

**Supplementary information to:  
Different Pharmaceutical Products need Similar Terminology, 2013**

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In order to support the writing of the terminology manuscript, a questionnaire was sent out to relevant stakeholders. These stakeholders included experts from regulatory authorities (e.g. EMA, FDA, CBG-MEB), large pharmaceutical industry (originator and generic), SMEs, other types of organizations (USP, WHO, EDQM, EGA) and hospital pharmacists. The responses varied from fully filled out questionnaires, to brief statements on general policies described on the website of these stakeholders, or reference to scientific publications on the terminology of biosimilars.

## Terminology matters!

(cf. Weise et al., Nature Biotechnology 29, 2011, 690-693)

### A questionnaire re the terminology used for biosimilars and non-biological complex drugs

#### Introduction/definition of the problem

Most of the terminology to be discussed in this questionnaire is used in the classical generic paradigm which considers two medicinal products bioequivalent if they are pharmaceutical equivalents or pharmaceutical alternatives and their bioavailabilities (rates and extents of absorption) after administration in the same molar dose are similar to such a degree that their effects, with respect to both efficacy and safety, will essentially be the same (EMA).

The determination of bioequivalence is based on a statistical comparison of two formulations of the same drug entity where the both one-sided 90% confidence intervals of the extent of drug absorption in healthy volunteers ( $AUC_{0-t}$ ) and  $c_{max}$  are within 80 and 125% of the reference product.

The goal of the bioequivalence studies is to show that the drugs are interchangeable with no risk for the patients. The terminology used for classical generics has also been adopted by other regulations, in particular concerning reimbursement, substitution and pharmacovigilance.

Whereas the term of bioequivalence is clearly defined, the application to compare pharmaceutical alternatives is also restricted to the classical small, well defined molecules. This is not more the case in complex medicinal products such as high molecular weight recombinant proteins or colloidal systems such as iron-sucrose nanoparticles or liposomes.

To enable the introduction of copies of the first original biological medicines after expiry of data protection or patents the EMA and other regulatory agencies have introduced the concept of biosimilar medicinal products and regulatory pathways for their market approval. These regulations themselves may have their ambiguities and lack of definitions. But the use of different terms has also led to questions at the level of selecting drugs for the patient, reimbursement policies (e.g., in reference pricing, drug safety, terminology in publications etc).

Very similar problems will occur with *non-biological* complex drugs (NBCD): Complex drugs other than biosimilars. Examples of NBCD, cf above, are iron sucrose complexes, glatiramoids and liposomes.

#### Goal

We are working on a paper to come to a global consensus on terminology concerning biosimilars and non-biological complex drugs.

#### Structure of the paper

The basis of the paper is to show that the classical generic paradigm - generic is bioequivalent and therefore exchangeable with the same efficacy and safety as the original does not apply to copies of biological medicines and non-biological complex drugs.

The paper is not only intended as a manual for regulatory authorities but also for editors and readers of scientific journals and health care professionals and decision makers re reimbursement.

Key terminology: two definitions to be challenged as a starting point

Non-Biological Complex Drug: a medicinal product, not being a biological medicine, where the active substance is not a homo-molecular structure, but consists of different (closely related) structures that can't be fully quantitated, characterized and described by (physico-)chemical analytical means.

Biosimilar: "A similar biological or "biosimilar" medicine is a biological medicine that is similar to another biological medicine that has already been authorized for use".

Could you be so kind and give definitions for the following terms being used in the framework of biosimilars and non-biological complex drugs?

Two drugs products are:

Identical.....

Therapeutic equivalent.....

Similar.....

Interchangeable .....

Exchangeable.....

Substitution(able).....

Switchable.....

Traceable.....

Other nomenclature relevant to this discussion .....

We would appreciate receiving your comments by October 21 2012.

Then, the first discussion re the results of this questionnaire will follow on Thursday October 27 2012, 10.30-12.00 am in Washington D.C. in the East Overlook Room during the AAPS meeting. You are welcome to attend this discussion.

Thanks in advance,

Yours,

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