



## **BIO POSITION STATEMENT**

### **Naming and Labeling Requirements for Biological Medicines**

#### **Summary**

**Medical product naming and labeling play an essential role in ensuring patient safety. These regulatory mechanisms will be increasingly important as biosimilar medicines (also known as “follow-on biologics”) enter the market. Current systems for naming and labeling of generic medicines were not designed to address the unique character of biosimilars, which are not identical or interchangeable with the innovative product. To avert inappropriate assumptions about product sameness and interchangeability, and to protect patient safety, each biological medicine should have a distinct international nonproprietary name (INN) and each biosimilar should have an original label that includes information about product substitution and interchangeability.**

#### **Introduction**

A “biosimilar” medicine is a distinct biological medicine claimed to be “similar” in terms of quality, safety and efficacy to a reference medicine that has already been granted marketing authorization. In this position statement, the Biotechnology Industry Organization (BIO) summarizes considerations that must be taken into account with respect to naming and labeling of biological medicines, including biosimilars. Unlike traditional “small-molecule” generic medicines, biosimilars are not identical to the reference innovative product. Current requirements for naming and labeling may lead to inappropriate assumptions about sameness and interchangeability of biological medicines. Therefore, requirements for naming and labeling should be clarified to accommodate the advent of biosimilars and to help ensure that all biological medicines continue to be used safely and appropriately by patients and health professionals.

**This position statement covers the following issues related to naming and labeling:**

- 1. A System for Unique Identification of Biological Medicines Should Be Established, Including Distinct International Nonproprietary Names (INNs)**
- 2. Each Biological Medicine Should Have an Original Label**
- 3. Information about Product Substitution and Interchangeability Should Be Included in the Label**

BIO members are concerned that patient safety and medicinal efficacy may be compromised if the issues listed above are not appropriately addressed. BIO will work with the European Medicines Agency (EMA) and its Committee for Medicinal Products for Human Use (CHMP), the United States Food and Drug Administration (FDA), and other authorities including the World Health Organisation (WHO) to ensure the establishment of science-based and transparent requirements for naming and labeling for biological medicines.

## **Key Issues Related to Naming and Labeling of Biological Medicines**

### **1. A System for Unique Identification of Biological Medicines Should Be Established, Including Distinct International Nonproprietary Names (INNs)**

Biosimilars are “similar” but not “identical” to the innovative product, and their safety and effectiveness profiles may differ from that of the innovative product. Assignment of the same nonproprietary name to a biological medicine and any biosimilar versions may be taken to imply that these products are pharmacologically interchangeable when they are not. To date, assignment of the same INN to different versions of a product has not presented a significant problem insofar as each version has had a brand name. BIO takes the position that in order to accommodate the advent of biosimilars each biological medicine should have a distinct INN.

The lack of unique identification for biological medicines could create public health concerns in the following areas:

- **Pharmacovigilance:** The first adopted EMA guideline on biosimilars (“Guideline on Similar Biological Medicinal Products [SBMPs]”, CHMP/437/04) contains the following requirement: “... in order to support pharmacovigilance monitoring, the specific medicinal product given to the patient should be clearly identified” (p. 4). BIO strongly supports this requirement. If patients receive multiple products without adequate record-keeping, it will be difficult or impossible to determine which product is responsible when adverse effects occur.

In its Sept. 2006 paper on INN policies for biosimilars (<http://www.fda.gov/cder/news/biosimilars.htm>) the FDA states “the USA does not see any reason to change present INN practices for pharmacovigilance purposes when there are other identification systems in place to allow product identification beyond the level of the non-proprietary name.” Because some countries do not have other such identification systems in place, and because physicians may use the INN in prescribing and as an indicator of interchangeability, BIO believes that assignment of distinct INNs to biological medicines is essential to ensure that adverse event reports are attributed to the right product and allow the development of appropriate responses to new safety information.

- **Inadvertent Substitution:** Because biological medicines may be only similar, but not identical to each other, patients could respond very differently to the innovative product and any biosimilar versions. Inadvertent substitution of one version of one medicine for another could have negative clinical consequences, for example, one version may cause a clinically significant immune reaction while another does not. A unique identification system would help ensure that patients are dispensed the precise medicine prescribed by the physician.
- **Traceability:** If an adverse event occurs with a biological medicine, it is critical that it be traced promptly to the correct manufacturer. This tracing would be greatly facilitated if all biological medicines had a distinct INN. This is particularly important in countries where prescribing by INN is routine and encouraged. Unless a unique identification system is in place, it will be substantially more difficult to correct medication errors in the prescribing of biological medicines and any biosimilar versions, and to ensure that products can be traced quickly and efficiently to avert an impact on patient safety.

**BIO recommends the following approaches for addressing the concerns described above:**

- **Development of distinct International Nonproprietary Names (INNs) for all biological medicinal products including biosimilars.** A distinct INN could consist of the same stem name as the innovator plus a unique suffix (such as “-alpha” or “-beta”).
- **Development of a political agreement among the European Commission and Member States to include biological medicinal products within a list of drugs that cannot be substituted by a pharmacist without prior consultation with a physician. We also urge the Commission to encourage Member States to require that for biological medicinal products a) marketing materials always include the distinct INN plus either the brand name or manufacturer name, and b) physicians include the brand or manufacturer name in all prescriptions.**

## **2. Each Biological Medicine Should Have an Original Label**

BIO believes that physicians and other healthcare professionals should be provided with specific information regarding each biological medicine in order to make an informed decision regarding the use of the product. Therefore, we believe it is essential that each biological medicine, and each biosimilar version of it, have its own individual or “original” label.

The original label for a biosimilar – as for any approved medicinal product – should be constantly supplemented throughout the life of the product with new safety information based on post-marketing clinical experience from the use of the product. Because biosimilars are “similar” but not “identical” to the innovative product, information in the

innovator's original label cannot be extrapolated to the biosimilar label, or vice versa. Furthermore, the label of the biosimilar may not contain, without appropriate authorization, any information that is still covered by patent law or other intellectual property rights.

### **3. Information About Product Substitution and Interchangeability Should Be Included in the Label**

Because biological medicinal products are each unique, switching patients from one such product to another may have important clinical implications, including safety implications. BIO believes that healthcare professionals and patients should be well informed about these potential implications, and that patients and their physicians should always be involved when any switch among such products is considered. Therefore, BIO recommends that information concerning product substitution and interchangeability be included in the original label for each biosimilar, and that competent authorities consider drafting requirements or guidance on the wording of such information.

We note that the U.S. Food and Drug Administration has permitted interchangeability only when two products are “therapeutic equivalents” as defined in *Approved Drug Products with Therapeutic Equivalence Evaluations* (the “Orange Book,” <http://www.fda.gov/cder/orange/obannual.pdf>), and that a biosimilar (follow-on protein product) and its respective reference product would not meet the Orange Book definition of therapeutic equivalents. In its Sept. 2006 paper on INN policies for biosimilars, cited above, the FDA states that it “has not determined how interchangeability can be established for complex proteins.” In BIO’s October 2005 comments to EMEA on its draft “Guideline on Similar Biological Medicinal Products containing Biotechnology-Derived Proteins as Active Substance: Non-Clinical and Clinical Issues” (CHMP/42832/2005) we asked EMEA to clarify that biosimilar medicines will not be considered interchangeable with the reference product “unless the EMEA affirmatively finds them to be so following scientific review, and that the EMEA will require robust data, including comparative clinical studies, to justify claims of interchangeability” (p. 6).

BIO would be pleased to work with regulatory authorities and other stakeholders to address the concerns identified in this position paper, and develop appropriate solutions that protect patient safety.

For more information please see <http://www.bio.org/healthcare/followon/>.

#### **About BIO**

BIO represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and 31 other nations. BIO members are involved in the research and development of healthcare, agricultural, industrial and environmental biotechnology products. For more information please see <http://www.bio.org>, or reach us at (US) 202-962-9200.