

**Proposal for a
Directive of the European Parliament and of the Council on
the application of patients' rights in cross-border healthcare**

EuropaBio's position paper on amendments 630, 631 and 633

Summary of position

Amendments 630, 631 and 633 (reproduced in Annex 1) have been tabled on Article 14 of the Cross-Border Healthcare Proposal, arguing for the introduction of identification of medical products on the basis of International Nonproprietary Names (INNs). Although this proposal could appear to represent a safe way to ensure that patients receive the correct product no matter what EU-member state their medications are dispensed in, EuropaBio is concerned that for biotechnology-derived medicines it could potentially have the opposite effect.

- **Biotech medicines are different from traditional small molecule medicines for example in their complexity molecular structure and weight. One major difference is that it is impossible to make exact copies – while with small molecule drugs one can make exact, generic copies.¹ As a result, the “similar, but not identical” nature of biosimilars raises questions about the INN prescription of biological products. Even small distinctions in any step from the cell line stage through to administration may cause different immunogenic responses in patients. These responses can be very acute and require a very prudent approach under medical control.**
- **The current INN system, whereby drugs with the same molecular structure (irrespective of their production processes) are given the same name, could easily lead to inadvertent substitution without the prescribing clinician being aware. It might therefore have clinical consequences and jeopardize patient safety and health outcomes. Therefore, inadvertent substitutions as abetted by amendments calling for compulsory INN prescription pose a potential risk to the patients' health, and interfere with the freedom of prescription of physicians.**

As a result, EuropaBio urges the honourable MEP to vote against amendments 630, 631 and 633, or support the inclusion of an exception clause for biological products.

About EuropaBio

EuropaBio's mission is to promote an innovative and dynamic biotechnology-based industry in Europe. EuropaBio, (the European Association for Bioindustries), has 68 corporate and 5 associate members operating worldwide, 4 Bioregions and 25 national biotechnology associations representing some 1800 small and medium sized enterprises.

Members of EuropaBio are involved in research, development, testing, manufacturing and commercialisation of biotechnology products and processes. Our corporate members have a wide range of activities: human and animal health care, diagnostics, bio-informatics, chemicals, crop protection, agriculture, food and environmental products and services. www.europabio.org

INN, biological medicinal products and amendments 630, 631 and 633

1. What is INN?

All medicines have an International Nonproprietary Name (INN), attributed to them by the WHO, and most have a brand name, too. Chemical pharmaceutical generics have the same INN as the originator product as they are exact copies of the originator – i.e. they are completely interchangeable. As such, prescribing chemical pharmaceuticals by INN does not pose any foreseeable health risks for patients.

More information about INN here: <http://www.who.int/medicines/services/inn/en/>

2. How are biological medicinal products different?

For biological medicinal products, the situation is different. Their production requires a high level of monitoring and quality testing: typically around 250 in-process tests are conducted for a biological, compared with around 50 tests for a traditional (chemical) medicine. The unique starting material and the complex manufacturing processes mean that it is not possible to exactly reproduce a biological in the same way a pharmaceutical (chemical) generic can be produced.

At European level, this has been officially acknowledged by the EMEA stating that: **“Biological medicinal products are usually more difficult to characterise than chemically derived medicinal products. In addition, there is a spectrum of molecular complexity among the various products (recombinant DNA, blood or plasma-derived, immunologicals, gene and cell-therapy, etc.). Moreover, parameters such as the three-dimensional structure [...] can be significantly altered by changes, which may initially be considered to be ‘minor’ in the manufacturing process. Thus, the safety/efficacy profile of these products is highly dependent on the robustness and the monitoring of quality aspects.”**¹.

As a result, although the objectives of the INN system – “clear identification, safe prescription and dispensing of medicines to patients, and communication and exchange of information among health professionals and scientist worldwide” – must be praised for generics, but not for biosimilars, EuropaBio is concerned that this system cannot be applied to complex biological products and particularly to ensure high standards of patient safety.

3. What would be an acceptable and safe solution?

The European Commission’s proposal for improving the EU pharmacovigilance system stresses the importance of being able to precisely trace a biological product. **Specifically, the Commission suggests that marketing authorisation holders should advise those completing adverse event reports to provide “the (invented) name and the batch number”**².

Also, in order to improve the pharmacovigilance of biological products including biosimilars, the Commission has proposed that Member States ensure that biological medicinal products that are the subject of adverse reaction reports be identifiable (i.e. traceable).

EuropaBio would like to see a revision of the INN nomenclature system so that each biotechnology-derived medicine is assigned a distinct INN.

¹ Guideline on Similar Biological Medicinal Products. Committee for Medicinal Products for Human Use (CHMP) European Medicines Agency. London. 2005. Available at: <http://www.emea.europa.eu/pdfs/human/biosimilar/043704en.pdf> (as consulted in February 2009)

² European Commission proposals to revise EudraLex Volume 9A. For more details please see: http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/docs/doc2008/2008_03/pc_vol9_03-2008.pdf (as consulted in February 2009)

Another alternative would be to ensure that biologicals are always commercialized with a brand name, the INN plus the manufacturer's name. No matter which of the two solutions is chosen, this would ensure that all – regulators, prescribers and patients alike – know exactly what medicine they are dealing with, and are able to track it back, also.

4. How are EU-Member States regulating in this field?

EuropaBio firmly believes in the freedom of prescription of physicians and also acknowledges that a number of countries such as France, Germany, Italy, Netherlands, Spain, Sweden and UK³, has either established legislative measures to prohibit the automatic substitution of biotech medicines or have given regulatory advice on the use of biologics (including prescription by brand).

The justification for such measures is that patient safety is put at risk. Biosimilars do not have the same set of safety/efficacy clinical data as original biological products and no clinical studies have been designed to assess the clinical outcome of repeated switches from a biological to its biosimilars.

EuropaBio calls for other countries allowing automatic substitution of generic medicines to take the necessary measures to prevent automatic and/or inadvertent substitution of biologics as they are not directly interchangeable. The European Parliament, on the grounds mentioned above, should reject the suggested amendments or support the inclusion of an exception clause for biological products.

More information about biosimilars, download the Europabio brochure *EuropaBio and Biosimilar Medicines* at:

http://www.europabio.org/Healthcare/documents/biosimilar_factsheet_December_2008.pdf

Contact:

Ludovic Lacaine

Healthcare Council Director, Europabio

Tel: +32 2 735 03 13

Email: l.lacaine@europabio.org

For more information: www.europabio.org

³ *Follow-On Biologics: Expect a Slow Start*, 2008, Morgan Stanley Research. As quoted by John Taylor in a letter to the US Federal Trade Commission. Available at: http://www.bio.org/letters/20081222_to_FTC.pdf (as accessed on February 2009)