EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Health systems and products
Medicinal products – authorisations, EMA

PHARM 620

PHARMACEUTICAL COMMITTEE
27 March 2013

Subject: **Interpretation of Pharmaceutical legislation – ECJ judgments**

Agenda item 4.a)

- **Case T-539/10, judgment of 7 March 2013, Acino v Commission**

By this judgement the Court dismissed Acino's request to annul Commission decisions that prohibited the supply, ordered the recall and varied the central marketing authorisation of several medicinal products for human use following a 'Good Manufacturing Practice' (GMP) Inspection' that discovered critical deficiencies in the production process of the active substance supplier in India. The Commission decisions consisted of provisional and final measures in the framework of an Article 20 referral.

As far as the legal side is concerned an interesting discussion point was whether GMP non-compliance can lead to the conclusion that "the qualitative and quantitative composition of a product is not as declared", which is one of the grounds in EU legislations that allows the Commission to act on the product and the marketing authorisation (Articles 116/117 of Directive 2001/83). The applicant took the view that the Commission would have to prove rather a concrete risk than a potential risk that the composition is not as declared. In its ruling the General Court followed the Commission approach that a potential risk is sufficient: " *S'il est vrai que de telles infractions graves [aux bonnes pratiques de fabrication] ne conduisent pas automatiquement à une atteinte à la composition qualitative et quantitative déclarée des médicaments concernés, il n'en demeure pas moins qu'elles impliquent, en tant que telles, un risque potentiel d'atteinte à cette composition et, ainsi, à la santé publique. (…) En effet, il y a lieu de relever que la Commission peut se limiter à fournir des indices sérieux et concluants, qui, sans écarter l'incertitude scientifique, permettent raisonnablement de douter de la composition qualitative et quantitative déclarée des médicaments en cause." (Para. 66)*

When verifying the legality of the EMA scientific opinion as part of the Commission decision the Court continues to exercise a quite detailed assessment, especially as regards its internal consistency and whether it establishes a comprehensible link between the

medical and/or scientific findings and its conclusions. It underlines again the importance of the quality of the scientific opinion.

- **Case C-535/11, Opinion of the Advocate-General of 31 January 2013, Novartis**

In the case at hand, the Court is asked to interpret the rules governing the placing of medicinal products for human use. The issue concerns a product for which company A has obtained a marketing authorisation under which, inter alia, the product is to be marketed in containers of a specified size. Company B then takes that product, draws it off into a smaller container and sells it against a medical prescription for an individual patient. The process does not lead to the product being changed in any way. Company B sells the product in that form without being in possession of a marketing authorisation. Is it entitled to do so?

The case relates to two centrally authorised products: Lucentis and Avastin, which both contain as active substance a growth inhibitor. Both products were used in the EU to treat patients with wet age-related macular degeneration; only Lucentis is authorised for this indication, though. Avastin, being the older of the two products, was used to treat AMD 'off-label' before Lucentis became available. However, it seems that it is continued to be used in several Member States for that indication.

In Germany, a company (Company B) tried to 'facilitate' the off-label use of Avastin by providing pre-filled syringes. Additionally, it offered pre-filled syringes of Lucentis drawing-off the content from the original vials into several sterile syringes. In doing so the company was able to produce several syringes/injections from one vial, with the respective effect on costs per unit (according to the SmPC only one vial per syringe should be used).

The company was taken to Court in Germany by the marketing authorisation holder with the purpose of stopping this activity, basically arguing that such modification of the products, if at all, could only be done by a marketing authorisation holder.

In its opinion the Advocate-General (AG) agreed that the operations of company B cannot be carried out without acquiring a separate marketing authorisation.

It would follows from Article 6(1) of Directive 2001/83 that if those operations/modifications to the product would have been offered by the marketing authorisation holder, the MAH would have needed a variation given that the requirement to obtain authorisation covers not only the initial placing of the product on the market but also any modification to the product. The AG argues that it would be illogical if a third party would be able to do the same modification without a marketing authorisation/variation. This would run counter to the aim of Directive 2001/83 to exercise control over the entire chain of distribution and could also be used to circumvent the general authorisation requirement.

Finally, the AG considers that contrary to pharmaceutical undertakings hospital and healthcare professionals may rely on the exemption provided by Article 3(1) of Directive 2001/83 ("products prepared in a pharmacy"): "*it seems to me that the exemptions I have just described will, in the normal course, allow health care services to prepare medicines on behalf of individual patients, even if those activities would otherwise require a marketing authorisation to be in place"* (para. 76 of the opinion).

The ruling of the Court is expected for 11 April 2013.

- **Interesting pending cases**

Cases **T-472/12** and **T-67/13** (Novartis v Commission), a direct action against the Commission concerning the application of the global marketing authorisation concept to products that received separate marketing authorisations under the 'old' Regulation (EEC) No 2309/93.

Case **T-547/12** (Teva Pharma v EMA), a direct action against the European Medicines Agency on the application of the global marketing authorisation concept in case of fixed combination products.

Cases **T-29/13**, **T-44/13** (AbbVie v EMA) and **T-73/13** (InterMune v EMA), another direct action against the European Medicines Agency deals with the disclosure of clinical trial data, which were submitted as part of a marketing authorisation application, under access to document legislation (Regulation (EC) No 1049/2001).

Case **C-512/12** (Octapharma France), preliminary reference to the Court on the classification of blood products (plasma) and the interaction between the Medicinal Product Directive 2001/83/EC and the 'Blood Directive' (2002/98/EC).

Case **T-140/12**, a direct action against the European Medicines Agency, focuses on the correct interpretation of Article 8 of the Orphan Regulation (EC) No 141/2000, which defines the concept of market exclusivity for orphan medicinal products.

Case **C-109/12** is another "borderline-products" case, relating to a vaginal capsule containing live lactobacilli which is intended to correct bacterial imbalance in the vagina. The national Court essentially asks, whether a product which is regarded by one Member State as a medical device in accordance with Directive 93/42/EEC and is provided with a CE marking, may be classified by another Member State as a medicinal product within the sense of Directive 2001/83/EC.

Action to be taken:

For information