Centralised authorisation of a generic product: but a generic of which product?

Elisabethann Wright

On 10 April 2006, the European Commission granted the first central authorisation for a generic version of a veterinary medicinal product. The event passed almost unnoticed, says Elisabethann Wright.

The authorisation resulted, however, in unfortunate consequences for the holder of the marketing authorisation for the reference product on which the approval of the generic product was based. The company would rightfully have expected a full 10-year period of protection under the original Regulation 2309/93, which governed its authorisation. Instead, its data protection period was reduced to just over eight years.

If the approach adopted by the European Commission in this case represents future Commission policy, it must create discomfort for holders of centralised authorisations for innovative products concerning the extent of the period of protection that they can expect these products to merit. This concern is in no way limited to veterinary products. Producers of human medicinal products might likewise encounter shorter than expected periods of protection for products whose marketing authorisations were submitted before the new EMEA Regulation took full effect on 20 November 2005. This result is neither legal nor fair.

The veterinary authorisation in question was granted in April 2006 to the company Omnipharm for a product called Flexicam. The Flexicam authorisation was for a generic version of the Boehringer Ingelheim product Metacam. The Flexicam authorisation covered a 1.5mg oral suspension for dogs.

Metacam had been initially approved at national level in several EU Member States. According to the European Public Assessment Report for Metacam, the product was eligible for grant of a Community marketing authorisation via the centralised system as it is a product intended for food-producing animals and its active ingredient, meloxicam, had not been authorised for use in food-producing animals on the date of entry into force of the original EMEA Regulation No 2309/93 (i.e. on 1 January 1995), as provided in Part B of that Regulation's Annex.

Consequently, on 7 January 1998, the European Commission issued a marketing authorisation, valid throughout the EU, for the veterinary medicinal product Metacam 5mg/ml solution for injection for cattle.

As the Metacam 5mg/ml solution for injection for cattle had thus been assessed under the centralised procedure, the European Commission deemed it necessary for the companion animal product also to be brought under the umbrella of the first authorisation. The companion animal products that were on the national markets of the EU Member States at that time were withdrawn once the centralised application was authorised.

The data protection provisions of Article 13(4) of the first Regulation 2309/93 provided that:

"Medicinal products which have been authorised by the Community in accordance with the provisions of this Regulation shall benefit from the 10-year period of protection referred to in point 8 of the second paragraph of Article 4 of Directive 65/65/EEC".

The new EMEA Regulation 726/2004 both repealed and replaced Regulation 2309/93. The new Regulation modified what was said in Article 13(4) and moved this provision to Article 14 (11). The new provision now provides that medicinal products authorised in accordance with the centralised procedure are to benefit from an eight-year period of data protection. However, the period of market protection remains at 10 years, with the possibility of an additional one-year extension, where a new indication is authorised according to a certain timetable.

Considering all this, following its product's authorisation in accordance with the centralised procedure under the original EMEA Regulation, Boehringer Ingelheim should have been entitled to expect that Metacam, in all its forms, would benefit from 10 years' protection from generic competition. This would mean protection until January 2008.

The generic authorisation of Flexicam, granted as it was in April 2006, was evidently within the 10-year protection period to which Metacam should have been entitled, according to a traditional interpretation of Article 13(1) of Regulation 2309/93. However, despite the fact that the European Commission, according to its own publications, can grant a generic authorisation only to generic versions of reference products that are themselves the subject of a central authorisation, the Commission apparently chose not to base its calculation of the protection period to which Metacam was entitled upon this provision. Rather, it chose to base its calculation on a period linked to a previous national authorisation.

The net effect of this, and of the authorisation of Flexicam earlier this year, was to deprive Metacam of part of the 10-year protection period that, as a product authorised in accordance with the centralised procedure, it should have been entitled.

The approach adopted in this case seems essentially to suggest that, on one hand, the European Commission has the power to grant a centralised authorisation for a generic of a nationally approved product, and yet, on the other hand, it has the power to ignore the protection period granted by EMEA Regulation 2309/93 to a product that it had, itself, previously authorised. The question arises as to whether there is a valid legal basis for such an approach.

The power of the European Commission to approve medicinal products in accordance with the centralised procedure was initially laid down in Regulation 2309/93. This Regulation was subsequently repealed and replaced by Regulation 726/2004[1]. However, the type of medicinal products that the Commission is permitted to authorise, in accordance with the centralised procedure, continues to be strictly dictated by its provisions.

Article 3(1) of Regulation 726/2004 identifies the types of products that must, by obligation, be authorised according to the centralised procedure. Article 3(2) of the Regulation identifies the types of product that may, at the option of the applicant, be the subject of an application for authorisation in accordance with the centralised procedure, provided it fulfils the criteria which that Article provides.

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The ninth recital in the preamble to the Regulation suggests that the optional procedure is open to generic products *"provided they are authorised from the outset at Community level"*. This position is generally reinforced by European Commission literature related the authorisation of generic products. As an example, according to the Notice to Applicants, authorisation according to the centralised procedure will be granted to *"a generic medicinal product of a centrally authorised medicinal product if not using the option in Article 3(3) of Regulation (EC) No 726/2004"*[2]. Article 3(3) permits competent national authorities to authorise generic versions of a centrally authorised product, provided that certain criteria are fulfilled.

It is possible that, under the new provisions introduced in Article 3(3), the European Commission will be able to authorise generic versions of innovative products initially authorised at national level in the Member States, provided that they fulfil the criteria laid down in that Article. However, nothing in the available information relating to Metacam suggests that these criteria were fulfilled in the present circumstances or that the Commission chose to exercise this power. By limiting the protection period that accompanies Metacam's centralised authorisation, not only is the Commission acting contrary to the specific provisions of the EMEA Regulation, but it is essentially authorising a generic product of a nationally authorised product through the centralised procedure.

This approach begs the essential question of the extent of the European Commission's power to authorise generic medicinal products through the centralised procedure. Specifically, from where does the Commission find a legal basis for its claimed power to authorise – through the centralised procedure – generics of products authorised through a national procedure that do not fall within the criteria in Article 3(2) of Regulation 726/2004? Were the requirements of Article 3(2) satisfied in the Flexicam application for centralised authorisation and acknowledged by the EMEA in accepting the application?

The European Commission is governed by strict provisions in Regulation 726/2004 concerning the type of innovative products that it may approve in accordance with the centralised procedure. Its approval of Flexicam before the expiry of the 10-year data protection granted to Metacam by Article 13(4) of Regulation 2309/93 suggests that it does not, apparently, consider itself to be governed by the same provisions when it comes to generic products. This raises concerns on two levels.

First, a legislative distinction has been established between the role of the European Commission and the role of the competent authorities of the Member States in the authorisation of medicinal products. If the authorisation of Flexicam signals the adoption of a policy position on the part of the Commission, the distinction between the roles of the institutions will be undermined. If the Commission were permitted to approve generics on the basis of prior national authorisations, the question arises as to whether it considers itself entitled to approve the same products that competent national authorities can approve – provided these are generic products. Such a result would inevitably lead to confusion, both for the relevant authorities and for applicants for marketing authorisation.

Second, the entitlement of Metacam to a 10-year period of protection has been diminished by the approach that has been adopted by the European Commission in the present case. There is no evident provision in either Regulation 2309/93 or Regulation 726/2004 on which this decrease can be justifiably based. If, again, this signifies a policy decision on the part of the Commission, all holders of central marketing authorisations, whether these are for veterinary products or for human products, should be concerned about the period of protection that they can expect for their product. This concern would relate particularly to products that were subject to a previous national authorisation granted in an EU Member State. ❊

Elisabethann Wright serves as counsel at international law firm Hogan & Hartson's Brussels office

[1] Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency.

[2] Volume 2A Procedures for marketing authorisation Chapter 1 Marketing Authorisation, 2.2, November 2005. ❊

Poland says no to human embryonic stem cell research

The Polish health ministry has decided to review the current Act on Family Planning and the Protection of Human Life with a view to banning research conducted on stem cells procured from human embryos. The draft Act, prepared jointly of the health and science ministry, is expected to be ready in September 2006.

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The current Act on Family Planning already includes paragraphs aimed at the protection of human life from the moment of conception, which indirectly bans embryonic stem cell research because it inevitably leads to the destruction of embryos, the Polish science ministry explains. This is also reflected in the decision of the Polish Constitution Tribunal of 28 May 1997. At the moment, however, there is no regulation in Poland that would directly ban human embryonic stem cell research. Therefore, the science ministry believes, it is necessary to introduce a separate paragraph to close the "loophole" and prevent the legislation from being contested in the future.

The stimulus to revise the current legal status of embryonic stem cell research in Poland came from the EU Competitiveness Council's July meeting during which the final version of the se venth framework programme (FP7) was agreed. The FP7 provides for financing of embryonic stem cell research from EU funds.

Poland, together with Slovakia, Austria, Lithuania and Malta, was against the programme because of this provision. According to the Polish government, the risk associated with the procurement of the stem cells outweighs the benefits such research could offer. It also argues that the society will not be able benefit from the results of the research in the near future, therefore conducting the research cannot be justified from the ethical point of view. ❊