General Court of the European Union
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Press and Information

Judgment in Case T-301/12
Laboratoires CTRS v Commission

The General Court annuls the Commission's decision refusing to grant a marketing authorisation for Orphacol

A marketing authorisation may be issued in respect of that orphan medicinal product on the basis of well-established medicinal use dating back more than 10 years

EU law[1] states that any marketing authorisation ('MA') application regarding a medicinal product for human use must be accompanied by the results of the pre-clinical tests and clinical trials of the medicinal product concerned. However, by way of derogation, a simplified procedure is applicable to, inter alia, orphan medicinal products (that is, products intended for the treatment of very rare and serious conditions). Thus, an applicant will not be required to provide the results of pre-clinical tests or clinical trials if he can demonstrate that the active substances of the medicinal product have been in well-established medicinal use within the EU for at least 10 years, with recognised efficacy and an acceptable level of safety. In that event, the test and trial results are to be replaced by appropriate scientific literature.

Laboratoires CTRS (Cell Therapies Research & Services) ('CTRS') has developed the medicinal product Orphacol, which contains cholic acid as an active substance. That orphan medicinal product is used to treat rare but very serious liver disorders. Those disorders, if not properly treated within the first weeks or months of life, can lead to death.

On 30 October 2009, CTRS applied to the European Medicines Agency ('EMA') for an MA for that medicinal product.

The Committee for Medicinal Products for Human Use ('CMPHU'), a part of the EMA, issued a positive opinion, followed by a revised opinion, which was also positive, in December 2010 and April 2011 respectively, recommending that an MA be granted. However, in July 2011 the Commission submitted to the Standing Committee on Medicinal Products for Human Use ('the Standing Committee') a draft decision refusing to grant CTRS an MA for Orphacol. In October 2011, the Standing Committee issued a negative opinion on the Commission's draft decision refusing to grant an MA. In the same month, the Commission submitted the draft decision refusing to grant an MA to the Appeal Committee. In November 2011, the Appeal Committee also issued a negative opinion on the Commission's draft decision refusing to grant an MA.

On 12 January 2012, CTRS brought an action before the General Court seeking a declaration that the Commission had failed to act in unlawfully failing to adopt a final decision in relation to its application for an MA for the medicinal product Orphacol and, in the alternative, applying for the annulment of the decision, allegedly contained in a letter of 5 December 2011 from the Commission, refusing to grant that MA.

[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 (EMA) (OJ 2004 L 136, p. 1), as amended by Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004 (OJ 2006 L 378, p. 1), and 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 (OJ 2001 L 311, p. 67), as amended by Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 (OJ 2004 L 136, p. 34).

On 4 July 2012[2], the General Court of the European Union declared that the application for a declaration of failure to act was inadmissible and that, because the Commission had replaced the decision refusing the MA allegedly contained in the letter of 5 December 2011 with a decision of 25 May 2012 refusing to grant the MA[3], there was no need to adjudicate on the application for annulment of the former decision.

On 10 July 2012, CTRS brought another action before the General Court seeking annulment of the decision of 25 May 2012. The Court decided to give the case priority treatment.

By its judgment delivered today, the General Court annuls the Commission's decision of 25 May 2012 refusing to grant the MA for the medicinal product Orphacol.

First of all, the Court notes that cholic acid has been used to treat patients in France between 1993 and October 2007 in the form of hospital preparations provided on medical prescription, prepared individually in accordance with the prescriptions of a pharmacopoeia and in compliance with the rules of good practice laid down in French legislation. They are thus prescribed in a hospital or pharmaceutical establishment, under strict medical supervision. Since that date, cholic acid capsules have been authorised for use in France under the brand name Orphacol. Next, the Court finds that those hospital preparations were intended to fulfil 'special needs' as defined in EU law[4], that is, they were supplied in response to individual situations which were justified by medical considerations, and that they were necessary to meet patients' needs. Therefore, CTRS was not obliged, when applying for the MA, to provide the results of pre-clinical tests or clinical trials required by EU law[5].

Accordingly, the General Court rejects the Commission's arguments alleging that there was no well-established medicinal use, and finds that well-established medicinal use of cholic acid has been demonstrated by CTRS.

In addition, the General Court finds that CTRS has shown that it was unable to provide comprehensive particulars on the efficacy and safety of the medicinal product concerned under normal conditions of use because of certain exceptional circumstances[6] within the meaning of EU law.

The Court notes that an MA applicant must justify in the non-clinical and clinical summaries the reasons why it is not possible to provide comprehensive information on the efficacy and safety of the orphan medicinal product concerned and must justify the risk/benefit balance for that product. CTRS has done so in the present case, providing a list of bibliographical references to studies on cholic acid and demonstrating that it was unable to provide comprehensive data for objective, verifiable reasons: namely, the rareness of the disorders in question and ethical considerations. As regards the first reason, at the time when the MA application was submitted (30 October 2009), only 90 patients had been diagnosed with the disorders, 19 of whom were treated in France. As regards the second reason, the CMPHU concluded (and its assessment was not challenged by the Commission) that, because participation in a clinical trial would expose patients to the risk of serious liver damage, or even death, it would be contrary to the principles of medical ethics to carry out a controlled study of the efficacy of cholic acid.

Accordingly, the Commission was wrong to conclude in its decision that the data submitted by CTRS should have been comprehensive, and that it could not invoke the existence of exceptional circumstances in its application made on the basis of well-established medicinal use.

Consequently, the General Court annuls the Commission's decision.

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2 Case T-12/12 Laboratoires CTRS v Commission.
3 Commission Implementing Decision C(2012) 3306 final refusing an MA under Regulation No 726/2004 for 'Orphacol – Cholic acid', an orphan medicinal product for human use.
4 Directive 2001/83/EC (Article 5).
5 Directive 2001/83/EC (Article 8(3)).
6 Regulation (EC) No 726/2004, Article 14(8).

NOTE: An appeal, limited to points of law only, may be brought before the Court of Justice against the decision of the General Court within two months of notification of the decision.

NOTE: An action for annulment seeks the annulment of acts of the institutions of the European Union that are contrary to European Union law. The Member States, the European institutions and individuals may, under certain conditions, bring an action for annulment before the Court of Justice or the General Court. If the action is well founded, the act is annulled. The institution concerned must fill any legal vacuum created by the annulment of the act.

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