The aims of new European Union pharmaceutical rules - by Linda Horton *et al* *

The new European Union rules on pharmaceuticals were published on April 30, 2004 (*Marketletters passim*), cover the authorization and regulation of human and veterinary medicines, provides for an increased role for the renamed European Medicines Agency and aims to speed up product approvals.

Furthermore, the new rules simplify authorization procedures and improve transparency without changing the basic principles of the existing system, in which a centralized authorization procedure exists alongside a decentralized procedure based on mutual recognition.

New rules also simplify authorization procedures and improve transparency without changing the basic principles of the system

The package consists of the following:

- regulation on authorization and supervision of medicinal products for human and veterinary use and on the EMA (replacing Regulation 2309/93 which set up the European Agency for the Evaluation of Medicinal Products);

- a directive on the community code relating to medicinal products for human use (amending the previous Directive 2001/83/EC);

- a directive on the community code relating to medicinal products for veterinary use (amending Directive 2001-/82/EC); and

- a directive on traditional herbal medicinal products (amending the community code Directive 2001/83/EC).

Timeframe for implementation

The three directives entered into force on April 30, 2004 (the date of official publication). Member states of the EU have until October 30, 2005, to implement these measures in national law.

The regulation on authorization and supervision of medicinal products is directly effective in the national law of the member states. No additional implementing legislation at the member state level is needed.

This regulation entered into force on the May 20, 2004 (the 20th day following its official publication). However, most of its provisions do not apply until November 20, 2005.

Authorization and supervision of medicinal products

Under the new regulation, assessment of new medicines by the EMA will be quicker, which will enable new medicinal products to be placed on the community market faster.

The authorization procedure will be changed so that more categories of medicine will be obliged to use the centralized procedure instead of seeking authorization in, first, a "reference member state" then in other member states through the decentralized mutual recognition system.

Currently, the centralized procedure must be used for the authorization of biotechnology products. Under the new rules, the centralized procedure becomes mandatory for medicines to treat AIDS, cancer, diabetes, neurodegenerative disorders and orphan diseases and, after four years, this procedure will be further extended to cover medicines for autoimmune and viral diseases. A general review clause will enable further extension of the EMA exclusive jurisdiction to medicines for other diseases.

Increasing and accelerating the availability of products

A "fast-track" registration procedure for products of significant therapeutic interest has been introduced, allowing these products to be assessed and authorized in an expedited way.

In addition, the possibility of a conditional marketing authorization has been introduced, which allows for a one-year authorization to be granted, provided that there is an important expected health benefit for the patients concerned and that the company agrees to carry out additional monitoring and clinical studies, which will be reviewed at the end of this period.

Finally, subject to further additional provisions, a European-wide system to make medicinal products available in advance of authorization for a compassionate use will also be possible. This will help to ensure that patients might be allowed to have access to products still undergoing investigation even if there are no clinical trials performed on the product in that country.

Better access to information for patients

The revised legislation provides for an overall increase in transparency and improves access to more information on the results of the pharmaceutical decision-making process, including assessment reports and the summaries of product characteristics.

Promoting innovation and clarifying generics regulation

One of the biggest changes brought by the new legislation is in the area of regulatory data exclusivity, which will now be harmonized across the 25 EU countries in a compromise policy called "8+2+1." Data submitted by companies for the approval of medicines will be protected

for 10 years across the EU from the time of first authorization. Therefore, it will not be possible to market generics until 10 years have elapsed.

This can be extended by an extra year if a further innovative indication for the medicine is authorized. It is, however, possible for a generic company to submit an abridged application, seeking to rely upon the innovator's data, eight years after the date of the marketing authorization of the innovative product. This improves the current situation in many countries in the EU 25 that at present only offer six (and in some cases three) years protection.

The aim of this change is to allow pharmaceutical companies more time to recoup investments made in research, before a generic product may be authorized, and thereby encourage innovation. The new "8+2+1" formula applies only to medicines approved after the legislation's effective date.

Regarding the generic pharmaceutical sector, the new "Bolar" rule introduces, for the first time, the possibility for companies to start development work on a product while the innovator's product is still under patent protection.

Clearer definitions

The new directives clarify key definitions and the scope of Directives 2001/83/EC and 2001/82/EC. The definition of "medicinal product" now clearly includes new therapies and the growing number of so-called "borderline" products between the medicinal product sector and other sectors.

The new definition specifies the type of action that the medicinal product may exert on physiological functions. It covers medicinal products such as gene therapy and radiopharmaceutical products, as well as certain medicinal products for topical use.

In order to clarify situations where a given product falls not only within the definition of medicinal product but also of other regulated products, the new directive will not be applicable where a product comes clearly under the definition of other product categories (food, food supplements, medical devices, biocides, cosmetics, *etc*).

Generic medicinal product is defined as "a medicinal product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies." This should provide greater legal certainty and better application of the regulatory procedures for generic medicines.

Traditional herbal medicinal products

The new directive provides for a simplified registration procedure for traditional medicinal products requiring fulfillment of European standards of quality, safety and efficacy. This harmonized procedure is aimed at safeguarding public health while ensuring free competition of products in the EU market.

Conclusion

Although most changes will not become effective until sometime in 2005, due, in part, to the accession of the 10 new member states, certain changes took place soon after publication of the new laws and those who deal with EU pharmaceutical issues are already modifying their vocabulary.

The EMEA has become the European Medicines Agency. Its Committee on Proprietary Medicinal Products has become the Committee on Human Medicinal Products. The composition of the CHMP will be revamped to make room for the 10 accession states.

The new legislation includes many important changes in the EU legislative framework for both regulation of product quality, safety and efficacy and also for innovator and generic rights.

These developments have potentially significant implications for pharmaceutical companies selling their products in the EU, particularly those exporting products from the USA to Europe.

**** Linda Horton is a partner at the international law firm Hogan & Hartson; also contributing to this article were: Wim Nauwelaerts, Klaus Goecke, Jacqueline Mailly, Gugliemo Adninolfi and Jamies Tomhave.***