JUDGMENT OF THE COURT (First Chamber)

17 July 2008 *

In Case C-448/06,

REFERENCE for a preliminary ruling under Article 234 EC from the Verwaltungsgericht Köln (Germany), made by decision of 24 October 2006, received at the Court on 2 November 2006, in the proceedings

cp-Pharma Handels GmbH

v

Bundesrepublik Deutschland,

THE COURT (First Chamber),

composed of P. Jann, President of the Chamber, A. Tizzano (Rapporteur), A. Borg Barthet, M. Ilešič and E. Levits, Judges,

* Language of the case: German.

Advocate General: J. Mazák,
Registrar: J. Swedenborg, Administrator,

having regard to the written procedure and further to the hearing on 18 October 2007,

after considering the observations submitted on behalf of:

— cp-Pharma Handels GmbH, by R. Köhne, Rechtsanwalt,

— the Greek Government, by S. Charitaki and S. Papaioannou, acting as Agents,

— the Polish Government, by E. Ośniecka-Tamecka, acting as Agent,

— the Commission of the European Communities, by B. Stromsky and B. Schima, acting as Agents,

after hearing the Opinion of the Advocate General at the sitting on 16 January 2008,

gives the following

Judgment

1 This reference for a preliminary ruling concerns the validity of Commission Regulation (EC) No 1873/2003 of 24 October 2003 amending Annex II to Council Regulation (EEC) No 2377/90 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin (OJ 2003 L 275, p. 9).

2 The reference was made in the course of proceedings between cp-Pharma Handels GmbH ('cp-Pharma') and Bundesrepublik Deutschland (Federal Republic of Germany) with regard to a decision of the competent German authority revoking the marketing authorisation for the medicinal product 'progesterone for veterinary use' in the form of a solution administered by intramuscular injection which had been granted to that company.

Legal context

Community legislation

The provisions concerning the establishment of maximum residue limits

— Regulation (EEC) No 2377/90

3 The first and third recitals in the preamble to Council Regulation (EEC) No 2377/90 of 26 June 1990 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin, as amended by Council Regulation (EC) No 806/2003 of 14 April 2003 (OJ 1990 L 122, p. 1; 'Regulation No 2377/90'), state as follows:

'… the use of veterinary medicinal products in food-producing animals may result in the presence of residues of foodstuffs obtained from treated animals;

…

… in order to protect public health, maximum residue limits ['MRLs'] must be established in accordance with generally recognised principles of safety assessment, taking into account any other scientific assessment of the safety of the substances concerned which may have been undertaken by international organisations, in particular the

Codex Alimentarius or, where such substances are used for other purposes, by other scientific committees established within the Community'.

4 Article 1(1)(b) of that regulation defines an MRL as the maximum concentration of residue resulting from the use of a veterinary medicinal product which may be accepted by the Community to be legally permitted or recognised as acceptable in or on a food.

5 Articles 2 to 5 of Regulation No 2377/90 provide for the classification in four separate annexes of pharmacologically active substances used in veterinary medicinal products for food-producing animals. Those substances are to be classified in Annex I if the MRLs have been established (Article 2 of the regulation), in Annex II where, 'following an evaluation …, it appears that it is not necessary for the protection of public health to establish [an MRL]' (Article 3 of that regulation) and in Annex IV where it appears that an MRL cannot be established because the residues, whatever their limit, present a hazard for the health of the consumer (first paragraph of Article 5 of the regulation). Finally, under the first paragraph of Article 4 thereof, a provisional MRL may be established for a substance used on the date of entry into force of the regulation, 'provided that there are no grounds for supposing that residues of the substance concerned at the level proposed present a hazard for the health of the consumer'. Substances for which provisional MRLs have been established are dealt with in Annex III to Regulation No 2377/90.

6 Pursuant to Article 6(1) of Regulation No 2377/90, '[i]n order to obtain the inclusion in Annex I, II or III of a pharmacologically active substance which is intended for use in veterinary medicinal products for administration to food-producing animals, an application to establish [an MRL] shall be submitted to the European Agency for the Evaluation of Medicinal Products set up by [Council] Regulation (EEC) No 2309/93 [of 22 July 1993 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products (OJ 1993 L 214, p. 1)], hereinafter referred to as "the Agency"'.

7 Article 7 of Regulation No 2377/90 provides:

‘1. The Committee for Veterinary Medicinal Products referred to in Article 27 of Regulation (EEC) No 2309/93 (hereinafter “the [CVMP]”) shall be responsible for formulating the Agency’s opinion on the classification of substances referred to in Annex I, II, III or IV to this Regulation.

…

5. The Agency shall forward the definitive opinion of the [CVMP] within 30 days of its adoption both to the Commission and to the applicant. The opinion shall be accompanied by a report describing the safety evaluation of the substance by the Committee, which shall give the grounds for its conclusions.

6. The Commission shall prepare draft measures taking account of Community legislation …’

8 Under Article 8(1) of Regulation No 2377/90, ‘[t]he Commission shall be assisted by the Standing Committee on Veterinary Medicinal Products’.

9 Article 14 of Regulation No 2377/90, in its original version, provided:

‘With effect from 1 January 1997, the administration to food-producing animals of veterinary medicinal products containing pharmacologically active substances which are not mentioned in Annex I, II or III shall be prohibited within the Community …’

10 In the version of Regulation No 2377/90 applicable to the dispute in the main proceedings, the date 1 January 1997 was replaced by 1 January 2000 for the majority of substances (including progesterone) whose use was authorised at 7 March 1997 and for which applications for establishment of an MRL had been filed with the Commission or the Agency before 1 January 1996.

— Regulation No 1873/2003

11 Regulation No 1873/2003 amended Annex II to Regulation No 2377/90 by including progesterone for female bovine, ovine, caprine and equine animals. The inclusion of that pharmacologically active substance is accompanied by the following footnote:

'Only for intravaginal therapeutic or zootechnical use and in accordance with [Council] Directive 96/22/EC [of 29 April 1996 concerning the prohibition on the use in stockfarming of certain substances having a hormonal or thyrostatic action and of ß-agonists, and repealing Directives 81/602/EEC, 88/146/EEC and 88/299/EEC (OJ 1996 L 125, p. 3)]'.

12 The sixth, eighth and tenth recitals in the preamble to Regulation No 1873/2003 are worded as follows:

'(6) The SCVPH [Scientific Committee on Veterinary Measures relating to Public Health] repeatedly confirmed that the use of hormones for growth promotion purposes in meat production poses a potential health risk to consumers due to their intrinsic pharmacological and toxicological properties and epidemiological findings. However, at present the data available on progesterone are insufficient to make any quantitative estimate of the risk arising from the exposure to residues in meat and meat products originating from treated animals. No threshold levels can be defined for progesterone in this regard.

…

(8) Animals also naturally produce progesterone. The level of endogenous secretion of progesterone in the animals is variable, depending notably on gender, age, breed and sexual cycle. Validated methods are available to detect progesterone in animal tissues. However, these methods cannot distinguish between naturally occurring hormones and residues of progesterone as a means of controlling that the restrictions of use established in Directive 96/22/EC are observed.

…

(10) The Commission considers that safeguards as to the possibility of misuse of veterinary medicinal products containing progesterone are necessary. Restricting the terms of the use of progesterone to administration only via the intravaginal route in female animals of bovine, ovine, caprine and equine species provides this additional safeguard needed to avoid misuse as the relevant veterinary medicinal products cannot, due to their specific presentation, be realistically used for prohibited purposes. It is therefore considered appropriate to include progesterone in Annex II to Regulation … No 2377/90 in accordance with the Annex to the present proposal for a Commission Regulation, which limits the use of progesterone to this specific purpose and product formulation.'

The other relevant provisions

— Directive 96/22

13 Directive 96/22, as amended by Directive 2003/74/EC of the European Parliament and of the Council of 22 September 2003 (OJ 2003 L 262, p. 17; 'Directive 96/22'), which is the version relevant to the dispute in the main proceedings, provides that Member States are to prohibit the administration to a farm animal of hormonal substances having a gestagenic effect, which includes progesterone.

14 By derogation and in a limited number of cases, Article 4(1) of Directive 96/22 states that Member States may authorise 'the administering to farm animals, for therapeutic purposes, of …, testosterone and progesterone … Veterinary medicinal products used for therapeutic treatment must comply with the requirements for placing on the market laid down in [Council] Directive 81/851/EEC [of 28 September 1981 on the approximation of the laws of the Member States relating to veterinary medicinal products (OJ 1981 L 317, p. 1)] and be administered only by a veterinarian, by injection or for the treatment of ovarian dysfunction in the form of vaginal spirals, but not by implant, to farm animals which have been clearly identified. …'.

— Directive 2001/82/EC

15 Article 6 of Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products (OJ 2001 L 311, p. 1) provides:

'In order that a veterinary medicinal product may be the subject of a marketing authorisation for the purpose of administering it to food-producing animals, the

active substances which it contains must be shown in Annex I, II or III of Regulation … No 2377/90.'

16 Article 96 of Directive 2001/82 provides:

'[Directives] 81/851/EEC, 81/852/EEC, 90/677/EEC and 92/74/EEC … are repealed …

The reference made to the said Repealed Directives shall be construed as references to this Directive …'

National legislation

17 The first sentence of Paragraph 30(1) of the German Law on medicinal products (Arzneimittelgesetz), in the version published on 11 December 1998 (BGBl. 1998 I, p. 3586; 'the AMG'), provides:

'An authorisation … must be revoked where one of the grounds for refusal under Paragraph 25(2)(3),(5),(5a), (6) or (7) subsequently arises.'

18 Paragraph 25(2)(7) of the AMG provides:

'The competent higher federal authority may refuse to grant an authorisation only if

…

7. the marketing of the medical product or its administration to animals would contravene legal provisions or a regulation, directive or decision of the Council or Commission …'

The dispute in the main proceedings and the question referred for a preliminary ruling

19 On 16 February 1999, cp-Pharma obtained an extension of the marketing authorisation for the veterinary medicinal product 'progesterone ad us. vet' for a period of five years. That authorisation concerned a solution for intramuscular injection, the active substance of which is progesterone, to be administered in cases of follicle cysts and 'nymphomania caused by follicle cysts'.

20 By decision of 22 January 2004, the competent authority revoked the marketing authorisation on the ground that progesterone was listed in Annex II to Regulation No 2377/90 for administration only via the intravaginal route. According to that authority, since no MRL has been established for other applications, the prohibition set out in Article 14 of that regulation applied to that medicinal product and therefore the authorisation had to be revoked.

21 Following the rejection of its objection to that decision to revoke the authorisation, cp-Pharma brought an action before the referring court seeking annulment of that decision on the ground that the Commission had disregarded the recommendation of the CVMP, which asked it to include progesterone in Annex II to Regulation No 2377/90 without limiting its use to intravaginal administration.

22 In the decision for reference, the Verwaltungsgericht Köln (Administrative Court, Cologne) takes the view that Regulation No 2377/90, in the event of the listing of a substance in Annex II thereto, does not empower the Commission to impose restrictions as to the methods of administration of that substance. Moreover, such a possibility appears, *mutatis mutandis*, to have been excluded by the Court in Case C-32/00 P *Commission* v *Boehringer* [2002] ECR I-1917, paragraph 55, in which it held that, where the substance in question is entered in Annex III to that regulation, the only limitation on the validity of an MRL envisaged by that regulation concerns the indication of the limited duration of its validity.

23 The referring court observes, in addition, that the CVMP had proposed that progesterone be entered in Annex II to Regulation No 2377/90 without any restrictions, as the risks to health through progesterone residues were estimated to be minimal.

24 Finally, that court notes that the provisions of Directive 96/22, establishing measures to avoid any misuse in the administration of progesterone as a veterinary medicinal product, provide expressly that that substance may be administered by injection.

25 Having regard to the foregoing, the Verwaltungsgericht Köln decided to stay the proceedings and to refer the following question to the Court for a preliminary ruling:

‘Is … Regulation … No 1873/2003 … partially void on account of a breach of higher-ranking Community law (Articles 1(1) and 3 of … Regulation … No 2377/90 in conjunction with Article 4(1) of … Directive 96/22 …), in so far as application of an

injection solution as a pharmaceutical form is excluded by virtue of the note marked (*) against the listing of progesterone in Annex II to … Regulation … No 2377/90?'

The question referred

26 Cp-Pharma and the Polish Government take the view, contrary to that of the Greek Government and the Commission, that Regulation No 1873/2003 is invalid in that Regulation No 2377/90 does not expressly authorise the Commission to establish an MRL solely for certain methods of administration of progesterone and Directive 96/22 permits Member States to authorise marketing of that substance in injectable form. Cp-Pharma adds that, in any event, the Commission could not adopt a measure concerning the MRL for progesterone which contradicts the opinion of the CVMP, while the Polish Government submits that Regulation No 1873/2003 is insufficiently reasoned with regard to the grounds on which the Commission decided not to follow that opinion.

27 In order to answer the question referred by the national court, it is appropriate to note that, as the Court has already held in paragraph 80 of the judgment in Case C-198/03 P *Commission* v *CEVA and Pfizer* [2005] ECR I-6357, the Commission must be given a discretion which is sufficient to allow it to determine, on a fully informed basis, the measures that are necessary and appropriate for the protection of public health.

28 That is evidently all the more justified with regard to a file such as that concerning progesterone which, as the Court has already recognised, is particularly complex since it raises questions which are delicate and controversial from a scientific viewpoint (*Commission* v *CEVA and Pfizer*, paragraph 81).

29 That complexity is due to the fact that progesterone, in addition to therapeutic treatment, is liable to be used unlawfully as a growth stimulate and, currently, there are no reliable methods of analysis permitting distinction between endogenous progesterone, produced naturally by the animals, and exogenous progesterone, resulting from the administration of medicinal products, and therefore monitoring of the abusive use of that substance. Furthermore, the Commission, when it adopted Regulation No 1873/2003, was faced with a situation of ongoing scientific uncertainty with regard to the possible harmful effects of progesterone, characterised by divergent scientific opinions adopted by the CVMP, on the one hand, and by the SCVPH and other international scientific bodies, on the other (see, to that effect, *Commission* v *CEVA and Pfizer*, paragraph 82).

30 In such circumstances, it is necessary to ascertain whether the Commission has exceeded the limits of its discretion by providing for the inclusion of progesterone in Annex II to Regulation No 2377/90 only in respect of its intravaginal use.

31 Although it is true that Article 3 of Regulation No 2377/90 does not expressly provide for the possibility of including a substance in Annex II thereto for only some of its methods of administration, that fact cannot, as the Advocate General observed in point 52 of his Opinion, prevent the Commission from nevertheless making such an inclusion. That approach may appear particularly appropriate where, as in the dispute in the main proceedings, the substance in question cannot be included in Annex I or III to that regulation, but where certain limitations on the methods of administration of that substance can make it possible to ensure that the presence of residues in animal tissue does not constitute a risk for human health, so that a total prohibition on marketing that substance following its inclusion in Annex IV to that regulation would be disproportionate.

32 As is apparent from the sixth and eighth recitals in the preamble to Regulation No 1873/2003, the fact that endogenous progesterone cannot be distinguished from exogenous progesterone made it impossible to establish an MRL, for the purposes of inclusion of that substance in Annex I or III to Regulation No 2377/90, which would exclude the existence of a risk to consumer health.

33 However, as the Commission has stated in its observations submitted to the Court and in its answers to the written questions put by the Court, without being contradicted on that point by the applicant in the main proceedings or by the governments which submitted observations to the Court, the inclusion of progesterone in Annex II to Regulation No 2377/90 exclusively in respect of intravaginal administration is likely to exclude risks to human health. As is apparent from those observations, in the case of administration by intravaginal spiral, the concentration of progesterone in the body of the animal increases significantly, then falls rapidly without leaving significant residues when the spiral is removed, whereas administration by injection leaves long-lasting residues potentially dangerous to human health.

34 In those circumstances, having regard both to the extent of the Commission's discretion and to all the factual circumstances in light of which Regulation No 1873/2003 was adopted, it does not appear that the approach followed by the Commission, taking account both of considerations of protection of human health and of requirements based on the principle of proportionality, disregarded the limits of the Commission's discretion.

35 Contrary to cp-Pharma's submissions, the fact that the CVMP had recommended the inclusion of progesterone in Annex II to Regulation No 2377/90 without any restriction as to its method of administration is not such as to call that conclusion into question.

36 In that regard, it is sufficient to note, firstly, that there is no provision of Regulation No 2377/90 which lays down that the opinions of the CVMP are binding and, secondly, that it follows expressly from the third recital in the preamble to that regulation that, in the course of establishing MRLs, the Commission must take account of any scientific assessment of the safety of the substances concerned which may have been undertaken by international organisations, in particular the Codex Alimentarius, or by other scientific committees established within the Community.

37 In other words, in the course of exercising its discretion, the Commission was in no way required to take account only of the opinion of the CVMP, which favoured

inclusion of progesterone in Annex II to that regulation, but could legitimately base its decision on other information and scientific assessments, including the opinions of the SCVPH, which had pointed out the risks to human health resulting from the presence of residues of that substance in foodstuffs of animal origin.

38 Nor did the Commission, contrary to the submissions of the Polish Government, infringe the obligation to give reasons by not specifically mentioning the scientific data which led it not to follow the opinion of the CVMP and by not indicating the extent to which the data contradicted that opinion.

39 It must be pointed out that the sixth recital in the preamble to Regulation No 1873/2003 refers expressly to the opinions of the SCVPH, differing from those of the CVMP, which had confirmed on several occasions both the risks arising from use of progesterone and the fact that it is impossible to establish MRLs for that substance. Furthermore, the eighth and tenth recitals in the preamble to that regulation state the reasons for which, according to the Commission, only intravaginal administration of progesterone can prevent the misuse of that substance.

40 Therefore, in accordance with the requirements of established case-law (see, inter alia, Case C-367/95 P *Commission* v *Sytraval and Brink's France* [1998] ECR I-1719, paragraph 63; Joined Cases C-346/03 and C-529/03 *Atzeni and Others* [2006] ECR I-1875, paragraph 73; and Case C-266/05 P *Sison* v *Council* [2007] ECR I-1233, paragraph 80), the reasoning given for Regulation No 1873/2003 shows in a clear and unequivocal fashion the reasoning followed by the Commission in such a way as to enable the persons concerned to ascertain the reasons for the measure and to enable the Court to exercise its power of review.

41 With regard to the argument raised by the Polish Government that Regulation No 1873/2003 infringes the principle of proportionality because it is based on a purely hypothetical risk to human health which is not supported by the scientific data set out in its reasoning, it suffices to note that, as has been recalled in paragraph 39 of

the present judgment, the existence of such a risk, confirmed by a number of scientific opinions, is clearly apparent from the reasoning of that regulation.

42 It should also be noted that the conclusion, set out in paragraphs 31 and 34 of the present judgment, that the Commission may restrict the inclusion of the substance in Annex II to Regulation No 2377/90 according to its method of administration is in no way called into question by the argument of the Polish Government that Regulation No 1873/2003 is incompatible with the provisions of Directive 96/22 which permit the administration of progesterone by intramuscular injection.

43 Firstly, it is appropriate to note that the conditions under which Article 4 of Directive 96/22 allows Member States to authorise the administration of progesterone to farm animals include that of compliance with the requirements relating to placing on the market laid down in Directive 81/851, which was repealed subsequently by Directive 2001/82.

44 Secondly, Article 6 of Directive 2001/82 expressly provides that, in order for a veterinary medicinal product to receive marketing authorisation for administration to food-producing animals, the active substances which that medicinal product contains must appear in Annex I, II or III to Regulation No 2377/90.

45 Accordingly, it is clear that Article 4 of Directive 96/22, read in conjunction with Article 6 of Directive 2001/82, permits Member States to authorise administration of progesterone to farm animals only if that substance is included in Annex I, II or III to Regulation No 2377/90 in accordance with the provisions thereof.

46 On the grounds set out in paragraphs 31 to 33 of the present judgment, the Commission could legitimately restrict the inclusion of progesterone in Annex II to that regulation to a specific method of administration, that is to say intravaginally. In

those circumstances, there is no incompatibility between the provisions of Regulation No 2377/90 and those of Article 4 of Directive 96/22.

47 Having regard to all of the foregoing, the answer for the referring court must be that examination of the question referred has disclosed no factor of such a kind as to affect the validity of Regulation No 1873/2003.

Costs

48 Since these proceedings are, for the parties to the main proceedings, a step in the action pending before the national court, the decision on costs is a matter for that court. Costs incurred in submitting observations to the Court, other than the costs of those parties, are not recoverable.

On those grounds, the Court (First Chamber) hereby rules:

Examination of the question referred has disclosed no factor of such a kind as to affect the validity of Commission Regulation (EC) No 1873/2003 of 24 October 2003 amending Annex II to Council Regulation (EEC) No 2377/90 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin.

[Signatures]