Global authorisation: Intention and Reality

Elisabethann Wright

The declared purpose of the 2001 Community Code on Medicinal Products was, in the interests of clarity and rationalisation, to codify and consolidate into a single text the existing EU legislative provisions on medicinal products for human use. But has the inevitable clash between the need for innovation and the desire for economic benefits from generic medicines clouded the issue? Elisabethann Wright examines the debate.

When the European Commission proposed a modification to the Community Code[1] it included a justification in the Explanatory Memorandum that accompanied the proposal for the addition of a definition of the terms "generic product" and "reference medicinal product" as necessary in order to bring the text into line with "commonly accepted terminology".

While this explanation suggests that the additions were simply for purposes of consolidation, justification for other modifications in the revision of the Community Code included the European Commission's belief that it was necessary to maintain an appropriate balance between innovations and the need to favour the production of generic medicines.

The fourth preamble to the revision, adopted as Directive 2004/27/EC [2], repeats the previously declared view that the main purpose of EU regulation on the production and distribution of medicinal products for human use should be to safeguard public health, with the additional requirement that this objective should be achieved by means which do not hinder the development of the pharmaceutical industry or trade in medicinal products in the EU.

The promotion of the EU pharmaceutical industry is something that the European Commission continues to seek to promote, most recently by the Innovative Medicines Initiative. This Initiative is intended to overcome research bottlenecks in the drug development process by promoting new methodologies and tools that are better at predicting the safety and efficacy of possible new drugs and medicines.

Nevertheless, the result of Directive 2004/27/EC, as it was finally adopted, may be to discourage, rather than encourage, achievement of at least some of the aims of the Community Code, particularly as regards the development of the EU innovative pharmaceutical industry.

This may, in particular, result from the introduction of the principle of "global marketing authorisation" by Directive 2004/27/EC. If this principle continues as it is currently interpreted by Member States, its implications for the encouragement of innovative pharmaceutical development in the EU will be the inverse of what it apparently aims to achieve.

According to the 14th preamble to Directive 2004/27, "since generic medicines account for a major part of the market in medicinal products, their access to the Community market should be facilitated in the light of the experience acquired".

There is no doubt as to the benefit that generic medicinal products bring. However, it must be questioned whether the negative consequences that the new provisions governing "global marketing authorisation" have for innovative products are proportionate to the benefits that generic medicinal products reap from the new legislation.

The definition of a "generic medicinal product" in the original proposal for a modification of the Community Code that was subsequently adopted as Directive 2004/27/EC reflected the definition of an "essentially similar product" provided by the European Court of Justice in its case law. This original definition of "generic product" was limited to medicinal products with the same qualitative and quantitative composition in active principles and the same pharmaceutical form as their reference product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability tests. The various immediate-release oral pharmaceutical forms were deemed to be one and the same pharmaceutical form.

However, by the time Directive 2004/27/EC was adopted, the definition of a generic product had evolved. As a result, the different salts, esters, isomers, mixtures of isomers, complexes or derivatives of an active substance were considered to be the same active substance, unless they differed significantly in properties with regard to safety and/or efficacy.

The revision further provided that, when a medicinal product had been granted an initial marketing authorisation, any additional strengths, pharmaceutical forms, administration routes, presentations, as well as any variations and extensions would also be granted such an authorisation or be included in the initial marketing authorisation. All these marketing authorisations were to be considered as belonging to the same global marketing authorisation, in particular for the purpose of an application for generic authorisation[3].

One could expect the European Commission to argue that the provisions of Directive 2004/27/EC that introduce the possibility for an additional year's data protection for new therapeutic indications – that bring a significant clinical benefit and an improvement to the quality of life and welfare of the patient – are intended to encourage the development of the pharmaceutical industry. However, apparently applying the European Commission's belief that it is, however, necessary to maintain an appropriate balance between such innovations and the need to favour the production of generic medicines, it is foreseen that this extra year will only be granted in the cases where the new indication is authorised during the first eight years of the ten years data protection period. The aim, according to the Explanatory Memorandum, is not to hinder the emergence of a generic market.

continued...

One of the results of this increased generic right is a need for applicants seeking marketing authorisation for innovative products to take some basic commercial decisions earlier in their strategy than they would, perhaps, have preferred. There is now a need to determine early in the process which of two avenues is the more commercially advantageous.

One such avenue is to submit a first application for marketing authorisation that covers a variety of therapeutic indications. This could permit the innovator, in an attempt to recoup the cost of investments, to exploit as many avenues as possible during the eight-year data protection/ten-year market production period provided by the Community Code. However, it also provides generous opportunities to generic manufacturers once these periods have expired.

Another avenue is to limit an initial application for marketing authorisation to one or a few therapeutic indications. This may, in principle, leave open to the innovator the opportunity to subsequently license the medicinal product to a third party to develop it for different therapeutic indications. However, in light of the provisions of Directive 2004/27/EC referred to above, which include all subsequent variations or extensions of the original authorisation within the global authorisation available to generic applicants, such licences would appear to have diminished commercial value. If the global authorisation provisions are to be interpreted as meaning that any new therapeutic indication for which the innovative product is approved is essentially to be considered part of the initial marketing authorisation, any subsequent therapeutic indication developed by a third party would appear not to be entitled to individual data and market protection.

It is arguable that, as a result, at least one of the declared intentions of the Community Code, that of supporting the innovative pharmaceutical industry, rather than being encouraged, risks being undermined. Innovative manufacturers are being faced with an invidious choice between an initial wide-ranging marketing authorisation application that may, depending on the nature of the medicinal product, be impossible to achieve in practice, and a gamble on the – increasingly unlikely – possibility of licensing a medicinal product to a third party with the possibility of developing the product further for an additional therapeutic use with accompanying data and marketing protection. The generic industry, on the other hand, is being presented with a wide selection of ready-made authorisations immediately following the expiry of the protection related to the initial authorisation of the innovative product.

This interpretation of the Community Code in its current form will undoubtedly contribute to another of the declared aims of the European Commission, the enhancement of access by generic products to the EU market.

The question must be asked, however, whether this is what the EU institutions intended to achieve by the 2004 revision to the Community Code.

One is tempted to make a comparison between the effects of these provisions of the Community Code, which will arguably discourage innovation in the EU, with the unintended but tangible effects of the provisions of Directive 2004/40/EC[4] concerning the exposure of workers to the effects of electromagnetic fields. The intended and laudable intention of Directive 2004/40/EC was to introduce exposure limit values to protect workers from all "*known short-term adverse effects in the human body…*" associated with electromagnetic fields. One of the effects of the Directive in practice is, however, to almost entirely exclude the use of MRI scanners in the EU.

It is acknowledged that exclusion of the use of MRI scanners was an unforeseen, but tangible, effect of the provisions of Directive 2004/40/EC and steps are being taken to address this consequence. Arguably, the unforeseen but tangible negative effect of the global authorisation on the EU innovative pharmaceutical industry needs to be equally recognised and addressed. ❊

Elisabethann Wright is Counsel at international law firm Hogan & Hartson's Brussels offices

---

[1] Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community Code relating to medicinal products for human use

[2] Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use

[3] A foot note in the European Commission's Notice to Applicants suggests that the concept of the "global marketing authorisation" originated from the decision of the Court of Justice in C-106/01 Novartis. This seems to be a remarkably wide interpretation of the conclusions of the Court in that judgement.

[4] Directive 2004/40/EC of the European Parliament and of the Council of 29 April 2004 on the minimum health and safety requirements regarding the exposure of workers to the risks arising from physical agents (electromagnetic fields) (18th individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC).