EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Health systems and products
Medicinal products – authorisations, EMA

PHARM 612

PHARMACEUTICAL COMMITTEE
22 October 2012

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

Agenda item 3.a)

- **Case C-221/10P, judgment of 19 April 2012, Artegodan**

By this judgement the Court dismissed Artegodan's appeal against a 2010 ruling of the General Court which dismissed the company's request for damages in respect of the loss which it considered to have suffered following a Commission decision which required Member States to withdraw the company's product from the market and which was later annulled.

The ruling is the final word in a long and complex legal case, which started in 2000 when the Commission adopted a decision ordering the withdrawal of several national marketing authorisations concerning amphetamine-like anorectic substances, including the product of Artegodan.

This decision was annulled by the General Court in 2002 (T-74/00) for two reasons: (i.) lack of competence [*to note, under today's legislation the Commission would be competent*] and (ii.) non-compliance with the legal conditions for withdrawing authorisations. The General Court considered that such decision can only be based on new scientific evidence and not on the change of the assessment criteria of the therapeutic efficacy of a medicinal product (in the specific case the withdrawal was reasoned with the absence of long-term efficacy of the product, an assessment criteria which was not used in the initial assessment of the product).

With its new ruling the Court overruled the second finding. It was pointed out that the scientific committee evaluating the benefit/risk ratio is entitled to use a different assessment criteria (looking at long-term efficacy instead of short-term efficacy) than initially, if that change can be reasoned with a new consensus in the scientific community as underpinned by e.g. new therapeutic guidelines or scientific conclusions.

- **Case C-145/11, judgment of 19 July 2012, Commission v. France**

The case deals with the powers of a concerned Member State when requested to validate a marketing authorisation application in a (veterinary) MRP/DCP procedure. According to the Court these powers are confined to the following three elements:

"À cet égard, il ressort de l'article 32, paragraphe 1, de cette directive qu'une demande d'autorisation de mise sur le marché d'un médicament vétérinaire soumise dans le cadre de la procédure décentralisée doit être considérée comme valide lorsqu'elle est fondée sur un dossier identique dans chacun des États membres concernés par la demande, lorsque ce dossier comprend l'ensemble des informations administratives et de la documentation scientifique et technique prévues aux articles 12 à 14 de la directive 2001/82 et lorsque les informations présentées contiennent une liste de ces États membres." (para. 33)

The Court moreover confirmed that the general purpose of the validation check done by the concerned Member State is to verify that the applicant complies with formal requirements ("Ces exigences visent à assurer le respect des aspects formels d'une telle demande."). It is instead for the reference Member State to evaluate the application in detail (para. 34).

Any substantive argument in relation to a marketing authorisation application, which a concerned Member State may have, may only be raised post-validation during the evaluation period, where the concerned Member State is entitled to challenge the assessment of the reference Member State:

"En effet, conformément à l'article 32, paragraphe 3, de la directive 2001/82, l'évaluation des documents présentés par le demandeur est effectuée par l'État membre de référence qui est choisi par le demandeur. Cet État membre doit préparer le rapport d'évaluation et les États membres concernés ont l'obligation d'approuver ce rapport à moins qu'ils n'invoquent un risque potentiel grave pour la santé humaine ou animale ou pour l'environnement, ainsi que le prévoient les articles 32, paragraphe 4, et 33, paragraphe 1, de ladite directive." (para. 34)

This judgment provides further clarification as regards the validation phase (according to the Court it is based on the Synthon findings – C-452/06). For reasons of the similarities between the veterinary Directive and the human Directive, the findings are equally applicable to the human sector (cf. para. 39).

- **Case C-308/11, judgment of 6 September 2012, Chemische Fabrik Kreussler**

In case C-308/11 the Court was asked to clarify the meaning of "pharmacological action" as used in the definition of a human medicinal product by function. The case was triggered by a dispute before a German Court concerning the question whether a mouthwash solution has to be considered as a cosmetic or a medicinal product and whether the product would exert a pharmacological action.

The answer of the Court builds on previous case law. For the purpose of defining the term 'pharmacological action' within the meaning of Article 1(2)(b) of Directive 2001/83, account may be taken of the definition of that term in the Guidance Document on the demarcation between the Cosmetic Products Directive 76/768 and the Medicinal Products Directive 2001/83 as agreed between the Commission Services and the competent authorities of the Member States.

In doing so, the national court must nevertheless ensure that the interpretation was derived in a manner consistent with the criteria laid down by the case-law relating to the interpretation of European Union legal acts.

Article 1(2)(b) of Directive 2001/83 must be interpreted as meaning that, for a substance to be regarded as exerting a 'pharmacological action' within the meaning of that provision, it is not necessary for there to be an interaction between the molecules of which it consists and a cellular constituent of the user's body, as an interaction between that substance and any cellular constituent present within the user's body may be sufficient.

A substance the molecules of which do not interact with a human cellular constituent may, by means of its interaction with other cellular constituents present within the user's organism, such as bacteria, viruses or parasites, have the effect of restoring, correcting or modifying physiological functions in human beings.

It follows that it is not a priori inconceivable that a substance the molecules of which do not interact with a human cellular constituent may constitute a medicinal product within the meaning of Article 1(2)(b) of Directive 2001/83.

The Court recalled though, that a case-by case analysis of the characteristics of a particular product remains necessary: "it must be pointed out that products containing a substance which exerts a pharmacological action cannot automatically be classified as medicinal products 'by function', for the purposes of Article 1(2)(b) of Directive 2001/83, unless the competent administration has made an assessment, with due diligence, of each product individually, taking account, in particular, of that product's specific pharmacological, immunological or metabolic properties, to the extent to which they can be established in the present state of scientific knowledge".

Additionally, the following points have to be covered in the case-by-case assessment: "account must be taken, in determining whether a product falls within the definition of a medicinal product 'by function' for the purposes of that provision, of all the characteristics of the product, including, inter alia, its composition, the manner in which it is used, the extent of its distribution, its familiarity to consumers and the risks which its use may entail". "Lastly, it must be added that, to be capable of being regarded as being a medicinal product by function, the product in question must, having regard to its composition – including its content in active substances – and if used as intended, be capable of appreciably restoring, correcting or modifying physiological functions in human beings."

- **Case E-7/11, judgment of the EFTA court of 29 March 2012, Grund**

The case deals with the attempt of an Icelandic nursing home to purchase Norwegian medicinal products from a Norwegian wholesaler for people in its care. It focusses on the question to what extent such transaction would be legal. It touches on issues such as control reports as provided by Article 51(1) of Directive 2001/83/EC, packaging requirements (language labelling exemptions under Article 63(3) of the Directive), parallel import and the meaning of 'placing on the market' in the context of medicinal products.

- **Interesting pending cases**

Case **C-535/11** initially focussed exclusively on the meaning of the term 'developed' as referred to in the annex to Regulation (EC) No 726/2004. The case is triggered by a pending national court case concerning the medicinal products Lucentis and Avastin. In this procedure the marketing authorisation holder of Lucentis challenge the legality of the activity of a service provider, which prepares pre-filled syringes of Lucentis and Avastin. In preparation of the oral hearing the Court asked the parties to the procedure to what extent Articles 3, 5 and 40 of Directive 2001/83/EC may be applicable in this case.

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