EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Health systems and products
Medicinal products – authorisations, EMA

PHARM 661

PHARMACEUTICAL COMMITTEE
22 October 2014

Subject: **Ongoing Court cases**

Agenda item 1a

- **Case C-269/13P, Judgment of 10 April 2014, Acino v COM**

Background: Following an inspection which revealed serious quality problems (GMP non-compliance) of a third-country API manufacturer for the company A., the Commission took measures to prevent any product that contained active substances produced in that factory from being placed on the EU market. In addition, the relevant marketing authorisations were modified (in the framework of an 'Article 20' referral) by deleting the factory from the list of authorised manufacturing sites.

The company considered these measures as being disproportionate; arguing that despite the quality problems in the factory, subsequent tests of the manufactured batches had shown that those problems did not affect the finished products. A. started therefore in 2010 an action before the General Court (first instance). In 2013 the General Court confirmed the position of the Commission. In July 2013 A. appealed against this decision before the Court of Justice. With its ruling of April, the Court dismissed the appeal.

Main considerations of the Court: The concerned Commission decisions were based on the conclusion that due to the GMP non-compliance it could no longer be considered that the "qualitative and quantitative composition" of the finished products was as declared. Such a deviation is one of the grounds allowing the Commission to vary, withdraw or suspend a marketing authorisation for a centrally authorised product or to withdraw the product form the market (Article 116/117 of Directive 2001/83).

While the Commission (based on the scientific opinion from EMA) has the burden of proof for such conclusion, the Court confirmed that the Commission is entitled to act on the basis of considerations which are "*based on solid and persuasive evidence to entertain reasonable doubts as to the declared qualitative and quantitative composition of the medicinal product at issue*" (para. 61). In view of the precautionary principle the Commission may act based on a potential risk. Non-compliance with GMP may constitute such a potential risk of impairment of the qualitative composition and,

therefore, of detriment to public health (para. 72). It was consequently justified to take action in the present case.

With its ruling the Court confirmed that competent authorities may suspend marketing authorisations or withdraw products from the market in case of serious GMP failures in a manufacturing site.

- **Case C-358/13 and C-181/14, Judgment of 10 July 2014, 'Legal highs'**

Background: The case centres on the scope of the definition of medicinal products by function and more particular on the term 'modifying' ("physiological functions") contained in the definition of medicinal product set forth in Article 1(2)(b) of Directive 2001/83/EC, for the purpose of ascertaining whether certain synthetic drugs ('legal highs') could be regarded as "medicinal products" within the meaning of the Directive. Those drugs elicit the effects of opioids, cannabinoids and other psychoactive substances. The emergence and spread of these substances, and the potential risks that they pose, have led national authorities to subject them to various restriction measures, including the classification as medicinal product.

Ruling: *The definition of medicinal products by function does not cover substances, which produce effects that merely modify physiological functions but which are not such as to have any beneficial effects, either immediately or in the long term, on human health, are consumed solely to induce a state of intoxication and are, as such, harmful to human health.*

Main considerations of the Court: Directive 2001/83 gives two different definitions of the term "medicinal product", a medicinal product by presentation and medicinal products by function. These definitions cannot be regarded as unconnected, they cannot be read a way as to render one element in conflict with another (para. 29).

The question referred by the national court concerns the words 'modify the physiological functions', which is used as part of the definition of a medicinal product by function. While the word 'modify' is neutral the Court states that it must be interpreted in a way that takes the purpose and scope of Directive 2001/83 into account. The Directive reflects the legislature's intention to highlight the beneficial effects which the substances concerned are meant to have on the functioning of the human organism and, as a consequence — be it immediately or over a period of time — on human health. The word 'modify' must, therefore, be interpreted as encompassing substances which are capable of having a beneficial effect on the functioning of the human organism and, as a consequence, on human health (para. 37).

Substances whose effects merely modify physiological functions and which are not such as to entail immediate or long-term beneficial effects for human health are not covered by the definition of a medicinal product.

The fact that the Court's conclusion will mean that the marketing of the substances at issue in the main proceedings may not be subject to criminal law sanctions cannot call that conclusion into question. The objective of imposing criminal law sanctions in respect of the introduction on the market of harmful substances cannot have any effect of the definition of the term medicinal product given in Directive 2001/83 or on any classification of such substances as medicinal products on the basis of that definition (para. 49).

- **Interesting pending cases**

Case **T-140/12**, (*Teva* v *EMA*), a direct action against the EMA, which focuses on the correct interpretation of Article 8 of the Orphan Regulation (EC) No 141/2000 defining the concept of market exclusivity for orphan medicinal products;

Cases **T-472/12, T-67/13** and **T-511/14** (*Novartis* v *Commission*), direct actions 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* v *EMA*), a direct action against the EMA on the application of the global marketing authorisation concept to fixed combination products;

Case **T-189/13**, a direct action against the Commission decision to delete certain indications from national marketing authorisations of tolperisone-containing oral formulations ('Article 31 referral');

Case **T-48/14** (*Pfizer* v *Commission/EMA*), direct action concerning the alleged failure to include a compliance statement under the Paediatric Regulation into the marketing authorisation;

Case **T-542/14** (*CTRS* v *Commission*), Orphacol III, direct action by a competitor against the marketing authorisation granted to the medicinal product Kolbam;

Case **C-104/13** (*Olainfarm*), a preliminary reference that deals with the use of well-established medicinal use products as a reference product for generic applications;

Joined case **C-544 and C-545/13,** a preliminary reference on the applicable advertising provisions for pharmacy and hospital preparations.

- **Withdrawn cases**

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

Case **C-661/13** (‘*BOLAR’*), preliminary reference concerning the application of the BOLAR provision in Article 10(6) of Directive 2001/83 to third parties, basically API suppliers, in circumstances where the protected substance is sold by the third party to a pharmaceutical company for BOLAR purposes.

Action to be taken:

For information