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Eduardo Mysler & Morton Scheinberg

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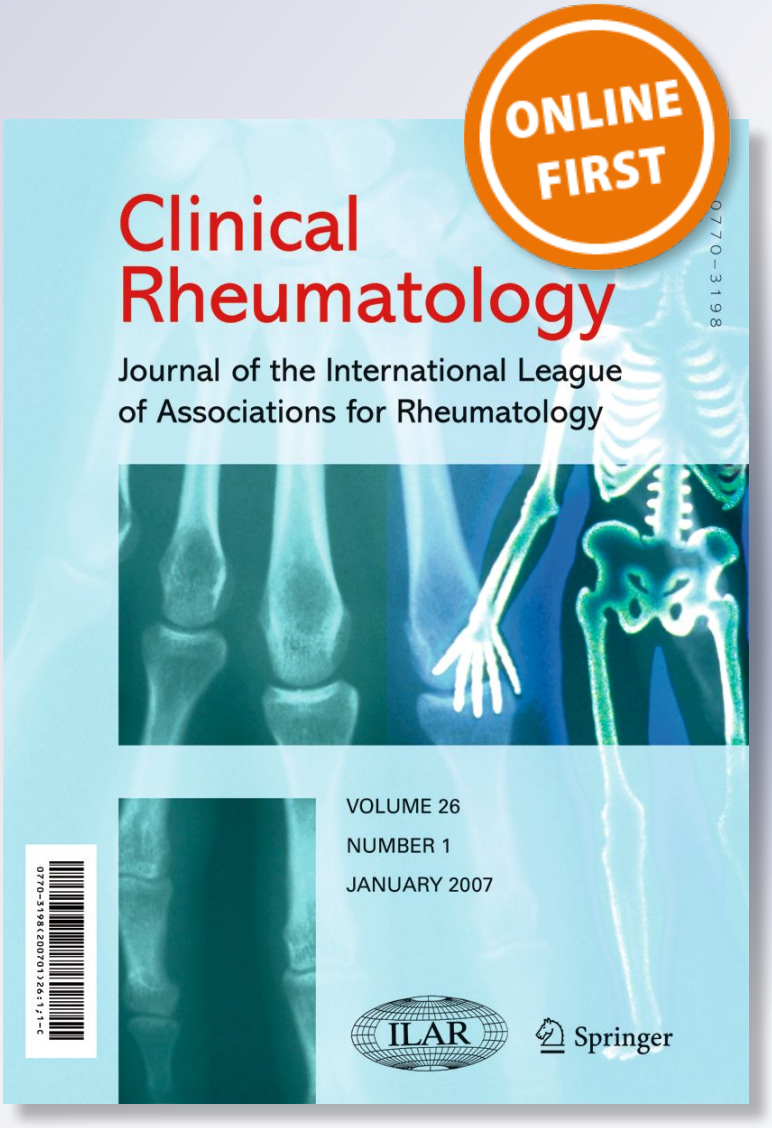

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EDITORIAL

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The treatment of inflammatory arthritis has been revolutionized in the past decade by the introduction of targeted biologic therapies. They are genetically engineered monoclonal or fusion proteins that could interfere with the biological activity of cytokines or inhibit T cell co-stimulation or could deplete B cell [1].

The patent for some of these agents that are currently used will soon expire, and a growing interest of the pharmaceutical industry is now in the development of "biosimilar" or copies of biological medical products. A copy which could claim to be a biosimilar to a reference or innovator, unlike a chemical generic, would not be identical depending on the chemical and biological characteristics of the molecule directly related to the manufacturing process which could not be precisely duplicated. Consequently, biosimilars would require an approach different from both originators and generics. Although biosimilars aim to mimic the innovator product in molecular size and complexity, during the manufacturing process, minor changes in production can have serious implications in terms of safety and efficacy [2].

Regulatory policy for biosimilars is being developed in several countries and in general following guidelines that were set up by the World Health Organization or the European Medical Agency. Besides general guidelines on quality, clinical issues are being defined and are continually being revised. They include indications of differences in the amino acid chain and glycosylation patterns on the biochemical quality side and the kind of clinical trial that would be require from the clinical side trying to measure efficacy and at the same time the possibility of extrapolation of indication. If a non-inferiority trial versus an equivalence trial would be required, it could affect not only the budget to develop the biosimilar but also the time of the launching as it will need many more patients. Also, the need for an extensive follow-up (for how long) to assure to the medical community the safety of the new drug and the possible immunogenicity is being debated. To perform the pharmacodynamic and pharmacokinetic assays previous or at the same time of the clinical trial is still not absolutely clear [3].

One of the main benefits of biosimilars should be a reduced cost when compared with the innovator. However, it is a general understanding that it will not be in the same order of magnitude as is in the cases of generic medicines due to elevated manufacturing costs and the need for extensive clinical and non-clinical studies. A growing interest in this area should be expected in the rheumatology community since the potential reduction in costs will lead to increasing number of patients having access to these drugs [4–7].

In Latin America, the regulation of biosimilars varies considerably between different countries, and in some the so-called biosimilars were approved before adequate clinical testing was performed. Others are in the process of creating their regulations. Some have decided to open the discussion with the academic community like in Colombia that after approving one biosimilar without clear guidelines is now creating and revising their own (Table 1).

Argentina has produced two different norms 7075 and 7729 from 2011 where it clearly states the requirement for well-defined non-clinical and clinical data to have the biological products approved and the 7729 where it states the requirement for biosimilars (http://www.anmat.gov.ar/boletin_anmat/noviembre_2011/Dispo_7729-11.pdf).

E. Mysler
Organizacion Medica de Investigacion,
Buenos Aires, Argentina

M. Scheinberg (✉)
Clinical Trials Section,
Hospital Abreu Sodré-AACD (a bone and joint hospital),
Sao Paulo, Brazil
e-mail: morton@osite.com.br

M. Scheinberg
Hospital Israelita Albert Einstein,
Sao Paulo, Brazil

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Table 1 Intended copies of biologics in Latin America licensed without biosimilar regulations

Etanercept (Etanar)	Manufactured in China	Licensed in Colombia
Rituximab (Reditux)	Manufactured in India	Licensed in Bolivia Chile and Peru
Rituximab (Kikuzubam)	Manufactured in Mexico	Licensed in Mexico

As in other countries, the problem with these Latin American guidelines is that they leave to the regulatory authority that is evaluating an individual drug the possibility of asking for more studies, double blind, randomized, or a simple clinical one arm study. This not only could create a double standard depending on who is presenting the dossier but also could place the patients at risk if all the so-needed assurance for the biosimilar are not cover

Resolution 55/2010 in Brazil has stated the ground for their approval of biosimilars. Although it is based on the WHO, it leaves to the regulatory authorities the decision on the type of study that will be required and other requisites that are crucial to produce a safe and efficacious drug [8].

Mexico has also their regulation reference (Articule 39 de la Ley Orgánica de la Administración Pública Federal y 222 Bis de la Ley General de Salud) that is even more vague in the requirements. It leaves to the regulatory authorities the need for clinical studies and the kind that will require for approval for individual drugs. There is even a statement which states that the closer the biochemical characteristics of the biosimilar to the innovator the less clinical proof of similar efficacy would be required. Still there is a requisite for clinical studies that compare the innovator with the biosimilar.

Costa Rica (Decree 37006 from Executive Power Thursday March 22nd 2012, point 5.6) has recently put in placed the regulation for biosimilars. Although it states that the Costa Rican authority is going to follow the FDA, WHO, or EMA guideless, it leaves again to the regulatory authority the opportunity to decide if another guidelines in some circumstances could be used to approve a certain drug.

The Chilean regulation, the closest to the WHO, requires preclinical and clinical studies for most of the biosimilars to get approval, but still leaves to the regulatory authority the final decision on the type of studies that should be required and the possible extrapolation of indications [9].

In summary, we are seeing a better situation that we had 5 years ago, where we had no regulation and some biosimilars were approved without clear studies to back them up. This new regulations is clearly welcome but more clear guidelines is needed. Biosimilars are a very needed resource in Latin American countries where we have a significant gap between the patients who have and the ones who do not have access to biological drugs. That gap should and must be closed but without putting at risk the same population that we are trying to help.

Disclosures None.

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