



July 3rd, 2013

Comité Consultivo Nacional de Normalización de Regulación y Fomento Sanitario
Oklahoma Número 14
Planta Baja, Colonia Nápoles
Código Postal 03810
México, D.F.

Re: PROYECTO de Norma Oficial Mexicana PROY-NOM-177-SSA1-2013: Que establece las pruebas y procedimientos para demostrar que un medicamento es intercambiable y un medicamento biotecnológico es biocomparable. Requisitos a que deben sujetarse los Terceros Autorizados, Centros de Investigación o Instituciones Hospitalarias que realicen las pruebas; PROYECTO de Norma Oficial Mexicana PROY-NOM-257-SSA1-2013: Autorización de medicamentos, registro, prórroga y modificaciones; Norma Oficial Mexicana de Emergencia NOM-EM-001-SSA1-2012.

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) thanks El Comisionado Federal para la Protección contra Riesgos Sanitarios y Presidente del Comité Consultivo Nacional de Normalización de Regulación y Fomento Sanitario, Mikel Andoni Arriola Peñalosa, for the opportunity to submit comments on the *PROYECTO de Norma Oficial Mexicana PROY-NOM-177-SSA1-2013*, the *PROYECTO de Norma Oficial Mexicana PROY-NOM-257-SSA1-2013*, and the *Norma Oficial Mexicana de Emergencia NOM-EM-001-SSA1-2012*.

BIO represents more than 1,100 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, thereby expanding the boundaries of science to benefit humanity by providing better healthcare, enhanced agriculture, and a cleaner and safer environment. As the Mexican government looks to establish a pathway to market for biosimilar biological products, BIO offers the following important considerations to ensure patient safety, as well as continued innovation in the life sciences.

A. Recognize Scientific Differences Between Traditional Drugs and Biologics

Biologics are complex medicines that are manufactured using living organisms. These drugs are different and far more complex than most traditional small-molecule chemical drugs and include many of the latest breakthrough medical therapies for serious and life-threatening illnesses. Due to their size and complexity, biologics generally cannot be scientifically characterized to the same degree as traditional small-molecule chemical drugs. Any pathway for the approval of biosimilar biologics must protect patient safety, recognize the differences between traditional small-molecule drugs and biologics, and



preserve incentives for innovation. Please note that the term “biocomparability” is generally associated with internal quality control studies performed by manufacturers of biologics in order to ensure the fidelity of their products after manufacturing process changes. Therefore, to avoid confusion, BIO encourages the Mexican government to adopt international convention and refer to follow-on biologics as “biosimilars” rather than “biocomparables.”

B. Protect Patient Safety by Requiring a Robust Package of Analytical, Nonclinical, and Clinical Data for Biosimilars

Patients should not have to accept greater risks or uncertainties using a biosimilar product rather than an innovator's product. Accordingly, approval of biosimilars must be based on the same rigorous standards of safety, purity, and potency applied for the approvals of innovator biotechnology products. It is important to note that the methods used to show that one traditional small-molecule drug is the same as another are different from, and insufficient for, biologics. Versions of a biological product made by different manufacturers must be evaluated on a case-by-case basis, because they will differ from each other in certain respects. While International Conference on Harmonisation (ICH) document Q5E *Comparability of Biotechnological/Biological Products Subject to Changes in Their Manufacturing Process* may be consulted, the methods used by innovators to demonstrate continued safety and effectiveness after a manufacturing process change are insufficient to demonstrate quality, safety, and effectiveness of a biosimilar made by a different manufacturer using a different process. As innovator companies' experiences with respect to pioneer biotechnology products have shown, it is possible for small product or manufacturing differences in biologics to result in significant safety and/or effectiveness differences. Clinical trial evidence and data are fundamental for evaluating and demonstrating the safety and effectiveness of biosimilars and must be conducted on a product-by-product basis. In particular, immunogenicity testing is necessary to avoid putting patients at risk of adverse effects from immune reactions.

C. Clearly Label Biosimilar Products to Inform Patients and Physicians

The labeling requirements for biosimilars should flow from the fundamental premise of these products – that they will be similar to, but not the same as, their reference products. It is critical that the unique attributes of biosimilars, including the clinical and post-marketing safety data generated specifically for the biosimilar products, be clearly reflected in the labeling. Labeling that does not clearly identify the differences between a reference product and a biosimilar could be misleading to prescribers and patients. The labeling should include a prominently-displayed, standard warning regarding the risks of substituting or alternating innovator and biosimilar products. The labeling of the biosimilar product should state which indications have been approved and which have not in clear language that a user can understand and locate. Identification of the actual indication(s) studied will provide an additional tool to inform prescribers' selections of biological products and prevent unsafe substitution.



D. Assign All Biologics Unique Non-Proprietary Names to Facilitate Post-Market Surveillance

Biosimilars must also be properly evaluated through robust, global post-marketing surveillance (pharmacovigilance), as well as post-marketing clinical studies and registries, as needed. Biosimilars should, therefore, be assigned international non-proprietary names (INNs) that are readily distinguishable from that assigned to the innovator's or another biosimilar manufacturer's versions of the products. Assigning identical names to products that are not the same would be confusing and misleading to patients, physicians, and pharmacists; could result in inadvertent substitution of the products; and would make it difficult to quickly trace and address adverse events that may be attributable to either the innovator or the biosimilar products.

E. Prohibit Substitution of Biosimilars at the Point of Dispensation

Biosimilar biologic products will be therapies that are similar to, but not the same as, an innovator therapy. Without additional, robust clinical and post-marketing data that provide a reasonable expectation that the biosimilar product will produce the same clinical result as the reference product in any given patient, the approval criteria for biosimilarity do not meet the heightened standards necessary to safely enable substitution for the innovator product at the point of dispensation. The prescribing physician is in the best position to evaluate a patient's treatment history and options, and thus it is important for the treating physician to be able to designate exactly which product he/she believes should be dispensed to the patient. Product determinations should include a patient's values and preferences following informed discussion of the biosimilar product's risks, benefits, and uncertainties.

F. Preserve Incentives for Innovation

It is critical that Mexico's pathway for biosimilars includes meaningful protections against unfair use of reference product-manufacturers' intellectual property (IP) and regulatory dossiers. Such protections preserve incentives to research, develop, manufacture, and launch in Mexico new innovative therapies and cures for patients suffering from serious, life-threatening conditions and unmet medical needs, as well as to develop and secure approval of new indications for such products. Protecting IP and regulatory data will also help to enhance patient safety and access to novel biologics in Mexico. In particular, BIO urges Mexico to clarify that –

- ***Substantial exclusivity will be provided to innovators' regulatory data to promote the development and commercialization of new medicines.*** The effectiveness of the intellectual property incentives that exist today for developing new biological pharmaceutical products is linked to the regulatory systems that govern these products. Data exclusivity promotes the development and commercialization of new medicines by encouraging innovative companies to conduct safety and efficacy studies on new products so that they can be brought to the market to treat patients. Data exclusivity is generally implemented by not permitting the approval of a follow-on product, such as a generic or a biosimilar,



that relies upon the data provided by a reference product until the end of the applicable protection term. Because data exclusivity is implemented by the health authorities, once an innovator's information is entitled to protection, it offers the innovator certainty and predictability regarding exclusivity in the marketplace. In the United States, biosimilar products cannot be approved until 12 years after the innovative biological product was approved.

- ***The biosimilar pathway will respect innovators' intellectual property and other legal rights.*** Biosimilars should only be approved in Mexico after all protections, including regulatory data (see above) and patent protections, are no longer available for the approved innovator product. In this regard, any biosimilar pathway should ensure that an innovator receives adequate notice of an application referencing its product or its data, so that any legal challenge involving the biosimilar product can be litigated promptly and prior to marketing approval of the biosimilar. Any biosimilar pathway also should fully respect existing trade secret protections for certain innovator data (such as chemistry, manufacturing and control data required as part of the new biological product approval process) and not permit the use of such information for the purpose of approving biosimilar products.
- ***Reference Biologic Products should only be those approved through the submission of a full regulatory dossier.*** No biosimilar should be considered as a reference biologic product (RBP).
- ***If a relevant reference product is approved in Mexico, a biosimilar applicant should not be permitted to circumvent Mexican IP or regulatory data protection by referencing a foreign-approved product instead.*** Where there is a relevant domestically-approved innovator product to serve as the RBP, the biosimilar applicant must either use that as its reference product or scientifically justify the relevance of a foreign-approved RBP to that original Mexican-approved innovator product, consistent with generally accepted international standards. In either case, it is critical that the regulatory data and IP protection of the domestically-approved innovator product be respected in order for Mexico's overall biologics regulation scheme to maintain the incentives necessary for innovators to seek approval of and launch novel medicines in the Mexican market.



CONCLUSION:

BIO appreciates this opportunity to comment on PROY-NOM-177-SSA1-2013; PROY-NOM-257-SSA1-2013; and NOM-EM-001-SSA1-2012. We would be pleased to provide further input or clarification of our comments, as needed.

Respectfully submitted,

A handwritten signature in black ink that reads "Joseph M. Damond". The signature is written in a cursive style with a large initial "J".

Joseph Damond
Senior Vice President, International Affairs
Biotechnology Industry Organization (BIO)