Reports of Cases

JUDGMENT OF THE GENERAL COURT (Fifth Chamber)

4 July 2013 *

(Medicinal products for human use — Application for authorisation to market the medicinal product Orphacol — Commission decision refusing to grant authorisation — Regulation (EC) No 726/2004 — Directive 2001/83/EC — Well-established medicinal use — Exceptional circumstances)

In Case T-301/12,

Laboratoires CTRS, established in Boulogne-Billancourt (France), represented by K. Bacon, Barrister, M. Utges Manley and M. Barnden, Solicitors,

applicant,

supported by

Czech Republic, represented by M. Smolek and D. Hadroušek, acting as Agents,

by

Kingdom of Denmark, represented by V. Pasternak Jørgensen and C. Thorning, acting as Agents,

by

French Republic, represented by D. Colas, F. Gloaguen and S. Menez, acting as Agents,

by

Republic of Austria, represented by C. Pesendorfer and A. Posch, acting as Agents,

and by

United Kingdom of Great Britain and Northern Ireland, represented initially by S. Behzadi-Spencer, acting as Agent, and subsequently by C. Murrel, and finally by L. Christie, acting as Agents, and by J. Holmes, Barrister,

interveners,

v

European Commission, represented by E. White, M. Šimerdová and L. Banciella, acting as Agents,

defendant,

* Language of the case: English.

supported by

Republic of Poland, represented initially by B. Majczyna and M. Szpunar, and subsequently by B. Majczyna, acting as Agents,

intervener,

APPLICATION for annulment of Commission Implementing Decision C(2012) 3306 final of 25 May 2012 refusing a marketing authorisation under Regulation (EC) No 726/2004 of the European Parliament and of the Council for 'Orphacol – Cholic acid', an orphan medicinal product for human use,

THE GENERAL COURT (Fifth Chamber),

composed of S. Papasavvas, President, V. Vadapalas (Rapporteur) and K. O'Higgins, Judges,

Registrar: S. Spyropoulos, Administrator,

having regard to the written procedure and further to the hearing on 12 April 2013,

gives the following

Judgment

Background to the dispute

1 The applicant, Laboratoires CTRS, has developed the medicinal product Orphacol, which is used to treat two rare but very serious liver disorders. Those disorders, if not properly treated within the first weeks or months of life, can lead to death.

2 On 30 October 2009, the applicant applied for a marketing authorisation ('MA') for that medicinal product under the procedure provided for by 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 (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 and Directive 2001/83/EC (OJ 2006 L 378, p. 1).

3 On 16 December 2010, the Committee for Medicinal Products for Human Use ('the CMPHU'), which is part of the European Medicines Agency, issued a positive opinion, recommending that an MA be granted in respect of that medicinal product. On 14 April 2011, in response to the European Commission's requests for clarification, that Committee issued a revised opinion, which was also positive.

4 On 7 July 2011, the Commission submitted to the Standing Committee on Medicinal Products for Human Use ('the Standing Committee') a draft decision refusing to grant the applicant an MA for the medicinal product Orphacol.

5 On 13 September 2011, the Standing Committee discussed the Commission's draft decision refusing to grant an MA, but did not proceed to a vote and postponed the discussion until its next meeting.

6 On 13 October 2011, the Standing Committee issued a negative opinion on the Commission's draft decision refusing to grant an MA.

7 On 24 October 2011, the Commission submitted the draft decision refusing to grant an MA to the Appeal Committee.

8 On 8 November 2011, the Appeal Committee also issued a negative opinion on the Commission's draft decision refusing to grant an MA.

9 On 12 January 2012, the applicant brought an action 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.

10 On 23 April 2012, the Commission submitted a revised draft decision to the Standing Committee; that draft decision also refused to grant the MA to the applicant.

11 On 8 May 2012, the Standing Committee met but was unable to issue an opinion, as a qualified majority could not be reached when the revised draft was put to the vote.

12 On 25 May 2012, the Commission adopted 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 ('the contested decision') stating, in essence, that the conditions for granting an MA were not met in the present case.

13 In its judgment of 4 July 2012 in Case T-12/12 *Laboratoires CTRS* v *Commission*, not published in the ECR, the Court declared that the application for a declaration of failure to act was inadmissible and that there was no need to adjudicate on the application for annulment submitted by the applicant, because the contested decision had replaced the decision refusing the MA contained in the letter of 5 December 2011.

Procedure and forms of order sought

14 By application lodged at the Registry of the General Court on 10 July 2012, the applicant brought the present action.

15 By a separate document lodged at the Court Registry on the same day, the applicant submitted an application for the case to be decided under an expedited procedure in accordance with Article 76a of the Rules of Procedure of the Court.

16 By decision of 26 July 2012, the Court (Fifth Chamber) rejected that application, but decided to give this case priority treatment.

17 On 12 September, 8 October, 9 October, 13 September and 26 September 2012, the Czech Republic, the Kingdom of Denmark, the French Republic, the Republic of Austria and the United Kingdom of Great Britain and Northern Ireland sought leave, respectively, to intervene in support of the form of order sought by the applicant. On 9 October 2012, the Republic of Poland sought leave to intervene in support of the form of order sought by the Commission. Those requests for leave to intervene were notified to the parties, which submitted their observations within the prescribed period. The requests were granted by order of the President of the Fifth Chamber of the Court of 23 October 2012.

18 Acting upon the report of the Judge-Rapporteur, the Court decided to open the oral procedure and, on 7 March 2013, by way of measures of organisation of procedure pursuant to Article 64 of its Rules of Procedure, asked the Commission and the French Republic to reply to written questions prior to the hearing. The Commission and the French Republic answered those questions within the prescribed period.

19 The parties presented oral argument and replied to the Court's oral questions at the hearing on 12 April 2013.

20 The applicant, supported by the Czech Republic in both its pleas, by the Kingdom of Denmark in the first plea, and by the French Republic, the Republic of Austria and the United Kingdom of Great Britain and Northern Ireland in the second plea, claims that the Court should:

— annul the contested decision;

— order the Commission to pay the costs.

21 In its observations on the statements in intervention, the applicant requests that the Court rule on both pleas in law, irrespective of its decision regarding the first plea.

22 The Commission, supported by the Republic of Poland in respect of the second plea, contends that the Court should:

— dismiss the action as unfounded;

— order the applicant to pay the costs.

Law

23 In support of its application, the applicant puts forward two pleas in law. The first plea alleges infringement of Regulation (EU) No 182/2011 of the European Parliament and of the Council of 16 February 2011 laying down the rules and general principles concerning mechanisms for control by Member States of the Commission's exercise of implementing powers (OJ 2011 L 55, p. 13), repealing Council Decision 1999/468/EC of 28 June 1999 laying down the procedures for the exercise of implementing powers conferred on the Commission (OJ 1999 L 184, p. 23). In the second plea, which this Court considers appropriate to examine first, the applicant submits that the three reasons set out in Annex I to the contested decision as to why the Commission gave a negative response to its MA application are manifestly incorrect. The Commission was wrong to conclude that (i) 'well-established medicinal use' of cholic acid had not been proved, (ii) the bibliographical data had to be comprehensive and the concept of 'exceptional circumstances' could not be relied on, and (iii) granting an MA in the present case would undermine the objectives of Regulation No 1901/2006 and the protection of innovation.

24 As a preliminary point, it should be noted that, in Decision C(2002) 5453 of 18 December 2002, adopted in accordance with Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products (OJ 2000 L 18, p. 1), the Commission designated cholic acid as an orphan medicinal product.

25 Moreover, it is clear from the case-file that no medicinal product containing cholic acid as an active substance has ever obtained an MA in the European Union. However, cholic acid capsules have been used as hospital preparations to treat patients in France between 1993 and October 2007, a use provided for by the second subparagraph of Article L. 5121-1 of the French Public Health Code. Since

that date, cholic acid capsules have been authorised for use in France under the brand name Orphacol, pursuant to Article L. 5121-12 of the Public Health Code (to be issued to a 'named individual patient for compassionate use').

26 It is clear from the second recital in the preamble to the contested decision that the MA application submitted by the applicant was made under Article 10a of 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 the basis of well-established medicinal use, and referred to the existence of exceptional circumstances as mentioned in Article 14(8) of Regulation No 726/2004.

27 Lastly, it should be noted that the CMPHU's revised opinion mentions a whole list, provided by the applicant, of bibliographical references to studies on cholic acid which were carried out in hospitals (in France in particular) going back over ten years from the date of the MA application. The CMPHU also concluded that the applicant had shown that it was unable to provide comprehensive documentation regarding the efficacy and safety of cholic acid by reason of the exceptional circumstances in which that substance had been used, and, at the end of its analysis, it decided that the applicant had sufficiently demonstrated that the benefits of Orphacol outweighed the risks and gave a positive opinion regarding the MA application.

The allegedly erroneous conclusion that well-established medicinal use of cholic acid has not been proved

28 The applicant, supported by the Czech Republic, the French Republic and the United Kingdom of Great Britain and Northern Ireland, points out that the CMPHU concluded that the use of cholic acid as a hospital preparation between 1993 and 2007 was sufficiently systematic and well documented to prove well-established medicinal use over a period exceeding 10 years.

29 The Commission, supported by the Republic of Poland, does not dispute that cholic acid has been used in the EU over a period exceeding 10 years, but contends that that use must be well established for the purposes of Article 10a of Directive 2001/83. That article, as an express derogation from the requirements relating to the provision of particulars laid down in Article 8(3) of Directive 2001/83, must be applied strictly. The condition that medicinal use be well established cannot be satisfied by referring to the hospital preparations provided for in French law because, first, they are not covered by Article 5(1) of Directive 2001/83 and, second, it follows from the wording of that provision that arrangements must be in place relating to the reporting and monitoring of the medicinal products concerned. In addition, at the hearing, in response to a question from the Court, the Commission argued that France could not have excluded hospital preparations from that directive by virtue of Article 5(1) thereof, as such an exclusion could apply only on a case-by-case basis.

30 The Republic of Poland argues that the applicant cannot rely on Article 5(1) of Directive 2001/83 and, in that regard, refers to the Opinion of Advocate General Jääskinen in Case C-185/10 *Commission* v *Poland* [2012] ECR, from which it infers that only Member States are entitled to exclude certain medicinal products from the provisions of Directive 2001/83.

31 In that regard, Article 8(3)(i) of Directive 2001/83 states that any MA application must be accompanied by the results of the pre-clinical tests and clinical trials of the medicinal product concerned.

32 However, Article 10a of Directive 2001/83 provides that, by way of derogation from Article 8(3)(i) of that directive, 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 Community for at least 10 years, with recognised efficacy and an acceptable level of safety in terms of the conditions set out in Annex I. In that event, the test and trial results are to be replaced by appropriate scientific literature.

33 Under the second indent of Part III-5 of Annex I to Directive 2001/83, when an applicant for an MA for an orphan medicinal product invokes the provisions of Article 10a of that directive and Part II-1 of that annex (well-established medicinal use), the systematic and documented use of the substance concerned can refer – by way of derogation – to the use of that substance in accordance with the provisions of Article 5 of that directive.

34 Under Article 5(1) of Directive 2001/83, a Member State may, in order to fulfil special needs, exclude from that directive medicinal products supplied in response to a bona fide unsolicited order, formulated in accordance with the specifications of an authorised healthcare professional and for use by one or more individual patients under his direct personal responsibility.

35 The wording of that provision makes it clear that implementation of the derogation which it contains is conditional on fulfilment of a set of cumulative conditions (Case C-185/10 *Commission* v *Poland* [2012] ECR, paragraph 30).

36 In the interpretation of that provision account must be taken of the fact that, in general, provisions which are exceptions to a principle must, according to settled case-law, be interpreted strictly (*Commission* v *Poland*, paragraph 31).

37 The power arising from Article 5(1) of Directive 2001/83 to exclude the application of the directive's provisions can be exercised only if that is necessary, taking account of the specific needs of patients. A contrary interpretation would conflict with the aim of protecting public health, which is achieved through the harmonisation of provisions relating to medicinal products, particularly those relating to the marketing authorisation (*Commission* v *Poland*, paragraph 33).

38 The concept of 'special needs', referred to in Article 5(1) of that directive, applies only to individual situations justified by medical considerations, and presupposes that the medicinal product is necessary to meet the needs of the patient (*Commission* v *Poland*, paragraph 34).

39 Also, the requirement that medicinal products are supplied in response to a 'bona fide unsolicited order' means that the medicinal product must have been prescribed by the doctor as a result of an actual examination of his patients and on the basis of solely therapeutic considerations (*Commission* v *Poland*, paragraph 35).

40 In the present case, in the contested decision the Commission concluded in particular that, since Directive 2001/83 did not address the concept of hospital preparations, it was necessary to ascertain whether the use of cholic acid as a hospital preparation could be assimilated to the use provided for in Article 5 of that directive. The Commission went on to conclude that hospital preparations did not meet the requirements of Article 5(1) of Directive 2001/83 and that, accordingly, they did not constitute well-established medicinal use for the purposes of Article 10a of Directive 2001/83, contrary to the conclusions of the CMPHU in its revised opinion.

41 In that regard, first of all, it should be noted that the second subparagraph of Article L. 5121-1 of the French Public Health Code states that hospital preparations are medicinal products prepared in accordance with the prescriptions of a pharmacopoeia and in compliance with the rules of good practice laid down in French legislation where there is no appropriate medicinal product prepared by a hospital's in-house pharmacy or by that hospital's authorised pharmaceutical establishment, in accordance with that legislation. Hospital preparations are provided on medical prescription to one or more patients by the hospital's in-house pharmacy.

42 Next, it should be noted that the French Republic, under the legislation currently in force, has excluded hospital preparations from the provisions of Directive 2001/83 from 1992, that is, prior to the use of cholic acid-based hospital preparations.

43 Indeed, in response to a written question from the Court, the French Republic explained, that it was at the stage of setting out the legal framework concerning hospital preparations in Law No 92-1279 of 8 December 1992 amending Book V of the Public Health Code and concerning medicine and medicinal products (*Journal Officiel de la République Française* (JORF) of 11 December 1992, p. 16888) that the French legislature excluded hospital preparations from the provisions of EU legislation on medicinal products for human use. Thus, the French Republic has excluded cholic acid-based hospital preparations from the provisions of that legislation since it started using that medicinal product, that is, since 1993. In addition, the French Republic indicated that hospital preparations had to be declared following the entry into force of Article 21 of Law No 98-535 of 1 July 1998 on stricter supervision and monitoring of the safety of healthcare products for human use (JORF of 2 July 1998, p. 910056). Lastly, the French Republic stated that each cholic acid-based hospital preparation had been prepared individually.

44 Those hospital preparations were intended to fulfil 'special needs', in that they were supplied in response to individual situations which were justified by medical considerations and that they were necessary to meet patients' needs. It is common case that there is no medicinal product on the market capable of treating the liver disorders in question, which are likely to lead rapidly to the death of any person who is diagnosed with those disorders.

45 Moreover, those hospital preparations were supplied in response to 'a bona fide unsolicited order', in that – as the French Republic explained at the hearing, without being contradicted on that point by the Commission – they were prescribed by a doctor as a result of an actual examination of his patients and on the basis of solely therapeutic considerations.

46 Accordingly, it must be found in the present case that the cholic acid-based hospital preparations complied with the conditions laid down in Article 5(1) of Directive 2001/83.

47 That finding is not undermined by any of the Commission's arguments.

48 First, the Commission's argument that hospital preparations are not covered by Article 5(1) of Directive 2001/83 cannot be accepted, as that provision does not exclude any type of medicinal product from its ambit.

49 Second, the Commission's argument that there is an obligation to report and monitor medicinal products covered by Article 5(1) of Directive 2001/83 cannot be upheld, given that the wording of that provision does not state, or even imply, that any such obligation exists.

50 Third, contrary to the arguments put forward by the Commission at the hearing, that provision does not state that a Member State may exclude medicinal products from the provisions of Directive 2001/83 only on a case-by-case basis, rather than on the basis of categories of medicinal products, such as hospital preparations.

51 As regards the Republic of Poland's argument that only Member States are entitled to exclude certain medicinal products from the provisions of Directive 2001/83, it is, in fact, the French Republic which has excluded hospital preparations from the provisions of that directive, as set out in paragraph 42 above.

52 It follows from the foregoing that the Commission's arguments and the Republic of Poland's arguments must be rejected.

53 Accordingly, the Commission was wrong to conclude that the use of cholic acid as a hospital preparation in France between 1993 and October 2007 did not constitute well-established medicinal use for the purposes of Article 10a of Directive 2001/83.

The allegedly erroneous finding that the data submitted in the MA application should have been comprehensive, leading to the wrongful rejection of the possibility of invoking exceptional circumstances

54 The applicant, supported by the Czech Republic, the French Republic and the United Kingdom of Great Britain and Northern Ireland, criticises the Commission's conclusion, in the contested decision, that an MA application made on the basis of well-established medicinal use, as provided for in Article 10a of Directive 2001/83 cannot, in the absence of comprehensive data regarding the efficacy or the safety of the medicinal product, be granted on the basis of the applicant invoking exceptional circumstances as referred to in Article 14(8) of Regulation No 726/2004.

55 The Commission, supported by the Republic of Poland, contends that an MA application cannot be submitted under Article 10a of Directive 2001/83 where comprehensive data on the efficacy and safety of the product are not available, and that the concepts of 'well-established medicinal use' and 'exceptional circumstances' are mutually exclusive. Thus, under Article 12 of Regulation No 726/2004, read in conjunction with Article 6 of that regulation, the Commission would have to refuse to grant the MA if the bibliographical application submitted did not specifically and completely include the particulars and documents referred to in Article 10a of Directive 2001/83.

56 In that regard, Article 6 of Regulation No 726/2004 states that each MA application must specifically and completely include the particulars and documents as referred to in, inter alia, Articles 8(3) and 10a of, and Annex I to, Directive 2001/83.

57 Moreover, under Article 12(1) of Regulation No 726/2004, the MA is to be refused if, after verification of the particulars and documents submitted in accordance with Article 6 of that regulation, it appears that the applicant has not properly or sufficiently demonstrated the quality, safety or efficacy of the medicinal product.

58 Article 14(8) of Regulation No 726/2004 and Article 22 of Directive 2001/83 provide that, subject to certain conditions, an MA may be granted in exceptional circumstances. An MA may be granted only if (i) the applicant can show that, for objective, verifiable reasons, he is unable to provide comprehensive data regarding the efficacy and safety, under normal conditions of use, of the medicinal product and (ii) it is based on one of the grounds set out in Annex I to that directive.

59 Furthermore, Part II-6 of Annex I to Directive 2001/83 provides that the MA may be granted subject to certain specific obligations, such as supplying the medicinal product concerned on medical prescription only and, in certain cases, administering that product only under strict medical supervision, possibly in a hospital, in certain circumstances. Those are when the applicant can show that he is unable to provide comprehensive data on the efficacy and safety under normal conditions of use, because the indications for use of the product in question are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, or comprehensive information cannot be provided having regard to the present state of scientific knowledge, or it would be contrary to generally accepted principles of medical ethics to collect such information.

60 In the present case, according to the CMPHU's revised opinion, the applicant has shown in its MA application 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, it is indeed clear from the case-file that, going on the basis of the number of cases observed in the EU over the last 15 years, at the time when the MA application was submitted, 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 in the context of the indications concerned, because such a study would involve dividing the patients into two groups, one receiving the treatment on trial and the other receiving a placebo, as the applicant explained at the hearing.

61 In addition, as has been stated in paragraph 27 above, in its MA application the applicant provided a list of bibliographical references to studies on cholic acid.

62 Moreover, it should be noted that the hospital preparations fulfilled the specific obligations referred to in Part II-6 of Annex I to Directive 2001/83: it is clear from the wording of the second subparagraph of Article L. 5121-1 of the French Public Health Code (see paragraph 41 above) that those preparations were provided on medical prescription by a hospital's in-house pharmacy.

63 However, according to the Commission, an MA cannot be granted without comprehensive documentation, and exceptional circumstances cannot be relied on where an MA application is submitted on the basis of well-established medicinal use.

64 Regarding the issue of comprehensive documentation, it should be noted that Part II-1(c) of Annex I to Directive 2001/83 provides for the possibility of an MA being granted even where information is missing, as long as the demonstration of an acceptable level of safety and/or efficacy can be supported although some studies are lacking. Therefore, an MA may be granted without comprehensive documentation. Moreover, as has just been noted, justification has been given in the present case for the absence of such documentation.

65 Nothing in Regulation No 726/2004 or Directive 2001/83 precludes the simultaneous application of the concepts of 'well-established medicinal use' and 'exceptional circumstances'.

66 The Commission's argument that Part II of Annex I to Directive 2001/83, covering derogations including those based on well-established medicinal use, does not provide for the possibility of invoking exceptional circumstances when the applicant is claiming such use cannot be decisive in the absence of any explicit statement to that effect.

67 On the contrary, it should be noted that, in the specific context of orphan medicinal products such as Orphacol, Directive 2001/83 expressly refers to the possibility of applying both the provisions relating to exceptional circumstances and those provisions relating to a claim of well-established medicinal use.

68 First, under the first indent of Part III-5 of Annex I to Directive 2001/83, when an orphan medicinal product is involved, the general provisions of Part II-6 (Exceptional circumstances) can be applied. The applicant must then justify in the non-clinical and clinical summaries the reasons why it is not possible to provide the complete information and must justify the benefit/risk balance for the orphan medicinal product concerned. As has already been noted (see paragraph 27 above), the applicant has done so in the present case.

69 Second, under the second indent of that provision, where an applicant for an MA for an orphan medicinal product invokes the provisions of Part II-1 of that annex (Well-established medicinal use), the systematic and documented use of the substance concerned can refer – by way of derogation – to the use of that substance in accordance with the provisions of Article 5 of that directive. In the present case, cholic acid has been used in accordance with that article, as is apparent from paragraph 41 et seq. above.

70 Therefore, those conditions have been met. Moreover, contrary to the Commission's assertions, the fact that the subparagraphs are divided into two separate indents does not mean that those provisions are mutually exclusive; such a meaning could be inferred only if the wording of that point had clearly stated that it would be impossible to implement both provisions simultaneously.

71 It follows that the Commission's arguments must be rejected.

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

The allegedly erroneous finding that granting an MA would undermine the objectives of Regulation No 1901/2006 and the protection of innovation

73 The applicant, supported by the Czech Republic and the United Kingdom of Great Britain and Northern Ireland, contests the third reason given by the Commission in the contested decision for refusing to grant the MA. This was that the granting of an MA would undermine both (i) the objectives of Regulation No 1901/2006, which requires – according to the Commission – that MA applications concerning new medicinal products for paediatric use be accompanied by paediatric studies and (ii) the protection of innovation, given that the Commission considers that the requirements of Article 10a of Directive 2001/83 must be strictly complied with in order to avoid either discouraging the publication of research or undermining innovation in the European Union.

74 Regarding the first argument, the Commission contends that, under Article 7(1) of Regulation No 1901/2006, applications for an MA for a medicinal product which is not yet authorised must include, in addition to the particulars and documents referred to in Article 8(3) of Directive 2001/83, the results of all studies performed and details of all information collected in compliance with an agreed paediatric investigation plan. Regarding the second argument, recital 4 in the preamble to Commission Directive 1999/83/EC of 8 September 1999 amending the Annex to Council Directive 75/318/EEC on the approximation of the laws of the Member States relating to analytical, pharmacotoxicological and clinical standards and protocols in respect of the testing of medicinal products (OJ 1999 L 243, p. 9) expresses the legislature's opinion that the possibility of submitting a bibliographical application ought not to undermine research and the publication of the results of clinical trials. The Commission argues that, if the requirements for proving well-established medicinal use over a 10-year period were to be relaxed by accepting that the use of active substances without an MA was sufficient to show such use, the reward system established by the legislation to encourage innovation would be seriously undermined.

75 As regards the first argument, under Article 9 of Regulation No 1901/2006, Article 7 of that regulation is not to apply to products authorised under, inter alia, Article 10a of Directive 2001/83.

76 It follows that the applicant has indeed shown that there is well-established medicinal use for the purposes of that provision.

77 It should be noted that the second argument is included in the contested decision, not as a ground for refusing to grant the MA applied for, but merely as a remark, which cannot undermine the finding made above. Moreover, in any event, the present case does not concern a relaxation of the requirements for proving well-established medicinal use, but the implementation of that use in exceptional circumstances, pursuant to Regulation No 726/2004 and Directive 2001/83.

78 Accordingly, the Commission was wrong to conclude in the contested decision that granting an MA in the present case would undermine the objectives of Regulation No 1901/2006 and the protection of innovation.

79 It follows from all of the foregoing that the Commission was wrong to refuse to grant the MA. Accordingly the contested decision must be annulled, without it being necessary to examine the first plea in law.

Costs

80 Under Article 87(2) of the Rules of Procedure, the unsuccessful party is to be ordered to pay the costs if they have been applied for in the successful party's pleadings. Since the Commission has been unsuccessful, it must be ordered to pay the costs, in accordance with the form of order sought by the applicant.

81 Under the first subparagraph of Article 87(4) of the Rules of Procedure, Member States which have intervened in the proceedings are to bear their own costs. Therefore, the Czech Republic, the Kingdom of Denmark, the French Republic, the Republic of Austria, the Republic of Poland and the United Kingdom of Great Britain and Northern Ireland must be ordered to bear their own costs.

On those grounds,

THE GENERAL COURT (Fifth Chamber)

hereby:

1. **Annuls Commission Implementing Decision C(2012) 3306 final of 25 May 2012 refusing a marketing authorisation under Regulation (EC) No 726/2004 of the European Parliament and of the Council for 'Orphacol – Cholic acid', an orphan medicinal product for human use;**

2. **Orders the European Commission to bear its own costs and those incurred by Laboratoires CTRS;**

3. **Orders the Czech Republic, the Kingdom of Denmark, the French Republic, the Republic of Austria, the Republic of Poland and the United Kingdom of Great Britain and Northern Ireland to bear their own costs.**

Papasavvas Vadapalas O'Higgins

Delivered in open court in Luxembourg on 4 July 2013.

[Signatures]