IPQ INTERNATIONAL PHARMACEUTICAL QUALITY
Inside the Global Regulatory Dialogue

IPQ "In the News," August 21, 2010

Biosimilar Products, Guidelines and Requests for Scientific Advice Continue to Increase in EU

The European Medicines Agency (EMA) portfolio of approved biosimilar products and guidelines and the related requests for scientific advice continue to expand, with interest increasing in particular in monoclonal antibodies.

The EMA is in the process of adding four more biosimilar product-specific guidelines: A new guideline on recombinant erythropoietins (EPO) was cleared in March to become effective in October, and new guidelines are under development on monoclonal antibodies, follitropin alpha (recombinant follicle stimulation hormone) and interferon beta.

Concept papers on the latter three have gone out for comment. The monoclonal antibody comment period ended in January and the period for follitropin alpha and IFN-beta closed in June. These four will accompany the agency's existing guides on recombinant human insulin, somatropin, granulocyte-colony stimulating factor (GCSF), low molecular weight heparin, and interferon-alpha.

These product class-specific guidelines address clinical, non-clinical and bioassay issues and fall under EMA's overarching "Guideline on Similar Biological Medicinal Products," released in late 2005. The umbrella guideline is accompanied by separate guidelines addressing quality and clinical/non-clinical issues for biosimilars, respectively, which were both released in mid-2006.

The number of biosimilar marketing authorization applications (MAAs) evaluated by EMA has reached 18. Of these, 14 have been approved, one turned down and three withdrawn.

The approvals have come in clusters for particular product classes:

● The first biosimilar authorizations in the EU were somatropin products from Sandoz and Biopartners, beginning with Sandoz' Omnitrope in April 2006.

● EMA's Committee for Medicinal Products for Human Use (CHMP) turned down the authorization of Biopartners' interferon alfa application filed in June 2006, which the company has indicated it intends to refile.

● In the 2007 timeframe, epoetin alfa authorizations were approved for Sandoz, Hexal, Medice, Stada and Hospira.

● In late 2007, Marvel Life Sciences withdrew its applications for short, intermediate and long-acting forms of recombinant human insulin.

● A series of filgrastim approvals in the EU began with a Ratiopharm product in February 2008. Biosimilars of the neutropenia therapy have subsequently been cleared for CT Arzneimittel, Teva, Hexal, Sandoz, and most recently for a Hospira filgrastim biosimilar in June.

The requests to the EMA from companies for scientific advice on biosimilars have been steadily rising as well. Advice was provided related to 13 applications in 2009, up from 2 in 2003..

The requests indicate an increasing interest in monoclonals in particular. Reflecting this interest, EMA held a well-attended workshop in July 2009 to focus on the issues in biosimilar monoclonal development.

Addressing biosimilars as part of a presentation on EU regulatory challenges over the coming decade at a CASSS CMC Strategy Forum in Vienna in late May, retiring EMA Quality of Medicines Head John Purves highlighted the growing EU experience as an "important reference for other regions in the world as well." Purves commented that "it will be interesting to see how the global development of biosimilars occurs in the future."

[See the IPQ "In the News" companion story for further insights from Purves at the Vienna forum on the challenges the EMA faces in regulating biosimilars, advanced therapies, personalized medicines, variations and QbD, and the need for increased industry/regulator dialogue to help address them.]