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DRAWN UP BY : Francesco Paolo Vatti, CET Group 5

SUBJECT: The situation of generic biotech drugs in Europe

PURPOSE: For information

TABLED TO: All Attendees



1. INTRODUCTION

After the elapse of patents, formerly patented drugs become available for any producer. Drugs identical to already authorised can have accelerated authorisation procedures in many Countries.

First patents about biotech drugs are now elapsing and new drugs are becoming available to any producer. So, the problem of the authorisation for marketing so-called “biogenerics” is arising. The potential world market for biogenerics has been estimated as ca. 1.5 billions Euro. A lot of firms are active in this field, particularly LG Chemicals (Korea), BioPartners (USA), Genemedix (UK), Cangene (Canada), Rijn Biotech (Holland), Wordhart (India), PC Gen (Argentina), Merck (Germany), Technopharma (Argentina), TEVA (Israel), RTG (USA), Biogenerics (Germany).

2. LEGAL FRAMEWORK

The legal situation in Europe is quite difficult to understand. The authorisation of generics is usually connected to their similarity to original drugs. However, an essential similarity is very difficult to assess, due to the highly complicated structure of such drugs. A rough legal framework was created in Europe in 2003 and several drafts of guidelines were proposed. A definitive version is expected relatively soon. Presently, rather than an essential similarity, which is usually very difficult to assess, a product comparability should be found in order to get an authorisation. This happened after realising that human growth hormone (HGH) can be synthesised from three different sources, getting anyway the same 191 amino acid sequence (comparability of product).



Nowadays the Directive 2004/27/EC indicates that as generic drug, a drug having the same qualitative and quantitative composition and the same pharmaceutical form as well as a biosimilarity with the reference drug is to be meant (art. 10(2)b). The biosimilarity should be shown through bioavailability tests.

According to art. 10(4), when a biotech drug does not fall in the above referenced provision of art. 10(2)b, for instance due to a difference in raw materials and/or in production process, results of preclinical tests and of clinical trials should be provided to the European Medicines Agency (EMA). A list of requirements is in Annex I of the Directive. Particularly, toxicological and clinical profiles must be provided.

EMA provided no accelerated process for getting authorisation and a new trial is usually required. Indeed, in addition to what has been described above, Art. 14(9) of Regulation (EC) No 726/2004 states that when an application is submitted for a marketing authorisation in respect of medicinal products for human use which are of major interest from the point of view of public health and particularly from the viewpoint of therapeutic innovation, the applicant may request an accelerated assessment procedure, while duly substantiating the request. However, it is presently expected by EMA that similar biological medicinal products would be of no major interest from the point of view of public health and particularly from the viewpoint of therapeutic innovation. This queer reason (how is it possible to know *a priori* whether an entire class of products will be of interest or not?) prevented EMA to set up an accelerated process.

3. AUTHORISATIONS OF BIOGENERICS IN EUROPE

Some biogenerics have already been submitted for authorisation in Europe: in particular Alpheon (recombinant human Interferon-alfa-2a, by BioPartners GmbH),



Omnitrope (somatropin, By Sandoz GmbH) and Valtropin (somatropin, by BioPartners GmbH).

EMA gave a negative opinion for the authorisation of Alpheon in June 2006, since it found major concerns about quality and identified differences between Alpheon and the reference product (Roferon-A) in the quality and clinical comparability exercise.

Both Omnitrope and Valtropin received their authorisation in April 2006, after 12 month trials, according to which they proved similar and with no further side effect with respect to the reference product (Genotropin for Omnitrope and Humatrope for Valtropin).

4. A FEW COMMENTS

From the above, it is apparent that European authorities do not see biotech generic drugs as particularly important for public health and they do not intend, at least presently, to provide an accelerated path for their approval. Valtropin requested 12 months for its authorisation.

It is questionable if the situation is in fact like European authorities think. If generic drugs are useful for public health, due to the availability of important active ingredients at price lower than brand drugs, it is not clear why the same should not apply for biotech drugs.

On the other hand, it is presently not clear which could be the interest of FICPI in this respect. A discussion on this point, at least among European members, could be advisable in order to set a FICPI position on this important matter.