ORDER OF THE PRESIDENT OF THE COURT
11 April 2001 *

In Case C-478/00 P(R),

Commission of the European Communities, represented by H. Støvlbæk, M. Shotter and K. Fitch, acting as agents, and B. Wägenbaur, avocat, with an address for service in Luxembourg,

appellant,

supported by

French Republic, represented by G. de Bergues and R. Loosli-Surrans, acting as agents,

intervener on appeal,

APPEAL against the order of the President of the Court of First Instance of the European Communities of 31 October 2000 in Case T-85/00 R *Roussel and*

* Language of the case: German.

Roussel Iberica v *Commission* [2000] ECR II-3613, seeking to have that order set aside,

the other parties to the proceedings being:

Laboratórios Roussel Ld.ª, established in Mem Martins (Portugal),

Roussel Iberica SA, established in Barcelona (Spain),

represented by B. Sträter and M. Ambrosius, Rechtsanwälte, with an address for service in Luxembourg,

applicants at first instance,

THE PRESIDENT OF THE COURT

after hearing Advocate General Stix-Hackl,

makes the following

Order

1 By application lodged at the Registry of the Court of Justice on 27 December 2000, the Commission of the European Communities brought an appeal pursuant to Article 225 EC and the second paragraph of Article 50 of the EC Statute of the Court of Justice against the order made by the President of the Court of First Instance on 31 October 2000 in Case T-85/00 R *Roussel and Roussel Iberica* v *Commission* [2000] ECR II-3613 ('the order under appeal'), by which the President of the Court of First Instance suspended operation of Commission Decision C(2000) 608 of 9 March 2000 concerning the withdrawal of marketing authorisations of medicinal products for human use which contain the following substances: 'clobenzorex', 'fenbutrazate', 'fenproporex', 'mazindol', 'mefenorex', 'norpseudoephedrine', 'phenmetrazine', 'phendimetrazine' and 'propylhexedrine' ('the contested decision').

2 By document lodged at the Registry of the Court of Justice on 14 February 2001, Laboratórios Roussel Ld.ª and Roussel Iberica SA ('the Roussel companies'), which were the applicants at first instance, submitted their written observations to the Court of Justice.

3 By application lodged at the Registry of the Court of Justice on 29 January 2001, the French Republic sought leave to intervene in the present proceedings in support of the Commission.

4 Pursuant to the first and fourth paragraphs of Article 37 of the EC Statute of the Court of Justice and Article 93(1) and (2) of the Rules of Procedure, the application by the French Republic for leave to intervene in the present proceedings should be granted.

5 The French Republic lodged its statement in intervention on 19 February 2001.

6 The parties presented oral argument at the hearing on 7 March 2001.

Legal background

7 On 26 January 1965, the Council adopted Directive 65/65/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (OJ, English Special Edition 1965–66, p. 20). That directive has been amended on several occasions, in particular by Council Directive 89/341/EEC of 3 May 1989 (OJ 1989 L 142, p. 11) and Council Directive 93/39/EEC of 14 June 1993 (OJ 1993 L 214, p. 22) ('Directive 65/65'). Article 3 of Directive 65/65 lays down the principle that no medicinal product may be placed on the market of a Member State unless an authorisation has first been issued by the competent authorities of that Member State in accordance with the directive or an authorisation has been granted in accordance with 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).

8 Article 4 of Directive 65/65 provides in particular that, in order to obtain a marketing authorisation as provided for in Article 3, the person responsible for placing the product on the market is to apply to the competent authority of the Member State concerned.

9 Article 5 of Directive 65/65 states:

'The authorisation provided for in Article 3 shall be refused if, after verification of the particulars and documents listed in Article 4, it proves that the medicinal product is harmful in the normal conditions of use, or that its therapeutic efficacy is lacking or is insufficiently substantiated by the applicant, or that its qualitative and quantitative composition is not as declared.

Authorisation shall likewise be refused if the particulars and documents submitted in support of the application do not comply with Article 4.'

10 Article 10 of Directive 65/65 provides that the authorisation is valid for five years and is renewable for five-year periods after consideration by the competent authority of a dossier containing in particular details of the data on pharmacovigilance and other information relevant to the monitoring of the medicinal product.

11 The first paragraph of Article 11 of Directive 65/65 provides:

'The competent authorities of the Member States shall suspend or revoke an authorisation to place a medicinal product on the market where that product proves to be harmful in the normal conditions of use, or where its therapeutic efficacy is lacking, or where its qualitative and quantitative composition is not as declared. Therapeutic efficacy is lacking when it is established that therapeutic results cannot be obtained with the [medicinal] product.'

12 Under Article 21 of Directive 65/65, an authorisation to market a medicinal product may not be refused, suspended or revoked except on the grounds set out in that directive.

13 Council Directive 75/318/EEC of 20 May 1975 on the approximation of the laws of Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of medicinal products (OJ 1975 L 147, p. 1), as amended by Directive 89/341 ('Directive 75/318'), provides, in the first paragraph of Article 1, that the Member States are to take all appropriate measures to ensure that the particulars and documents which must accompany applications for authorisation to place a medicinal product on the market pursuant to points 3, 4, 6, 7 and 8 of the second paragraph of Article 4 of Directive 65/65 are submitted by the persons concerned in accordance with the annex to Directive 75/318.

14 The seventh and eighth recitals in the preamble to Directive 75/318 are worded as follows:

'... the concepts of "harmfulness" and "therapeutic efficacy" referred to in Article 5 of Directive 65/65/EEC can only be examined in relation to each other and have only a relative significance depending on the progress of scientific knowledge and the use for which the medicinal product is intended; ... the particulars and documents which must accompany an application for authorisation to place a medicinal product on the market [must] demonstrate that potential risks are outweighed by the therapeutic efficacy of the product; ... failing such demonstration, the application must be rejected;

... the evaluation of "harmfulness" and "therapeutic efficacy" may be modified in the light of new discoveries and standards and protocols must be amended periodically to take account of scientific progress'.

15 The Second Council Directive (75/319/EEC) of 20 May 1975 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (OJ 1975 L 147, p. 13), as amended by Directive 93/39 ('Directive 75/319'), provides for a number of arbitration procedures before the Committee for Proprietary Medicinal Products ('the CPMP') of the European Agency for the Evaluation of Medicinal Products. Such a procedure is applied where a Member State considers, in the context of the procedure for the mutual recognition of national marketing authorisations which is provided for by Article 9 of Directive 75/319, that there are grounds for supposing that the authorisation of the medicinal product concerned may present a risk to public health (Article 10 of that directive), where divergent decisions have been adopted concerning the grant, suspension or withdrawal of national authorisations (Article 11), in specific cases where the interests of the Community are involved (Article 12), and in the case of variations of harmonised authorisations (Articles 15, 15a and 15b).

16 Article 12 of Directive 75/319 provides that the Member States among others may, in specific cases where the interests of the Community are involved, refer the matter to the CPMP for the application of the procedure laid down in Article 13 before reaching a decision on a request for a marketing authorisation or on the suspension or withdrawal of an authorisation, or on any other variation to its terms which appears necessary, in particular to take account of the information collected in the context of the pharmacovigilance system provided for in Chapter Va of Directive 75/319.

17 Article 15a of Directive 75/319 states:

'1. Where a Member State considers that the variation of the terms of a marketing authorisation which has been granted in accordance with the provisions of this Chapter or its suspension or withdrawal is necessary for the protection of public health, the Member State concerned shall forthwith refer the matter to the Committee for the application of the [procedures] laid down in Articles 13 and 14.

2. Without prejudice to the provisions of Article 12, in exceptional cases, where urgent action is essential to protect public health, until a definitive decision is adopted a Member State may suspend the marketing and the use of the medicinal product concerned on its territory. It shall inform the Commission and the other Member States no later than the following working day of the reasons for its action.'

18 Article 13 of Directive 75/319 sets out the procedure before the CPMP. Article 14 lays down the procedure to be followed after the Commission receives the opinion of the CPMP. The third subparagraph of Article 14(1) states that 'where, exceptionally, the [Commission's] draft decision is not in accordance with the opinion of the Agency, the Commission shall also annex a detailed explanation of the reasons for the differences'.

Facts and procedure

19 The Roussel companies hold marketing authorisations for medicinal products containing fenproporex. The facts of the case are set out in the order under appeal as follows:

'9 On 17 May 1995 the Federal Republic of Germany made a referral to the CPMP in accordance with Article 12 of Directive 75/319, as amended by Directive 93/39, expressing its fears as regards anorectics, which include medicinal products containing fenproporex, liable to cause serious pulmonary artery hypertension.

10 The procedure initiated by this referral led to the adoption of Commission Decision C(96) 3608 of 9 December 1996 ["the decision of 9 Decem-

ber 1996"], based on Article 14(1) and (2) of Directive 75/319, instructing Member States to vary certain clinical information which had to appear in the national authorisations to place the medicinal products in question on the market.

11 By letter of 7 November 1997 addressed to the chairman of the CPMP, the Belgian Ministry of Social Affairs, Public Health and the Environment expressed *inter alia* its fears that there was a causal link between cardiac valve disorders and the use of anorectics containing amfepramone or phentermine. It therefore requested the CPMP, pursuant to Articles 13 and 15a of Directive 75/319, to issue a reasoned opinion on the medicinal products concerned.

12 By letter of 31 August 1998, likewise addressed to the chairman of the CPMP, the Austrian Ministry of Labour, Health and Social Affairs pointed out that, in addition to phentermine and amfepramone, clobenzorex, fenbutrazate, fenproporex, mazindol, mefenorex, norpseudoephedrine, phenmetrazine, phendimetrazine and propylhexedrine belonged to the same group of amphetamine-related anorectics. The Austrian Ministry added that all those substances probably had the same properties and the same side-effects and requested the CPMP, pursuant to Article 15a of Directive 75/319, to issue a reasoned opinion relating to the medicinal products concerned.

13 On 31 August 1999 the CPMP gave its opinion on medicinal products containing clobenzorex, fenbutrazate, fenproporex, mazindol, mefenorex, norpseudoephedrine, phenmetrazine, phendimetrazine and propylhexedrine. It concluded that those medicinal products had an unfavourable benefit/risk balance and recommended that the authorisations to place them on the market should be withdrawn.

14 On the basis of that opinion, the Commission prepared a draft decision which was sent to the applicants amongst others on 20 January 2000. On 9 March 2000 the Commission adopted the decision concerning the withdrawal of marketing authorisations of medicinal products for human use which contain the substances "clobenzorex", "fenbutrazate", "fenproporex", "mazindol", "mefenorex", "norpseudoephedrine", "phenmetrazine", "phendimetrazine" and "propylhexedrine"... Article 2 of the contested decision refers to the views expressed by the CPMP in the opinion. Article 3 provides that the Member States are to withdraw the marketing authorisations for all the medicinal products mentioned in Annex I to the contested decision within 30 days of its notification.'

20 By application lodged at the Registry of the Court of First Instance on 6 April 2000, the Roussel companies brought an action before the Court of First Instance under the fourth paragraph of Article 230 EC for annulment of the contested decision or, in the alternative, its annulment in so far as it entails the withdrawal of the marketing authorisations for medicinal products for human use containing fenproporex in Spain and Portugal.

21 By separate document lodged at the Court Registry on the same day, the Roussel companies made an application for suspension of operation of the contested decision, together with an application on the basis of Article 105(2) of the Rules of Procedure of the Court of First Instance for an urgent decision on the claim for interim relief.

22 On 18 April 2000 the President of the Court of First Instance granted the application based on Article 105(2) of the Rules of Procedure and ordered that operation of the contested decision should be suspended until the making of the order terminating the proceedings for interim relief.

23 Apart from the contested decision, the Commission adopted two other decisions on 9 March 2000, concerning the withdrawal of marketing authorisations for

medicinal products for human use which contain phentermine (C(2000) 452) and amfepramone (C(2000) 453). All those decisions concern medicinal products for the treatment of obesity, which had already been referred to in the decision of 9 December 1996, and they were prompted by a re-evaluation of those medicinal products under Article 15a of Directive 75/319 which had been requested by two Member States. The evaluation procedure resulted in a number of opinions of the CPMP, adopted by its members almost unanimously, recommending withdrawal of the marketing authorisations for all the medicinal products for very similar reasons. The Commission decisions of 9 March 2000 are founded on those opinions.

24 Nine applications for interim relief were made in respect of the three decisions referred to in the preceding paragraph. By order of 28 June 2000 in Case T-74/00 R *Artegodan* v *Commission* [2000] ECR II-2583, the President of the Court of First Instance decided one of those applications and ordered suspension of the operation of Decision C(2000) 453 in relation to Artegodan GmbH. No appeal was brought against that order. The President of the Court of First Instance decided the other eight applications for interim relief by order of 19 October 2000 in Case T-141/00 R *Trenker* v *Commission* [2000] ECR II-3313 and by seven orders of 31 October 2000: in Case T-76/00 R *Bruno Farmaceutici and Others* v *Commission* [2000] ECR II-3557, Case T-83/00 R II *Schuck* v *Commission* [2000] ECR II-3585, Case T-83/00 R I *Hänseler* v *Commission* [2000] ECR II-3563, Case T-84/00 R *Roussel and Roussel Diamant* v *Commission* [2000] ECR II-3591, Case T-132/00 R *Gerot Pharmazeutika* v *Commission* [2000] ECR II-3635, Case T-137/00 R *Cambridge Healthcare Supplies* v *Commission* [2000] ECR II-3653, and the order under appeal. Those eight orders, against which the Commission has brought appeals, and the order in *Artegodan* v *Commission* are founded on almost identical grounds.

The order under appeal

25 By the order under appeal, the President of the Court of First Instance granted the Roussel companies' application for interim relief and ordered suspension of the operation of the contested decision in their regard.

26 The President of the Court of First Instance held that the condition relating to the establishment of a prima facie case was satisfied in the case in point. In this connection, he set out the following factors at paragraph 32 of the order under appeal:

'32 As regards the question of a prima facie case, the pleas raised by the applicants do not prima facie appear to be entirely unfounded. First, it appears that the competence of the Commission to adopt the contested decision depends on the nature of the decision of 9 December 1996, which is open to debate. Second, the Commission has not adduced convincing evidence to explain why that decision and the contested decision reached diametrically opposed results. The pleas raised by the applicants therefore deserve detailed consideration, a consideration which, however, in fact and in law, goes beyond the scope of the present interim proceedings.'

27 As regards the question of urgency, the President of the Court of First Instance concluded that the damage which immediate operation of the contested decision could cause would be serious and irreparable. In reaching that conclusion, he relied on the following considerations:

'42 In the present case, immediate operation of the contested decision means the complete withdrawal from the market of the medicinal products referred to in Article 1 of the decision. It therefore means that, if operation of the contested decision is not suspended, substitute medicinal products, the existence of which is acknowledged by the parties, will very probably take the place of the products withdrawn. The confidence of consumers, doctors and pharmacists in a medicinal product is particularly sensitive to statements that the product presents a danger to patients' health. Even if those statements are subsequently disproved, it is often impossible to restore confidence in the withdrawn product, other than in special cases where the

qualities of the medicinal product are especially valued by users and there is no perfect substitute product, or where the manufacturer enjoys an exceptionally good reputation, so that it cannot be said that he will be unable to repossess the market shares he held before withdrawal. However, such circumstances are not present here.

43 Moreover, if the contested decision were to be annulled by the Court of First Instance and the applicants thus authorised to resume marketing their medicinal products, the financial damage suffered by them because of a fall in sales as a result of loss of confidence in their products could not in practice be quantified sufficiently completely for the purposes of making reparation.'

28 The President of the Court of First Instance found that in the case in point the balance of interests favoured suspension of operation of the contested decision, on the basis of the following considerations:

'48 It appears highly probable that the operation of the contested decision would entail the definitive loss of the applicants' position in the market, even if the court hearing the main application were to annul the decision.

49 In opposition to the commercial interests of the applicants, the Commission submits that suspension of operation of the contested decision could harm public health. On this point, it must be emphasised that in principle the requirements of the protection of public health must unquestionably be given precedence over economic considerations (order [of the Court of Justice] in

[Case C-180/96 R] *United Kingdom* v *Commission* [[1996] ECR I-3903], paragraph 93; judgment in Case C-183/95 *Affish* v *Rijksdienst Keuring Vee en Vlees* [1997] ECR I-4315, paragraph 43; order of the Court of First Instance in Case T-136/95 *Industria del Frio Auxiliar Conservera* v *Commission* [1998] ECR II-3301, paragraph 58; and order of the President of the Court of First Instance in Case T-70/99 R *Alpharma* v *Commission* [1999] ECR II-2027, paragraph 152).

50 However, it must be noted that in this context the mere reference to the protection of public health cannot exclude an examination of the circumstances of the case, in particular of the relevant facts.

51 In the present case, the Commission has indeed established that there is uncertainty as regards the risks associated with medicinal products containing fenproporex, even if those risks are slight. Nevertheless, although the decision of 9 December 1996 and the contested decision are based on identical data, the measures taken by the Commission in 1996 and 2000 for the protection of public health with respect to those risks differ fundamentally. In those circumstances, the Commission was obliged to show that the protective measures in the decision of 9 December 1996 proved to be insufficient to protect public health, so that the protective measures it adopted in the contested decision were not manifestly excessive. However, the Commission has not been able to show this.

52 Moreover, the fact that the health risks which determined the adoption of the contested decision had already been taken into account in the Commission's decision of 9 December 1996 and had resulted in a change to the compulsory information concerning medicinal products supplied on prescription indicates that implementation of the contested decision is not urgent.'

The appeal

Arguments of the parties

29 The Commission founds its appeal on seven pleas in law.

30 By its first plea, the Commission, supported by the French Government, complains that the President of the Court of First Instance failed to apply properly, or at all, the precautionary principle in his balancing of the interests. This principle means that the Commission may take protective measures without having to wait until the reality and seriousness of those risks become fully apparent (Case C-157/96 *National Farmers' Union and Others* [1998] ECR I-2211, paragraph 63).

31 The basis of the second plea is that the President of the Court of First Instance misunderstood the nature of the contested decision and the process leading to its adoption.

32 The Commission submits that, when it adopts measures to protect public health with regard to medicinal products, the scientific process of assessing risk is not undertaken by it but by scientific experts, namely the members of the CPMP. It is on the basis of that assessment that the Commission then takes its policy decision ('risk management' decision), weighing the result of the risk assessment with other factors to be taken into account. The lack of reference to the scientific opinion of the CPMP in the order under appeal reveals a fundamental misunderstanding of the procedure leading to the adoption of the contested decision.

33 According to the Commission, the reason why, on 9 March 2000, it adopted a decision which differed from that of 9 December 1996 is directly connected with the final opinion of the CPMP dated 31 August 1999. The Commission points out that the statement of reasons for the contested decision referred to the fact that, in the CPMP's view, medicinal products containing fenproporex lacked therapeutic efficacy in the treatment of obesity when assessed on the basis of accumulated scientific knowledge acquired over the years and current medical recommendations.

34 Between the adoption of the decision of 9 December 1996 and that of the contested decision, the guidelines concerning the therapeutic efficacy of medicinal products for the treatment of obesity and the medical guidelines on the treatment of obesity had changed, causing the CPMP to alter its scientific assessment. Those guidelines represent a fundamental change in the scientific community's assessment of how to treat obesity. By failing to take account of that fundamental factor and focusing exclusively on the identicalness of the data upon which both the abovementioned decisions are based, the President of the Court of First Instance made a material error in assessing the balance of interests. Nor is it clear from the order under appeal that the President of the Court of First Instance took account of the fact that the contested decision introduced a higher level of health protection than that resulting from the decision of 9 December 1996.

35 The French Government essentially agrees with that line of argument, submitting that the President of the Court of First Instance distorted the content of the contested decision within the meaning of the judgment in Case C-164/98 P *DIR International Film and Others* v *Commission* [2000] ECR I-447, at paragraphs 48 and 49. Such a distortion is the result of a partial reading of the decision. The President of the Court of First Instance did not take Annex II to the decision into consideration in that he failed to note that the CPMP examined additional scientific data subsequent to 1996 and omitted the fact that, according to the CPMP, the medicinal products containing fenproporex did not have the required efficacy.

36 In its third plea, the Commission complains that the order under appeal 'exceeds the proper boundaries of judicial review'. It submits that the President of the

Court of First Instance erred in law by substituting his assessment as to the appropriate level of public health protection for that of the body competent to exercise its discretion in that field, namely the Commission. The French Government essentially endorses this plea, pointing out that the Court has previously held, in Case C-120/97 *Upjohn* [1999] ECR I-223, at paragraphs 33 and 34, that complex assessments in the medico-pharmacological field can be subject only to limited judicial review.

37 The fourth plea alleges breach of the requirement to balance the interests involved. The President of the Court of First Instance erred in law by failing to balance properly the interests concerned, in that he examined and took into account only the economic damage to the undertakings seeking suspension of the operation of the contested decision, without taking proper account of the seriousness and the irreparable nature of harm to patients treated with the medicinal product in question. The President of the Court of First Instance did not accord to the protection of public health the precedence that is required by the Court of Justice's case-law, when the risks to human health had been established by the scientific experts on the CPMP.

38 The fifth plea concerns an error of law with regard to the standard of proof required of the Commission. The President of the Court of First Instance proceeded on the assumption that the Commission, assisted by the CPMP, is, on its own, in a position to demonstrate that a medicinal product lacks therapeutic efficacy or is harmful in the normal conditions of use. The Commission points out that the provision of data on the safety and therapeutic efficacy of a medicinal product is largely dependent on the holder of the marketing authorisation and that it is neither the Commission's nor the CPMP's role to conduct clinical trials. The approach of the President of the Court of First Instance with regard to the standard of proof would prevent the Commission from reviewing its marketing authorisation decisions unless relevant new data had arisen.

39 The sixth plea alleges material errors in relation to the finding, made in point 51 of the order under appeal, that, while there is uncertainty as regards the risks

associated with medicinal products containing fenproporex, such health risks are 'slight'. The documents submitted to the Court of First Instance clearly show that the risks associated with those medicinal products, in particular the increased risk of primary pulmonary hypertension and cardiac valve disorders, are not 'slight'. The President of the Court of First Instance replaced the CPMP's assessment with his own.

40 The seventh plea alleges a lack of reasoning in the order under appeal with regard to the assessment by the President of the Court of First Instance that the risks associated with medicinal products containing fenproporex are slight. In the Commission's submission, no explanation is given, either in paragraph 51 or elsewhere in the order under appeal, making it possible to understand the reasons for such an assessment.

41 As regards the precautionary principle, the Roussel companies allege that the Commission has failed to cite any specific provision of Community law in support of its argument. That principle has been implemented, in the case of the law on medicinal products, in Directives 65/65 and 75/319 and it is solely by reference to those two directives that the withdrawal of a marketing authorisation should be analysed. While the applicant must substantiate the efficacy and safety of the medicinal product in order to obtain a marketing authorisation, the situation is very different where the marketing authorisation has been granted, since it can be withdrawn only under the conditions laid down in Article 11 of Directive 65/65. It is for the competent authority of the Member State concerned to prove that the conditions for withdrawal are met. The President of the Court of First Instance complied with that legal framework when finding that the Commission had not shown that the existing measures did not protect public health sufficiently.

42 So far as concerns the second plea put forward by the Commission, the Roussel companies submit that the order under appeal mentions the opinion of the CPMP in paragraph 13 and that it was not necessary to refer to it again in paragraphs 45 to 53 of the order, since the Community judicature is not required in proceedings for interim relief to mention expressly every fact or legal point. In any event, the

scientific data did not change from 1996 to 2000, because the guidelines referred to by the Commission concern evaluation criteria which cannot be applied to medicinal products which are already authorised. Furthermore, in considering that decisions to withdraw authorisation are designed to establish an even higher level of protection of public health, the Commission overlooks the fact that decisions to grant marketing authorisation presuppose a positive assessment of the benefit/risk balance. The Commission has already authorised the marketing of the medicinal products because their benefits outweigh the risks. Following the Commission's logic, the marketing of a medicinal product should be refused as soon as there is the slightest risk of an adverse effect.

43 Furthermore, the Commission now gives the impression that the contested decision was adopted for reasons relating to the safety of the medicinal product when, in reality, the withdrawal was ordered because of a new assessment of its efficacy. The appeal also seeks to give the impression that the Commission took account of urgent considerations relating to the protection of public health although, first, the duration of the procedure exceeded the limits imposed by Articles 13 and 14 of Directive 75/319 and, second, the Commission did not bring an appeal against the order in *Artegodan* v *Commission*, cited above.

44 As to the third plea, the Roussel companies contend that the President of the Court of First Instance did not evaluate medicinal products containing fenproporex himself, but merely established that the contested decision and that of 9 December 1996 are based on identical data. In those circumstances, he inferred a specific duty on the Commission to give reasons.

45 With regard to the fourth plea, alleging an error of law in the balancing of the interests, the Roussel companies submit that the President of the Court of First Instance took account of the public health risks, as shown by paragraph 52 of the order under appeal. However, he simply found that those risks had already been taken into consideration by the decision of 9 December 1996.

46 As to the fifth plea, alleging an error of law concerning the standard of proof, the Roussel companies maintain that the Commission's contentions reveal a false understanding of Directive 65/65. It is true that the applicant must prove that the conditions are met for the grant of a marketing authorisation but, once the authorisation has been granted, the legal framework is altered. Under Article 10 of Directive 65/65, marketing authorisations are valid for five years and if, on their renewal, the competent authorities have doubts concerning the safety or efficacy of the medicinal product, they may ask for further studies to be carried out. That provision thus enables the competent authorities to obtain new scientific data. In addition, the pharmacovigilance system serves to provide information on any adverse effects and enables the consequences to be drawn.

47 As regards the sixth plea, alleging material errors in relation to the finding made in paragraph 51 of the order under appeal, the Roussel companies submit that a question of fact is involved and that, in any event, the assessment of the President of the Court of First Instance is correct inasmuch as the contested decision refers only to uncertainty concerning adverse effects of medicinal products containing fenproporex.

48 To rebut the seventh plea, the Roussel companies contend that the obligation to state reasons does not apply to the same degree to the court adjudicating on the substance of the case and to one hearing an application for interim relief, and that the latter cannot be required to deal expressly with every point of fact or law. The grounds adopted by the President of the Court of First Instance constitute, in the light of the circumstances of the case, a valid basis for the order under appeal and allow the Court of Justice to exercise its powers of review.

Findings

49 In accordance with Article 225 EC and Article 51 of the EC Statute of the Court of Justice, appeals are limited to points of law and lie solely on the grounds of

lack of competence of the Court of First Instance, a breach of procedure before it which adversely affects the interests of the appellant or the infringement of Community law by the Court of First Instance.

50 The Court of First Instance has exclusive jurisdiction to find the facts, save where a substantive inaccuracy in its findings is attributable to the documents submitted to it, and to appraise those facts. That appraisal thus does not, save where the clear sense of the evidence has been distorted, constitute a point of law which is subject, as such, to review by the Court of Justice on appeal (see, in particular, Case C-390/95 P *Antillean Rice Mills and Others* v *Commission* [1999] ECR I-769, paragraph 29).

51 It is in the light of those considerations that the appellant's pleas should be considered.

52 First of all, since there is a question of an absolute bar, the Court must consider of its own motion whether the appeal is inadmissible in so far as it disregards the binding authority of the order in *Artegodan* v *Commission*, cited above, such a plea having been raised in Case C-459/00 P(R) *Commission* v *Trenker*, decided by an order made today [2001] ECR I-2823.

53 It need only be observed that the conditions governing the admissibility of appeals laid down by Article 49 of the EC Statute of the Court of Justice are assessed in relation to the case at issue and that alone. The fact that the grounds of an order of the Court of First Instance which has become definitive are identical to those of an order subject to appeal does not prevent the appellant from contesting such grounds (see, with regard to a judgment of the Court of First Instance upholding an objection of illegality raised against a legislative measure,

Joined Cases C-432/98 P and C-433/98 P *Council* v *Chvatal and Others* [2000] ECR I-8535, paragraph 22).

54 Accordingly, the appeal is admissible.

55 The plea concerning distortion of the content of the contested decision should be considered first.

56 In this connection, it is clear from the grounds of the order under appeal relating both to the establishment of a prima facie case and to the balancing of interests that the following considerations were decisive in the reasoning of the President of the Court of First Instance:

— '... the Commission has not adduced convincing evidence to explain why [the decision of 9 December 1996] and the contested decision reached diametrically opposed results' (paragraph 32);

— '... although the decision of 9 December 1996 and the contested decision are based on identical data, the measures taken by the Commission in 1996 and 2000 for the protection of public health with respect to those risks differ fundamentally. In those circumstances, the Commission was obliged to show that the protective measures in the decision of 9 December 1996 proved to be insufficient to protect public health, so that the protective measures it adopted in the contested decision were not manifestly excessive' (paragraph 51);

— '... the health risks which determined the adoption of the contested decision had already been taken into account in the Commission's decision of 9 December 1996 and had resulted in a change to the compulsory information concerning medicinal products supplied on prescription' (paragraph 52).

57 Those findings are not based on even a cursory analysis of the statement of reasons for the contested decision as set out in Annex II to the decision, to which Article 2 refers.

58 Annex II to the contested decision, which sets out the scientific conclusions of the CPMP in order to indicate the reasons leading to the withdrawal of the marketing authorisations for the medicinal products listed in Annex I to the decision, contains first of all an analysis of the efficacy of those products. It is concluded in Annex II that medicinal products containing fenproporex 'lack therapeutic efficacy in the treatment of obesity when assessed on the basis of accumulated scientific knowledge acquired over the years and current medical recommendations'.

59 In reaching such a conclusion, Annex II states that fenproporex lacks therapeutic efficacy in the treatment of obesity when used for three months or less. It is explained that 'rapid weight regain occurs once treatment is discontinued and there are no controlled studies which demonstrate that a limited short-term effect has any long-term clinically relevant influence on body weight or provides a clinical benefit within an anti-obesity programme'. It is also pointed out that longer-term use would increase the potential risks, in particular of drug abuse and drug dependence. It is concluded that 'in no case (short-term nor long-term) clobenzorex, fenbutrazate, fenproporex, mefenorex, norpseudoephedrine, phenmetrazine and phendimetrazine can be envisaged for a safe and efficacious treatment of obesity'.

60 According to Annex II, therapeutic efficacy in treating obesity requires a significant and long-term lowering of body weight, over at least one year. It states: 'This is based on accumulated scientific knowledge acquired over the years and is laid down in current medical recommendations; this is reflected in the Note for Guidance on Clinical Investigation of Drugs Used in Weight Control (CPMP/EWP/281/96). This is also expressed in current guidelines, e.g. the Scottish guideline (1996), a guideline from the Royal College of Physicians (1998) and in a guideline from the American Society for Clinical Nutrition (1998).'

61 The importance of those reasons given the subject-matter of the contested decision and in the light of the applicable law concerning the evaluation of medicinal products should be noted.

62 Under Article 5 of Directive 65/65, the evaluation of every medicinal product relates to its efficacy, its harmlessness and its quality. Compliance with those three conditions is intended to protect public health. The very concept of the protection of public health means that the medicinal product in question not only must not be harmful but also must be effective. As the footnotes to Article 10(1) of Directive 75/319 and Article 7a of Directive 65/65 state, 'the expression "risk to public health" refers to the quality, safety and efficacy of the medicinal product'.

63 The importance attached to the efficacy of the medicinal product, which is fundamental to the contested decision, is due to the fact that the first subparagraph of Article 1(2) of Directive 65/65 adopts the 'presentation' criterion when defining a medicinal product. The Court has consistently held that this criterion is designed to catch not only medicinal products having a genuine therapeutic or medical effect but also those which are not sufficiently effective or do not have the effect which their presentation might lead to expect,

in order to protect consumers not only from harmful or toxic medicinal products as such but also from a variety of products used instead of the proper remedies (see, most recently, Case C-219/91 *Ter Voort* [1992] ECR I-5485, paragraph 16).

64 Consequently, as follows from the very wording of Article 11 of Directive 65/65, the competent authority is required to suspend or revoke a marketing authorisation not only where the medicinal product proves to be harmful or its quality not to be as declared, but also where it proves not to be effective.

65 The degree of harmfulness which the competent authority may regard as acceptable thus depends on the benefits which the medicinal product is considered to provide. As the seventh and eighth recitals in the preamble to Directive 75/318 state, the concepts of 'harmfulness' and 'therapeutic efficacy' can only be examined in relation to each other. Accordingly, the reasons which have led a competent authority to preserve a marketing authorisation for a medicinal product notwithstanding certain harmful effects may cease to apply if that authority considers that the benefits justifying such an authorisation, that is to say the existence of a therapeutic effect, are no longer present. It is stated in the introduction to the annex to Directive 75/318, as amended by Commission Directive 91/507/EEC of 19 July 1991 (OJ 1991 L 270, p. 32), that after issue of the marketing authorisation any new data or information are to be submitted to the competent authorities 'in order to monitor the benefit/risk assessment'.

66 It is clear that, in its assessments regarding the establishment of a prima facie case and the balance of interests, the order under appeal makes no mention of the considerations in the statement of reasons for the contested decision relating to the change in the scientific criteria for evaluating medicinal products for the treatment of obesity and to the lack of therapeutic efficacy of medicinal products containing fenproporex.

67 In accordance with the very wording of the contested decision, such a change appears to be a decisive factor in the evaluation of those medicinal products by the CPMP and the Commission.

68 Furthermore, because of that omission, the risks to which paragraphs 51 and 52 of the order under appeal refer concern only the harmfulness of the medicinal product considered in isolation, without the harmfulness being related to the medicinal product's lack of therapeutic efficacy.

69 It follows from the foregoing that, inasmuch as the order under appeal fails to take account of essential aspects of the statement of reasons for the contested decision and, therefore, distorts the latter's content, it is vitiated by an error of law.

70 Accordingly, without it being necessary to rule on the remaining pleas, the appeal must be allowed and the order under appeal set aside.

71 In accordance with the first paragraph of Article 54 of the EC Statute of the Court of Justice, if the appeal is well founded the Court of Justice is to quash the decision of the Court of First Instance. It may then itself decide the matter directly, where the state of the proceedings so permits, or refer the case back to the Court of First Instance for judgment. Since the state of the proceedings so permits, it is appropriate to give a final decision on the application for interim relief.

The application for interim relief

Prima facie case

72 The Roussel companies put forward several pleas in law to establish a prima facie case for the interim relief sought.

73 First, they submit that the Commission was not competent to adopt the contested decision. Article 15a of Directive 75/319 does not constitute a valid legal basis for the procedure used in the present case. Article 15a allows a Member State to initiate the procedure provided for in Articles 13 and 14 of the directive only in the case of marketing authorisations which have been granted in accordance with Chapter III of the directive. However, the authorisations in question are national authorisations, not authorisations granted in accordance with that chapter. The fact that they were varied by the decision of 9 December 1996, following a procedure initiated under Article 12 of Directive 75/319, does not affect that conclusion.

74 The Roussel companies add that Article 15a of Directive 75/319 requires the suspension or withdrawal of a marketing authorisation to be necessary for the protection of public health. However, that condition is not met or, at the very least, ceased to be met during the procedure, after it was established that the risks had not changed since the decision of 9 December 1996 and that the cases relied on by the Kingdom of Belgium in its request submitted under Article 12 of Directive 75/319 were not significant.

75 According to the Commission, the decision of 9 December 1996 constitutes a marketing authorisation granted in accordance with Chapter III of Directive 75/319. It adds that that decision was adopted on the basis of Article 12 of Directive 75/319 and resulted in harmonisation of the marketing authorisations for the medicinal products listed in it, which include those produced by the Roussel companies. The Commission observes that that decision substantially alters, on the basis of Community law, the national marketing authorisations in such a way that, following expiry of the period set in Article 3 thereof, the medicinal products concerned may be marketed only if their presentation includes the clinical information set out in the decision.

76 When the judge hearing an application for suspension of the operation of a measure assesses whether there is a prima facie case, his task is not to give a final decision on the interpretation of the provisions applicable to the dispute.

77 Subject to that proviso, first, it must be acknowledged that, even though the decision of 9 December 1996 did not precede the issue of the national marketing authorisations, it cannot be inferred from that circumstance that following its adoption the Member States had absolute freedom so far as concerns preservation of those national authorisations, with the risk that the harmonisation achieved by that decision would be undone. At first sight, the Roussel companies' argument would render redundant Commission decisions concerning marketing authorisations already issued, adopted in accordance with the procedure laid down in Articles 13 and 14 of Directive 75/319.

78 Second, as the Commission correctly points out, even if the doubts which were expressed by the Member State concerned with regard to the harmlessness of medicinal products containing fenproporex and which justified the referral to the CPMP proved not to be founded at the end of the procedure, that could not result in the referral being retroactively regarded as unfounded.

79 Accordingly, the arguments put forward by the Roussel companies do not appear, on an initial analysis, to establish that the Commission was not competent to adopt the contested decision.

80 Second, the Roussel companies submit that the procedure before the CPMP and the Commission in this instance was marked by a serious breach of the procedural rules laid down in Articles 13 and 14 of Directive 75/319, since the CPMP and the Commission did not comply at all with the time-limits prescribed by those provisions. They add that the fourth subparagraph of Article 14(1) of Directive 75/319 should be interpreted as requiring the Commission to forward the draft decision simultaneously to the Member States and the holders of marketing authorisations. However, the draft decision was forwarded to the Member States on 5 January 2000, but to the holders of marketing authorisations only on 20 January 2000.

81 The Commission maintains that the delays held against it were due to the large number of medicinal products subject to the examination procedure in the present case and to the fact that that examination was particularly thorough. It adds that those delays did not prejudice the Roussel companies. It also submits that Article 14 of Directive 75/319 does not impose any obligation to notify the draft decision to holders of marketing authorisations.

82 On an initial analysis, it does not appear to follow from the terms in which Articles 13 and 14 of Directive 75/319 are couched that the time-limits the exceeding of which the Roussel companies criticise are mandatory in nature. The Roussel companies contend in a general manner that those time-limits are designed to protect the interests of undertakings, but they do not specify at all what particular prejudice was caused by the delays recorded or to what extent the

delays had any effect on rights of the defence or the content of the contested decision.

83 Furthermore, irrespective of whether the Commission was required to forward the draft decision to the Roussel companies, an obligation whose existence the Commission denies, it is clear that the Roussel companies have not even sought to show that the alleged delay in sending the draft decision resulted in specific prejudice to their rights of defence. The draft decision was consistent with the opinion of the CPMP, a document which was already in their possession, and Article 14 of Directive 75/319 makes no express provision for participation by the holder of the marketing authorisation at that stage of the procedure.

84 In those circumstances, the Roussel companies' arguments do not succeed in establishing, on an initial analysis, that the procedural irregularities pleaded prejudiced their rights of defence or had the slightest effect on the outcome of the procedure.

85 Third, the Roussel companies plead that the contested decision fails to comply with the first paragraph of Article 11 of Directive 65/65, which lays down the conditions to be met for the withdrawal of a marketing authorisation, and Article 21 of that directive. They submit that the statements of the CPMP and the Commission concerning the efficacy of the medicinal products concerned clearly show that their negative evaluation is the result of balancing safety against the potential benefit of those products. This balancing is clearly wrong and constitutes a misuse of powers.

86 They add that the scientific conclusions of the CPMP infringe the rule concerning allocation of the burden of proof contained in Article 11 of Directive 65/65. The effect of that provision is that the burden of proving the merits of the grounds for

a decision withdrawing authorisation lies with the competent authorities. The CPMP expected the Roussel companies to adduce appropriate evidence of the efficacy of fenproporex whereas it should itself have proved the inefficacy of that substance.

87 The Roussel companies contend that the opinion of the CPMP took account of the most recent guidelines, which is possible only in the case of a new application for a marketing authorisation under Article 5 of Directive 65/65 or extension of a marketing authorisation pursuant to Article 10. Nor do those guidelines justify the requirements suggested by the CPMP. An error of assessment was thus made in applying the guidelines.

88 Contesting those arguments, the Commission submits that the conditions under Article 11 of Directive 65/65 are satisfied here. The CPMP clearly established that medicinal products containing fenproporex lack the therapeutic efficacy needed for the grant of a marketing authorisation. Accordingly, the benefit/risk assessment was unfavourable. The Commission adds that the CPMP was not only entitled to rely on the guidelines in force but also required to carry out a benefit/risk analysis with regard to fenproporex in the light of scientific knowledge.

89 It is to be observed that the arguments of the Roussel companies set out in paragraphs 85 to 87 of this order mainly concern the way in which the Commission exercised the discretion available to it when assessing the need for a measure withdrawing a marketing authorisation. It is not in dispute that any decision withdrawing a marketing authorisation which is adopted in accordance with the procedure laid down in Articles 13 and 14 of Directive 75/319 must comply with the substantive conditions under Article 11 of Directive 65/65, which relate to the efficacy, safety and quality of the medicinal product. This type

of decision is thus the outcome of complex assessments in the medico-pharmacological field.

90 In principle, such assessments are subject to limited judicial review. According to the Court's case-law, where a Community authority is called upon, in the performance of its duties, to make complex assessments, it enjoys a wide measure of discretion, the exercise of which is subject to a limited judicial review in the course of which the Community judicature may not substitute its assessment of the facts for the assessment made by the authority concerned. Thus, in such cases, the Community judicature must restrict itself to examining the accuracy of the findings of fact and law made by the authority concerned and to verifying, in particular, that the action taken by that authority is not vitiated by a manifest error or a misuse of powers and that it did not clearly exceed the bounds of its discretion (see, with regard to withdrawal of a marketing authorisation for a medicinal product, *Upjohn*, cited above, paragraph 34).

91 In the present case, it does not appear, prima facie, that the contested decision, which is founded on the CPMP's opinion, is vitiated by a manifest error or a misuse of powers or that the Commission clearly exceeded the bounds of its discretion.

92 It follows from the foregoing considerations that, without prejudice to the assessments to be made when the substance of the case is examined, the pleas put forward by the Roussel companies in the proceedings for interim relief do not, on an initial examination, prevail over those which the Commission relies on to contend that the contested decision is lawful.

93 Nevertheless, inasmuch as the pleas relied on by the Roussel companies do not appear to be entirely without foundation, the interim relief sought cannot be refused after examination of whether a prima facie case is established without also examining the urgency that is pleaded and the balance of the competing interests.

Urgency and balancing of interests

94 The Roussel companies submit that if operation of the contested decision is not suspended they will suffer serious and irreparable damage.

95 Withdrawal of the marketing authorisations which they hold would have the consequence of obliging doctors to prescribe competing products. The Roussel companies state that, even if the withdrawal of the marketing authorisations were annulled, it would not be possible to reintroduce the medicinal products concerned under the same conditions, since it will prove very difficult and often impossible to re-establish in the market medicinal products which have been absent for a long time. They add that this difficulty in re-establishing products in the market is due to the fact that it is not easy to persuade doctors to prescribe medicinal products which have previously been withdrawn from the market, particularly where the withdrawal occurred following a pharmacovigilance procedure.

96 The Commission maintains that the condition relating to urgency is not fulfilled.

97 First, the possibility of a marketing authorisation being withdrawn is one of the normal business risks of any pharmaceutical undertaking. It is for the undertaking concerned to protect itself against the financial consequences of such a withdrawal by an appropriate policy, such as product diversification and adequate turnover.

98 Second, from the initiation of the procedure provided for in Article 15a of Directive 75/319 and, in any event, from 31 August 1999, the date on which the final opinion of the CPMP was issued, the Roussel companies could have expected the Member States to be asked by the Commission, in the form of a

decision, to withdraw marketing authorisations for medicinal products containing fenproporex.

99 It is settled case-law that the urgency of an application for suspension of the operation of a measure must be assessed in the light of the need for an interlocutory order in order to avoid serious and irreparable damage to the party seeking the suspension. In this connection, it is enough, particularly where damage depends on the occurrence of a number of factors, for that damage to be foreseeable with a sufficient degree of probability (see, for example, the orders in Case C-280/93 R *Germany* v *Council* [1993] ECR I-3667, paragraphs 22 and 34, and in Case C-335/99 P(R) *HFB and Others* v *Commission* [1999] ECR I-8705, paragraph 67).

100 In the present case, immediate operation of the contested decision means the complete withdrawal from the market of the medicinal products referred to in Article 1 of the decision. Therefore, if operation of the contested decision is not suspended, it is probable that substitute medicinal products, whose existence is acknowledged by the parties, will be prescribed instead of the withdrawn medicinal products while the proceedings on the merits of the case take place.

101 The risk therefore exists that, if the contested decision is annulled, it will then be difficult for the Roussel companies to recover the market shares which they held before the contested decision came into operation.

102 However, the Roussel companies merely plead difficulties in recovering market shares, in particular because there may be a loss of confidence in the medicinal products in question, and have not demonstrated at all that obstacles of a structural or legal nature would prevent doctors from prescribing such medicinal products again and those companies from regaining a significant proportion of those market shares following the putting into place, in particular, of appropriate publicity measures for doctors.

103 Furthermore, the damage alleged is purely financial in nature and, in principle, purely pecuniary damage cannot be regarded as irreparable or even as reparable only with difficulty since it may be the subject of subsequent financial compensation (order in Case 141/84 R *De Compte* v *Parliament* [1984] ECR 2575, paragraph 4).

104 Nevertheless, the judge hearing the application for interim relief must examine the circumstances of each case (*De Compte* v *Parliament*, cited above, paragraph 4).

105 In that regard, the Roussel companies form part of a very substantial multinational group of companies. As is apparent from the documents produced by those companies at the request of the President of the Court of First Instance, the turnover corresponding to the medicinal products covered by the contested decision represents a negligible part of the group's overall turnover. The financial losses which would result from implementation of the decision could probably be made up for by sales of other products and are therefore not in any way capable of weakening the financial health of the Roussel companies.

106 In addition, account should be taken of the fact that the Roussel companies operate in a market, the human medicinal products market, which is highly regulated.

107 In a sector where major investment is often required and the competent authorities may be led to intervene rapidly when public health risks become

apparent, for reasons which cannot always be foreseen by the undertakings concerned, it is for those undertakings, if they are not to bear themselves the loss resulting from such intervention, to protect themselves against its consequences by adopting an appropriate policy.

108 It was already pointed out in the decision of 9 December 1996, which, moreover, was not challenged by the Roussel companies, that medicinal products containing fenproporex had harmful effects. In those circumstances, the possibility that a decision could be adopted withdrawing or suspending the marketing authorisations held by those companies had to be taken into account as one of the risks which they normally had to bear once a referral had been made to the CPMP by a Member State because it considered that variation of the terms of the marketing authorisation or its suspension or withdrawal was necessary to protect public health.

109 In any event, even if the risk that damage which is irreparable or reparable only with difficulty would, following application of the contested decision, be suffered while the proceedings on the substance of the case take place were regarded as satisfactorily established, the Roussel companies' interest in obtaining suspension of the operation of the contested decision could not prevail in the present case over the interest of the Community in the immediate withdrawal of the marketing authorisations held by them, with a view to protecting public health.

110 It must be remembered that, in principle, the requirements of the protection of public health must unquestionably be given precedence over economic considerations (order in *United Kingdom* v *Commission*, cited above, paragraph 93).

111 In the present case, it is not in dispute that the CPMP's opinion, to which the contested decision refers, pointed out, as regards effects on the central nervous

system, that the medicinal products in question have 'serious effects such as psychotic reactions or psychosis, depression and convulsions' and that the potential for drug abuse and drug dependence is 'well known'. It also found that 'there were concerns related to the safety profile of [medicinal products containing fenproporex] concerning the risk of primary pulmonary hypertension and other serious cardiovascular... adverse reactions...'. Those considerations bear out the assessments already made on the safety of those medicinal products in 1996.

112 It was following the CPMP's assessments that medicinal products containing fenproporex lacked therapeutic efficacy in the treatment of obesity that the Commission, relying on the opinion of that committee, concluded that the benefit/risk assessment was unfavourable.

113 Without prejudice to the assessments to be made in the proceedings on the substance of the case, the judge hearing the application for interim relief cannot, in the absence of evidence of manifest error or misuse of powers, substitute his own assessments for those of the CPMP, which are the result of an in-depth *inter partes* procedure which led it to recommend the withdrawal of the marketing authorisations for medicinal products containing fenproporex.

114 Having regard to those assessments, it is evident that suspending the operation of the contested decision would be liable to make the users of those medicinal products run serious risks and, in terms of public health, would risk causing harm which could not be remedied if the substantive action were subsequently dismissed.

115 It follows from all the foregoing considerations that the application for interim relief must be dismissed.

On those grounds,

THE PRESIDENT OF THE COURT

hereby orders:

1. The order of the President of the Court of First Instance of the European Communities of 31 October 2000 in Case T-85/00 R *Roussel and Roussel Iberica* v *Commission*, ECR II-3613, is set aside.

2. The application for interim relief is dismissed.

3. Costs are reserved.

Luxembourg, 11 April 2001.

R. Grass
Registrar

G.C. Rodríguez Iglesias
President