceutical chapter apply to laws, regulations, procedures, administrative rulings, and implementing guidelines concerning all aspects of the pricing and reimbursement process, including, but not limited to, health technology assessments or other medical assessments of the clinical effectiveness of a pharmaceutical, demand-side measures and "clawback" mechanisms.
- Clarify that the obligation to address substantive comments in writing and explain any substantive revisions made to proposed regulations should be completed before the proposed regulations are adopted.
- Include an obligation to ensure that all applications are processed within a reasonable, specified period, clarifying EU Member States should be subject to all applicable provisions associated with the timelines mandated in the EU Transparency Directive.
- Include language providing that if an application is inadequate or insufficient, the relevant authority must notify the applicant of what additional information is required to resume the application review process in a timely manner.

- Clarify that the relevant regulatory authority should not request any additional information which is not explicitly required under national legislation or administrative guidelines to complete the decision-making process.
- Detail the requirements for providing an applicant with a pricing and/or reimbursement decision (including a negative decision), including that the decision must specify the basis for the determination, with specific reference to objective and verifiable criteria.
- Require that the final reimbursement notice should advise the applicant of its rights and the relevant timelines for seeking an independent review of the reimbursement decision.
- Require each Party to ensure access for stakeholders with legitimate commercial interests to full information about each Party's pricing and reimbursement systems and processes, including to a positive list of products covered, if any, published at least annually, and a negative list, if any published at least every six months.
- Require that confidential information contained in agreements signed between private sector actors (e.g., bio-pharmaceutical companies) and government entities that were entered into with the explicit understanding that the details included in those agreements will be kept confidential.

D. Dissemination of Information to Patients and Health Care Professionals

The TTIP should include language permitting manufacturers to make information available to health professionals and patients about their approved medicines via their internet sites, predicated on such information being truthful, not misleading and balanced.

E. Other Barriers to Market Access/Patient Access

Reflecting on the experience of BIO member companies in the EU market for bio-pharmaceutical products, BIO requests USTR to supplement the foregoing provisions, which are largely based on provisions found in previous U.S. and EU trade agreements, with the following provisions intended to address additional, practical impediments to EU market access:

- Requirement to respect the payment terms established by U.S. law/the EU's Late Payments Directive, respectively.
- Requirement that any "clawback" or rebate tax levied in response to an economic crisis should not disproportionately burden pharmaceutical manufacturers temporarily holding an exclusive position (i.e., any tax should be borne by the entire supply chain), and should be subject to a transparent, annual review process that affords those subject to the tax the opportunity to comment on whether it remains necessary

to continue the tax. Revenues raised by such taxes should be earmarked to cover healthcare expenditures.

3) The Regulatory Process for Agricultural Biotechnology

Comments in this section build upon previous submissions from both BIO and its partner EuropaBio. We encourage the U.S. and the EU to find a long-term solution to normalize trade in products derived through agricultural biotechnology. BIO believes that this can be accomplished within the existing legal and regulatory framework. Doing so would be to the mutual benefit to consumers, farmers and the economies of the United States and the European Union.

Agricultural biotechnology is an important tool that is being embraced globally to help address challenges such as food and energy security, environmental sustainability, and changing climactic conditions. With that promise in mind, it is critical that the US and EU take full advantage of the TTIP to forge a new trading relationship that can keep pace with the rapid adoption of agricultural biotechnology globally.

Most significantly, the TTIP should result in increased predictability and implementation of existing EU laws and regulations consistent with legislated timelines, and should also seek to incorporate internationally recognized approaches to risk assessment. The TTIP should provide for a mechanism to reduce risk of trade disruption resulting from gaps between the approval in the U.S. and EU. The TTIP should also establish improved dialogue and greater accountability at the ministerial and technical levels to address both existing trade issues, as well as promote cooperation as innovation in agriculture continues to evolve.

The comments which BIO submitted to USTR provide more detail on specific objectives it is seeking with respect to the EU's regulatory process.