ORDER OF THE PRESIDENT OF THE COURT OF FIRST INSTANCE
7 April 2000 *

In Case T-326/99 R,

Nancy Fern Olivieri, resident in Toronto (Canada), represented by P. Sands and J. Marks, Barristers, and R. Stein, Solicitor, with an address for service in Luxembourg at the Chambers of Nathan & Noesen, 18 Rue des Glacis,

applicant,

v

Commission of the European Communities, represented by R. Wainwright, Legal Adviser, and H. Støvlbæk, of its Legal Service, acting as Agents, with an address for service in Luxembourg at the office of C. Gómez de la Cruz, also of its Legal Service, Wagner Centre, Kirchberg,

defendant,

supported by

Apotex Europe Ltd, having its registered office in Leeds (United Kingdom), represented by P. Bogaert and M. Le Berre, of the Brussels Bar, S. Fries,

* Language of the case: English.

Rechtsanwalt, Baden-Württemberg, and G. Castle, Solicitor, with an address for service in Luxembourg at the Chambers of A. Lutgen, 1 Rue Jean-Paul Brasseur,

intervener,

APPLICATION for suspension of the operation of the Commission decision of 25 August 1999 granting marketing authorisation for the medicinal product for human use known as 'Ferriprox' (OJ 1999 C 270, p. 2),

THE PRESIDENT OF THE COURT OF FIRST INSTANCE OF THE EUROPEAN COMMUNITIES

makes the following

Order

Legal framework

Relevant provisions of Regulation (EEC) No 2309/93

1 Article 5 of 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) provides:

'The Committee for Proprietary Medicinal Products established by Article 8 of Directive 75/319/EEC... shall be responsible for formulating the opinion of the Agency on any questions concerning the admissibility of the files submitted in accordance with the centralised procedure, the granting, variation, suspension or withdrawal of an authorisation to place a medicinal product for human use on the market arising in accordance with the provisions of this Title and pharmacovigilance.'

2 Article 6(1) provides: 'An application for authorisation for a medicinal product for human use must be accompanied by the particulars and documents referred to in Articles 4 and 4a of Directive 65/65/EEC, in the Annex to Directive 75/318/EEC and in Article 2 of Directive 75/319/EEC.'

3 Article 7 provides:

'In order to prepare its opinion, the Committee [for Proprietary Medicinal Products]:

(a) shall verify that the particulars and documents submitted in accordance with Article 6 comply with the requirements of Directives 65/65/EEC, 75/318/

EEC and 75/319/EEC, and examine whether the conditions specified in this Regulation for issuing a marketing authorisation for the medicinal product are satisfied;

...'

4 Article 11 provides:

'Without prejudice to other provisions of Community law, the authorisation provided for in Article 3 shall be refused if, after verification of the information and particulars submitted in accordance with Article 6, it appears that the quality, the safety or the efficacy of the medicinal product have not been adequately or sufficiently demonstrated by the applicant. ...'

5 Article 13(2) provides:

'In exceptional circumstances and following consultation with the applicant, an authorisation may be granted subject to certain specific obligations, to be reviewed annually by the Agency.

Such exceptional decisions may be adopted only for objective and verifiable reasons and must be based on one of the causes mentioned in Part 4 G of the Annex to Directive 75/318/EEC.'

6 Article 68(2) states:

'An authorisation to place on the market a medicinal product coming within the scope of this Regulation shall not be granted... except in accordance with the procedures set out in this Regulation.'

Relevant provisions of the Annex to Directive 75/318/EEC

7 The text of 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 1975 L 147, p. 1) has been replaced by that of the Annex to Commission Directive 91/507/EEC of 19 July 1991 (OJ 1991 L 270, p. 32).

8 Part 4 of the Annex to Directive 75/318 lays down the requirements to be complied with by the particulars and documents accompanying applications for authorisation to market a medicinal product.

9 The second recital in Part 4 of that annex defines a clinical trial as 'any systematic study of medicinal products in human subjects whether in patients or non-patient volunteers in order to discover or verify the effects of and/or identify any adverse reaction to investigational products, and/or to study their absorption, distribution, metabolism and excretion in order to ascertain the efficacy and safety of the products'.

10 Part 4.C of the Annex governs the presentation of the results of clinical trials. Point (1) of Part 4.C states as follows:

'The particulars of each clinical trial must contain sufficient detail to allow an objective judgment to be made:

...

— final report signed by the investigator and for multicentre trials, by all the investigators or the coordinating (principal) investigator.'

11 Part 4.G of the Annex deals with the documentation to be produced for applications for authorisation made in exceptional circumstances. It is worded as follows:

'When, in respect of particular therapeutic indications, the applicant can show that he is unable to provide comprehensive data on the quality, efficacy and safety under normal conditions of use, because:

— the indications for which the product in question is intended are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, or

— in the present state of scientific knowledge comprehensive information cannot be provided, or

...,

marketing authorisation may be granted on the following conditions:

(a) the applicant completed an identified programme of studies within a time period specified by the competent authority, the results of which shall form the basis of a reassessment of the benefit/risk profile,

(b) the medicinal product in question may be supplied on medical prescription only and may in certain cases be administered only under strict medical supervision, possibly in a hospital...,

(c) the package leaflet and any medical information shall draw the attention of the medical practitioner to the fact that the particulars available concerning the medicinal product in question are as yet inadequate in certain specified respects.'

Facts

12 Thalassemia major is an inherited disease characterised by severe anaemia. Its treatment necessitates frequent blood transfusions. Such transfusions, however, result in the harmful accumulation of iron in a patient's organs. Since the body has no natural means of eliminating excess iron, this gradual accumulation of iron causes damage, in particular to the heart and liver, which reduces the patient's life expectancy.

13 The pharmacological therapy at present available to counter iron overload is deferoxamine. Treatment with deferoxamine, however, is uncomfortable, since it is administered by subcutaneous infusion, which must be carried out several times a week and may last up to 12 hours per day. It may also cause hypersensitivity to the substance.

14 Dr Nancy Fern Olivieri is an internationally recognised specialist in this disease. In her research work into the treatment of persons suffering from thalassemia, she has, since 1989, carried out detailed investigations and major trials of deferiprone, which is an iron-chelation agent administered orally.

15 From 1989 to May 1996, the applicant took part, as an investigator, in three clinical trials of deferiprone, which were in part financed by the company Apotex and are referred to as trials LA-01, LA-02 and LA-03. She was the principal investigator in trials LA-01 and LA-03.

16 Trial LA-01, which was a randomised trial of deferiprone and deferoxamine, was designed to evaluate the relevant effectiveness of the two substances. Trial LA-03 was designed to assess the long-term effectiveness and safety of deferiprone. On 24 May 1996 Apotex prematurely terminated trials LA-01 and LA-03.

17 Trial LA-02 was a targeted safety study of bone marrow function and joint disease. The applicant was not involved in this trial up to the date of its conclusion.

18 None of the reports on the three clinical trials bears the applicant's signature.

19 In a study made after the LA-01 and LA-03 trials, the applicant concluded that deferiprone was toxic to the heart and liver and that its use carried considerable risks concerning the development of cardiac disease and the occurrence of liver fibrosis. She immediately discontinued human trials of the product.

20 On 6 February 1998, Apotex Europe Ltd (hereinafter 'Apotex') submitted an application under Article 4(1) of Regulation No 2309/93 to the European Agency for the Evaluation of Medicinal Products (hereinafter 'the Agency') for marketing authorisation for the medicinal product 'Ferriprox', the active ingredient of which is deferiprone. This medicinal product, which has the advantage of being administered orally, is, like deferiprone, designed to counter iron overload.

21 This medicinal product was the subject of the centralised authorisation procedure.

22 In the course of the evaluation procedure, Apotex provided written and oral explanations and the Committee for Proprietary Medicinal Products (hereinafter 'the CPMP') delivered an opinion on 27 January 1999 in favour of granting marketing authorisation for the medicinal product, having regard to the 'exceptional circumstances' referred to in Article 13(2) of Regulation No 2309/93 and Part 4.G of the Annex to Directive 75/318.

23 Since Apotex did not appeal against this, the favourable opinion of the CPMP was considered as final and on 4 March 1999 was transmitted by the Agency to the Commission. This information was made public in April 1999.

24 On being apprised of this information, the applicant expressed to the Agency, from 28 April 1999, her concerns as to the health risks involved in the marketing of Ferriprox. She stressed in particular the risk of liver fibrosis to which patients receiving deferiprone would be exposed.

25 On 20 May 1999, the Chairman of the CPMP informed the Commission that the CPMP was considering potentially important new information regarding the safety of deferiprone which was to be rapidly reviewed in the light of previous data in order to determine whether the benefit/risk ratio had been altered. The CPMP asked the Commission to indicate what procedure should be followed in such a case. Apotex was also invited at the same time to supplement the documentation on its application file with any additional available information or to confirm that all data currently available on the risk of liver fibrosis had been transmitted to the Agency.

26 By letter of 15 June 1999, the Commission requested the CPMP to examine whether 'there are important new questions of a scientific or technical nature, which have not been addressed in the opinion of the Agency'.

27 During May and June 1999, the applicant remained in regular contact with the Agency, both indirectly through her lawyers and directly, in relation to her concerns regarding deferiprone.

28 On 21 June 1999, an *ad hoc* expert working group (hereinafter 'the *ad hoc* working group') established within the Agency was convened to examine the new information relating to the safety of the product and the implications of that information.

29 After considering the recommendations of the *ad hoc* working group, the CPMP concluded that the favourable opinion concerning granting of the marketing authorisation for Ferriprox should be upheld in view of 'exceptional circumstances'; however, it also recommended a revision of the draft Summary of Product Characteristics and Package Leaflet in order to extend the information with regard to the risk of liver fibrosis. The CPMP adopted a revised opinion on 23 June 1999 and the Agency informed the Commission to that effect on 7 July 1999.

30 The CPMP's revised opinion was incorporated into a revised draft decision. After the Standing Committee on Medicinal Products for Human Use, referred to in Article 73 of Regulation No 2309/93, had delivered a favourable opinion on the revised draft decision on 13 August 1999, the Commission, on 25 August 1999, adopted the decision granting marketing authorisation for the medicinal product for human use known as Ferriprox (hereinafter 'the contested decision'), which was notified to Apotex on 2 September 1999. In accordance with Article 12(3) of Regulation No 2309/93, notice of the marketing authorisation was published in the *Official Journal of the European Communities* on 24 September 1999 (OJ 1999 C 270, p. 2).

Procedure

31 By application lodged at the Registry of the Court of First Instance on 19 November 1999, the applicant brought an action seeking the annulment of the contested decision and of the CPMP's revised opinion of 23 June 1999.

32 By separate document lodged the same day, the applicant brought the present application for suspension of operation of the contested decision.

33 The Commission lodged its observations on that application for interim relief on 9 December 1999.

34 On 17 January 2000, the applicant submitted a written reply to the Commission's observations. Invited to set out its views on a specific point developed in the applicant's reply, the Commission lodged fresh observations on 28 January 2000.

35 By letter of 4 February 2000, lodged at the Registry of the Court of First Instance on 7 February 2000, the applicant requested that the Commission produce several documents which it had mentioned in its observations, in addition to other documents.

36 On 7 February 2000, the applicant lodged an amended version of her reply to the Commission's observations of 28 January 2000, together with new annexes.

37 On 10 February 2000, the Commission produced a number of the documents identified in the applicant's letter of 4 February 2000. It pointed out, however, that other documents could not be made available either on grounds of the confidentiality of the data which they contained or because the Commission did not hold the documents in question.

38 By application lodged at the Court Registry on 1 December 1999, Apotex applied for leave to intervene in support of the forms of order sought by the Commission in the proceedings for interim relief.

39 That application for leave to intervene was notified to the parties, pursuant to Article 116(1) of the Rules of Procedure of the Court of First Instance. The parties submitted their observations within the prescribed periods.

40 By order of 1 February 2000, the President of the Court of First Instance granted Apotex leave to intervene, and Apotex was authorised to present its submissions orally at the hearing.

41 The parties presented oral argument on 15 February 2000.

42 On 16 February 2000, the Commission lodged a non-confidential version of the document contained in Annex 1 to its observations. This document was immediately notified to the other parties.

Law

43 Under the combined provisions of Articles 242 EC and 243 EC and Article 4 of Council Decision 88/591/ECSC, EEC, Euratom of 24 October 1988 establishing a Court of First Instance of the European Communities (OJ 1988 L 319, p. 1), as amended by Council Decision 93/350/Euratom, ECSC, EEC of 8 June 1993 (OJ 1993 L 144, p. 21), the Court may, if it considers that the circumstances so require, order suspension of operation of the contested measure or prescribe any necessary interim measures.

44 Article 104(2) of the Rules of Procedure provides that applications for interim measures must state the circumstances giving rise to urgency and the pleas of fact and law establishing a prima facie case for the interim measures applied for. Those conditions are cumulative, so that an application for suspension of operation must be dismissed if one of them is not met (order of the President of the Court of 30 June 1999 in Case T-70/99 R *Alpharma* v *Council* [1999] ECR II-2027, paragraph 42). The judge hearing an application for interim relief must also, where appropriate, balance the interests involved (order of the President of the Court of Justice of 29 June 1999 in Case C-107/99 R *Italy* v *Commission* [1999] ECR I-4011, paragraph 59; orders of the President of the Court of 21 July 1999 in Case T-191/98 R *DSR-Senator Lines* v *Commission* [1999] ECR II-2531, paragraph 22, and of 25 November 1999 in Case T-222/99 R *Martinez and de Gaulle* v *Parliament* [1999] ECR II-3397, paragraph 22).

Admissibility

Arguments of the parties

45 The applicant considers that she must be regarded as having *locus standi.*

46 First, she is individually concerned by reason of her right to participate in the procedure for the adoption of the contested decision conferred on her by the relevant rules, that is to say, point (1) of Part 4.C of the Annex to Directive 75/318, which requires the final report of each clinical trial to be signed by the investigator.

47 She points out that the CPMP based itself on trials LA-01 and LA-03 for its evaluation of Ferriprox, these being trials in which she was the principal investigator and the results of which were incorporated in reports which she did not sign. Consequently, Article 6(1) of Regulation No 2309/93, which states, with reference to the Annex to Directive 75/318, that reports sent to the Agency must bear the signature of the investigator, was ignored.

48 Furthermore, the *ad hoc* working group recognised the importance of the role played by the applicant in the evaluation procedure, together with the seriousness of the issues which she raised.

49 Second, the applicant is individually concerned by reason of certain specific attributes. The authorisation was in fact granted on the basis of the trials which she had conducted. She is therefore the only person in a position to confirm that

the results of the clinical trials were correctly presented by Apotex in its application for authorisation. She is also the only person whose reputation will be affected by the Commission's reliance on the reports on the clinical trials for which she was principally responsible and the conclusions of which have been misrepresented.

50 The Commission challenges the applicant's *locus standi* on the ground that she is concerned neither directly, within the meaning of the judgment in Case 25/62 *Plaumann* v *Commission* [1963] ECR 95, nor indirectly by the contested decision.

51 In the first place, the rules applicable do not confer on third parties any right to participate in the procedure for authorisation to place a medicinal product on the market. Those rules do not accord any procedural guarantees allowing a third party to put forward legitimate interests on infringement of which reliance can be placed (see, *inter alia*, Case 169/84 *Cofaz and Others* v *Commission* [1986] ECR 391, paragraph 23, Case 75/84 *Metro* v *Commission* [1986] ECR 3021, paragraph 22, Case T-37/92 *BEUC and NCC* v *Commission* [1994] ECR II-285, paragraph 36, and Case T-96/92 *CCE de la Société Générale des Grandes Sources and Others* v *Commission* [1995] ECR II-1213, paragraph 31 et seq.). The obligation on the investigator to sign the reports describing the trials carried out, pursuant to Article 6 of Regulation No 2309/93, which refers to the Annex to Directive 75/318, does not provide a 'procedural guarantee' for that person. Consequently, the applicant's participation in the procedure leading to the adoption of the contested decision is not, in itself, of such a kind as to distinguish her individually in relation to that decision in so far as the applicable rules do not confer on her a subjective right to be heard or to have her interests taken into account (order in Case T-60/96 *Merck and Others* v *Commission* [1997] ECR II-849, paragraph 73).

52 Next, the results of trials LA-01 and LA-03, set out in the reports not signed by the applicant, were not determinative in the assessment made by the CPMP. The absence of a signature can be explained by the discovery of problems in the

conduct of the trials which justified Apotex in terminating them. In any event, Apotex was obliged, under the applicable rules, to submit all information relating to the evaluation of the medicinal product in question, including reports which had not been signed by the investigator.

53 Finally, since the marketing authorisation was granted due to 'exceptional circumstances', it could be issued without all the requisite clinical data.

54 Second, the Commission submits that the applicant is not individually concerned by reason of specific attributes and/or a factual situation.

55 The effects which the contested decision may have on the applicant's reputation are not such as to distinguish her individually. The Commission points out in this regard that Regulation No 2309/93 does not allow it to take account of factors such as those relied on by the applicant. It follows from Article 68 of that regulation that the criteria of safety, efficacy and product quality apply to the exclusion of all other criteria in deciding whether to grant authorisation (Case 301/82 *Clin-Midy and Others* v *Belgium* [1984] ECR 251; Case C-83/92 *Pierrel and Others* v *Ministero della Sanità* [1993] ECR I-6419; and Case C-127/95 *Norbrook Laboratories* v *MAFF* [1998] ECR I-1531).

56 Moreover, even if the applicant were the only person able to confirm whether or not the results of the trials which she conducted had been misrepresented by Apotex, she would still not be individually distinguished in relation to the contested decision, since the concerns which she raised were examined by the Agency and the CPMP issued a revised opinion.

57 Nor is the applicant directly concerned by the contested decision. She has failed to establish that the contested decision has a direct adverse effect on her

reputation. The applicant's fears are inadequately supported and thus not sufficiently conclusive to demonstrate a causal link between the contested decision and its alleged negative effects in her regard. In any event, any harm caused to the applicant's reputation would not result from that decision but rather from the alleged misrepresentation of the conclusions of her reports submitted by Apotex.

Findings of the President

58 Under the second subparagraph of Article 104(1) of the Rules of Procedure, an application for interim measures is admissible only if it is made by a party to a case before the Court of First Instance. That rule is not a mere formality but presupposes that the substantive action, to which the application for interim measures relates, can in fact be examined by the Court.

59 According to settled case-law, the issue of the admissibility of the main action should not, in principle, be examined in proceedings for interim relief, so as not to prejudge the Court's decision on the substance of the case. It may nevertheless appear necessary, when, as in the present case, it is contended that the main action to which the application for interim measures relates is manifestly inadmissible, to establish whether there are any grounds for concluding prima facie that the main action is admissible (order of the President of the Court of Justice in Case 376/87 R *Distrivet* v *Council* [1988] ECR 209, paragraph 21; orders of the President of the Court of First Instance of 30 June 1999 in Case T-13/99 R *Pfizer Animal Health* v *Council* [1999] ECR II-1961, paragraph 121, and of 15 February 2000 in Case T-1/00 R *Hölzl and Others* v *Commission* [2000] ECR II-251, paragraph 21).

60 In the present case, the contested decision was not addressed to the applicant. She must therefore show that there are factors which suggest that the decision is of direct and individual concern to her, within the meaning of the fourth paragraph of Article 230 EC.

61 In order to demonstrate that the contested decision is of individual concern to her, the applicant invokes, in particular, the right conferred by the relevant legislation to participate in the procedure leading to adoption of the measure.

62 It has consistently been held in this regard that the fact that a person is involved, in whatever manner, in the process leading to the adoption of a Community measure can individually identify that person in relation to the measure in question only if the Community legislation confers on that person certain procedural guarantees (orders in Case T-585/93 *Greenpeace and Others* v *Commission* [1995] ECR II-2205, paragraphs 56 and 63, and of 8 July 1999 in Case T-12/96 *Area Cova and Others* v *Council* [1999] ECR II-2301, paragraph 59; judgments in Joined Cases T-481/93 and T-484/93 *Exporteurs in Levende Varkens and Others* v *Commission* [1995] ECR II-2941, paragraph 55, and in Case T-398/94 *Kahn Scheepvaart* v *Commission* [1996] ECR II-477, paragraphs 48 and 49).

63 None of the provisions of the applicable Community legislation requires the Commission, prior to issuing marketing authorisation for a medicinal product, to follow a procedure during which persons other than the party requesting authorisation would have, *inter alia*, the right to be heard.

64 However, point (1) of Part 4.C of the Annex to Directive 75/318 provides that the particulars supplied in respect of each clinical test must contain sufficient detail to allow an objective judgment to be made and states that the final report must be signed by the investigator and, in the case of multicentre trials, by all the investigators or by the coordinating (principal) investigator.

65 While that provision does not constitute a procedural guarantee, inasmuch as it does not provide for the investigator's participation, before the Agency and the Commission, in the procedure leading to adoption of the measure, it is none the less possible that, if that provision is ignored, an investigator who did not sign the final report submitted to the Agency could be individually distinguished in relation to the measure authorising marketing of the medicinal product in question. The conduct of the clinical trials by the investigator is an indispensable precondition to any application for authorisation and the investigator's signature on the final report guarantees the authenticity of the data which that report contains.

66 It is also important to point out here that Regulation No 2309/93 and the measures to which it refers lay down precise rules governing the presentation of applications for marketing authorisation, the way in which they are to be processed, and subsequent decisions. In particular, Article 6(1) of Regulation No 2309/93 provides that 'An application for authorisation for a medicinal product for human use must be accompanied by the particulars and documents referred to in Articles 4 and 4a of Directive 65/65/EEC, in the Annex to Directive 75/318/EEC and in Article 2 of Directive 75/319/EEC.' Compliance with the requirements set out in Article 6(1) of that regulation is vital to ensure attainment of the essential objective of safeguarding public health (see, by way of analogy, *Norbrook Laboratories*, cited above, paragraphs 40 and 41).

67 In the present case, in determining only whether the main action is prima facie admissible, the fact that the reports on trials LA-01 and LA-03, in which the applicant was the principal investigator, were not signed by her cannot escape observance.

68 Furthermore, it has been held that an applicant can claim that he is affected by a measure in a manner which differentiates him from any other person, whatever

the nature, economic or otherwise, of the interests affected (order in *Greenpeace and Others* v *Commission*, cited above, paragraph 50). Consequently, it cannot be ruled out that the applicant, who is a recognised specialist in the treatment of persons suffering from thalassemia major and was the principal investigator in trials LA-01 and LA-03, may be able to invoke an interest in preserving the health of those persons.

69 It follows that, in so far as the applicable legislation was drawn up for the purpose of ensuring a high level of protection of public health and the applicant invokes the interest which she has in defending the protection of public health, there are factors which suggest that the applicant may be individually concerned by the contested decision.

70 Moreover, since the risk that public health may be adversely affected will stem directly from the placing of Ferriprox on the market, the applicant is, prima facie, directly concerned by the contested decision. Apotex's intention to act on the marketing authorisation granted for Ferriprox is not in doubt (see, by analogy, the judgment in Case T-435/93 *ASPEC and Others* v *Commission* [1995] ECR II-1281, paragraph 60).

71 In light of the foregoing, there are factors indicating that the main application, to which the application for interim measures relates, might be declared admissible.

Prima facie case

Arguments of the parties

72 In her application for interim measures, the applicant refers to the pleas which she has raised in her action for annulment as disclosing a prima facie case for granting suspension of operation of the contested decision.

73 First, the contested decision is based on the information contained in the application for authorisation submitted by Apotex. However, contrary to Articles 7 and 11 of Regulation No 2309/93, that information was never verified.

74 Second, manifest errors were committed in the assessment of that application. Known research work carried out by the applicant and by independent researchers into the safety and efficacy of deferiprone was not taken into account, or at any rate not taken properly into account.

75 Third, the provisions of Article 13 of Regulation No 2309/93, under which marketing authorisation for a medicinal product may be granted in 'exceptional circumstances', were misapplied. In particular, in acting pursuant to those provisions, the Commission failed to achieve a reasonable balance between the increased risk of harm associated with the use of deferiprone and the therapeutic efficacy of the product for patients. Further, the Commission failed to take proper account of the fact that a very small number of patients are affected by the disease and that most of them can be treated with the safe, tried and tested methods already available. The Commission was thus unable to justify, in this case, the existence of exceptional circumstances.

76 Fourth, in applying the exceptional circumstances procedure under Article 13(2) of Regulation No 2309/93 on the ground that deferiprone was a necessary treatment for that category of patients unable to use alternative products, the Commission infringed the principle of proportionality. Since only 40 patients world-wide fall into this category, the appropriate decision would have been to limit application of deferiprone to that category in a stringently controlled clinical trial. In this way, patients who did not fall within this category would not unnecessarily have been exposed to serious health risks.

77 Fifth, and finally, the precautionary principle has been infringed. The applicant stresses in this connection that the conclusions of the *ad hoc* working group note that the data which she provided 'reinforce the already existing doubts'. The granting of authorisation in such circumstances is incompatible with the precautionary principle since that principle dictates caution in cases of doubt.

78 In her reply to the Commission's observations, the applicant claims that the Commission undervalued the risks of deferiprone for human health. She contends that desensitisation and diethylenetriamine pentaacetic acid ('DTPA') therapy are therapeutic solutions in place of deferiprone for the group of patients for which she is authorised, namely those suffering from allergy or hypersensitivity to deferoxamine. Although not authorised for that purpose, DTPA could none the less be lawfully prescribed by doctors for indications other than those for which it was authorised.

79 Furthermore, no proof has been provided that patients with problems of allergy or toxicity with deferoxamine have subsequently been treated more safely with

deferiprone, or could be so treated. The trials which were to be conducted by Apotex (based on information from reference trial LA-06), pursuant to the conditions of marketing authorisation, were no more than a continuation of trial LA-02. The latter trial did not involve patients unable to tolerate deferoxamine treatment and trial LA-06 does not make it possible to obtain reliable information on safety in using deferiprone with respect to liver fibrosis and cardiac diseases. It follows that the absence of evidence ought to have induced the CPMP to require Apotex to conduct a further clinical trial before drafting an opinion favourable to granting marketing authorisation.

80 The applicant also takes the view that the assessment of deferiprone was based on incomplete and misleading information given by Apotex, particularly the information contained in the report on trial LA-01, annexed to the Commission's observations, in which the applicant was the principal investigator.

81 The applicant also challenges, first, the use made of serum ferritin to evaluate the efficacy of deferiprone and the conclusions which the Commission draws from this and, second, the assessment of the toxicity of deferiprone for the liver and heart.

82 All of the errors described by the applicant in her reply could have been avoided if the completeness and accuracy of the information which Apotex supplied to the Agency had been verified.

83 At the hearing, the applicant, in reply to a question put by the President in these interlocutory proceedings, expressly confirmed that she was raising a plea of infringement of essential procedural requirements inasmuch as the reports on trials LA-01 and LA-03, in which she had been the principal investigator, had not been signed by her.

84 The Commission considers first of all that the applicant has failed to establish that manifest errors of assessment were committed. Proper account was taken of

the matters submitted by the applicant in the CPMP's evaluation report of January 1999 and in the addendum of June 1999 to that report. The CPMP examined and checked in detail both the data notified in the application for authorisation and the data provided by the applicant concerning the efficacy and safety of deferiprone.

85 Contrary to what the applicant asserts, the CPMP did verify the information contained in the application for authorisation, as required by Articles 7 and 11 of Regulation No 2309/93. There is no requirement to conduct an independent investigation or to make special inquiries going beyond the validation carried out by the Agency's secretariat.

86 Further, the obligation on the CPMP to carry out a thorough review of the data contained in the marketing authorisation application in order to verify the quality, safety or efficacy of the medicinal product was complied with in the case of deferiprone.

87 The Commission challenges the contention that deferiprone is ineffective. Deferiprone has in fact proved to be effective for all those tested. It follows from the published results that keeping serum ferritin at levels below 2 500 mcg/l was the most important factor in survival without heart disease among patients suffering from thalassemia. On the basis of the data contained in the authorisation application submitted by Apotex, the CPMP concluded that deferiprone was effective in preventing an increase in serum ferritin levels for a period of at least one year. In particular, trial LA-02 demonstrated that those levels remained below 2 500 mcg/l in 54% of patients after one year, it being pointed out that a similar proportion (58%) of patients included in the trial had serum ferritin levels below 2 500 mcg/l at the start of the trial. Moreover, after one year of therapy, the mean serum ferritin levels had in fact declined.

88 The Commission adds that a subgroup analysis showed that, even in the more heavily iron-loaded patients (more than 5 000 mcg/l at the start of the trial), the mean serum ferritin levels decreased progressively with time.

89 Likewise, the Commission challenges the claim that the toxicity of deferiprone has been established in respect of cardiac and hepatic functions. Despite a detailed examination of the information supplied by the applicant and by Apotex, the *ad hoc* working group formed the view that the new data were inconclusive regarding the relationship between deferiprone therapy and liver fibrosis. It accordingly concluded that there was no basis on which to reconsider the opinion recommending that marketing authorisation be granted under exceptional circumstances.

90 In the recommendations which it presented to the CPMP, the *ad hoc* working group made the following proposals: to maintain the restricted indication; to inform the physician about the inconclusive nature of the relationship between liver fibrosis and deferiprone and to recommend monitoring in a specific population, namely that suffering from hepatitis C; to obtain written confirmation from Apotex that they will provide the sales figures in each Member State to ensure that deferiprone will not be prescribed outside the approved indication; and to obtain more information from Apotex and other sources as soon as that information becomes available. All of these recommendations were adopted by the CPMP in its revised opinion.

91 The Commission further points out that, in so far as no medicinal product is entirely without risk, the degree of acceptable risk will depend on the therapeutic value and uniqueness of the medicinal product in question. In the present context, failure to treat thalassemia will result in premature death of patients and treatment with deferiprone may prolong the life of patients for whom there was hitherto no alternative therapy to deferoxamine.

92 Second, the Commission challenges the assertion that errors were made in the application of Article 13 of Regulation No 2309/93. The exceptional decisions referred to in that article may be adopted only for objective and verifiable reasons and must be based on one of the causes mentioned in Part 4.G of the Annex to Directive 75/318. The Commission cites the first of the exceptions referred to in Part 4.G (see paragraph 11 above) and points out that the applicant has conceded that thalassemia is a rare disorder. Application of those provisions was therefore justifiable.

93 Furthermore, the conditions attached to the CPMP's revised opinion are very restrictive. The group of patients for whom deferiprone is authorised is sufficiently limited, in the first place, by the restrictions on prescription, since only physicians experienced in the treatment of patients suffering from thalassemia can prescribe deferiprone and, second, by its use, which is limited to patients for whom deferoxamine therapy is contra-indicated or for whom such therapy presents serious toxicity. The Commission also points out that the indications relating to the prescription of Ferriprox warn physicians that the available data are inconclusive with regard to whether deferiprone may worsen liver fibrosis and with regard to the effects which it may have on cardiac function. On the recommendation of the *ad hoc* working group, a further warning was included concerning the existence of a connection between liver fibrosis and hepatitis C among thalassemia patients.

94 Marketing authorisation for a medicinal product under exceptional circumstances also requires an applicant to complete within specified time frames an identified programme of studies, the results of which form the basis of an annual reassessment of the product's benefit/risk profile. Failure to meet this obligation may result in suspension or withdrawal of the marketing authorisation. In addition, Apotex is required to maintain detailed records of all suspected adverse reactions occurring within and outside the Community which are reported to it by health care professionals. Finally, in the event that urgent action is required to

ensure safe use of the product, the Commission has the power to impose an 'urgent safety restriction' under Article 1(3) of Commission Regulation (EC) No 542/95 of 10 March 1995 concerning the examination of variations to the terms of a marketing authorisation falling within the scope of Council Regulation (EEC) No 2309/93 (OJ 1995 L 55, p. 15), as amended.

95 Third, the Commission considers that there has been no infringement of the principle of proportionality. Where an institution enjoys discretionary powers within a particular sphere, the legality of a measure adopted in that sphere can be affected only if the measure is manifestly inappropriate having regard to the objective which the institution is seeking to pursue (Case C-180/96 *United Kingdom* v *Commission* [1998] ECR I-2265, paragraph 97). That is not the case with regard to the contested decision. In particular, the applicant errs in her assertion that most of the patients eligible for treatment with deferiprone can be treated with the safe, tried and tested methods already available. The alternative forms of treatment proposed by the applicant (DTPA therapy and lower-dose deferoxamine therapy) are unsatisfactory. Finally, the Commission states that there is no alternative to deferiprone in the patient group for whom it is authorised.

96 Finally, the Commission points out that, with regard to authorisations for medicinal products, the precautionary principle is incorporated into the concepts of safety and efficacy which have to be taken into account, as well as the extensive data which must be submitted to the CPMP for evaluation before an authorisation can be recommended. Compliance with this principle forms part of the duty of the Commission and the CPMP to follow the rules laid down by Regulation No 2309/93.

97 At the hearing, Apotex stated that it fully endorsed the Commission's observations.

Findings of the President

98 The applicant essentially takes the view that the defects in the procedure leading to the adoption of the contested decision taint that decision with manifest errors of assessment. One of the alleged defects, namely the fact that the reports on the clinical trials attached to the authorisation application did not bear the investigator's signature, constitutes, in her view, a breach of an essential procedural requirement.

99 In this regard, the third recital in Part 4 of the Annex to Directive 75/318 provides that '[e]valuation of the application for marketing authorisation shall be based on clinical trials including clinical pharmacological trials designed to determine the efficacy and safety of the product under normal conditions of use, having regard to the therapeutic indications for use in human beings'. Part 4.C of this Annex provides that the final report on each clinical trial to be attached to the authorisation application must be signed by the investigator.

100 It is common ground that the reports on clinical trials LA-01 and LA-03 attached to the authorisation application which Apotex submitted were not signed by the applicant in her capacity as principal investigator.

101 It must therefore be determined whether the lack of a signature on those reports can be regarded, prima facie, as an infringement of an essential procedural requirement, within the meaning of the second paragraph of Article 230 EC, thereby justifying annulment of the contested decision. To that end, it is necessary to examine the purpose served by the rule allegedly infringed and what effect any infringement could have had on the tenor of the contested decision.

102 The obligation on the investigator in the clinical trial to sign the final report is a formality which, being an integral part of the process by which a decision granting marketing authorisation for a medicinal product is elaborated, is capable of affecting its validity. This formality is necessary in that it makes it possible to guarantee the authenticity of the information contained in the report attached to the authorisation application, in particular the results of the trials; in so doing, the signature guarantees that the evaluation of the medicinal product is not based on material inaccuracies. It follows that failure to satisfy this formality may affect the legality of the decision that is adopted at the conclusion of the procedure should it be established that the final report, which was not approved by the investigator, misled the Agency and the Commission on an essential point owing to inaccuracies or omissions.

103 However, the rules do not exclude the possibility that, in some cases, reports of clinical trials not signed by the investigator may be annexed to the authorisation application. Those rules require that all information relevant to the evaluation of the medicinal product concerned, whether favourable or unfavourable to the product, must be included in the authorisation application. The introduction to the Annex to Directive 75/318 expressly provides that '[i]n particular, all relevant details shall be given of any incomplete or abandoned pharmacotoxicological or clinical test or trial relating to the medicinal product'.

104 It follows that, whether or not signed by the investigator, the report on a clinical trial included in the authorisation application always constitutes a vital element for the purposes of evaluating the efficacy and safety of the medicinal product to which it relates.

105 A procedure for granting marketing authorisation for a medicinal product will therefore be vitiated by an irregularity such as to result in its annulment if the Agency and, consequently, the Commission have been unable correctly to

evaluate the health advantages and risks of the medicinal product because the report on the relevant clinical trial contains, on one or more essential points, inaccurate or incomplete information which the additional data forwarded to the Agency during the course of the procedure could not rectify.

106 In this case, it is clear in particular from the case-file that the report on trial LA-01 was included — together with the reports on trials LA-02 and LA-03 — in the authorisation application submitted by Apotex. It is also clear from the documents in the case that the Agency must have taken account of trial LA-01, if only to reject it, as a basis on which to assess the efficacy of deferiprone (see the Agency document of 2 December 1999 entitled 'Ferriprox — Overview of the procedure', p. 2; the CPMP Assessment Report of 27 January 1999 (Annex 1 to the Agency document, pp. 13 to 15); and the scientific discussion contained in the 'European Public Assessment Report' drawn up by the CPMP on 25 August 1999 (Annex 4 to the Agency document)).

107 The applicant contends that the report on trial LA-01, annexed to the Commission's observations, contains a narration of the facts and interpretations which are incorrect and misleading. In this context, it must be pointed out that the conclusions reached on 11 June 1999 by Professor Olalla Marañón, the co-rapporteur designated by the CPMP to draft an evaluation report on the document submitted by the applicant, stated that:

'The letters sent by a Principal Investigator of the main clinical trials are disturbing. It should be ensured that all factual information has been submitted and is correct. This issue should be discussed by the CPMP' (point 5).

108 If the Court were in fact to find that the authorisation for the marketing of Ferriprox was issued pursuant to an Agency evaluation based on a clinical trial report containing material inaccuracies or substantially incomplete information,

such a finding would be of crucial importance for the purposes of assessing the legality of the contested decision. The applicant's arguments concerning the conditions under which the Agency evaluated the efficacy and safety of Ferriprox must therefore be examined in detail. However, such an examination cannot be carried out in the context of the present application for interim measures.

109 Since prima facie the applicant's arguments cannot be considered to be entirely baseless, the other conditions for granting suspension of operation must now be examined.

Urgency and the balance of interests

Arguments of the parties

110 In order to demonstrate the urgency in suspending operation of the contested decision, the applicant invokes, first, the danger which deferiprone represents for public health and, second, the existence of serious and irreparable damage in the harm done by the contested decision to her reputation.

111 With regard to the first point, the applicant considers that suspension of operation is the only measure which can offer adequate protection for public health.

112 The three clinical trials conducted by the applicant, or under her supervision, allowed her to conclude that deferiprone was ineffective for approximately half of the persons treated. Failure to eliminate iron overload from patients' bodies exposes them to the danger of premature death. Proof was also obtained as to the

toxicity of this substance. Prolonged use of deferiprone involves significant risks of liver fibrosis and cardiac disease and, consequently, premature death of the patients concerned.

113 Such results led the applicant to suspend all human trials and discontinue all administration of deferiprone under her control.

114 The applicant goes on to argue that the conditions linked to the marketing authorisation do not guarantee that the appropriate precautions will be taken to prevent the harmful consequences of absorbing deferiprone. The conditions to which the authorisation of Ferriprox is subject do not sufficiently limit the group of patients for whom this medicinal product may be prescribed, fail to ensure that patients and doctors are properly informed as to the existence and seriousness of the risks of liver fibrosis and cardiac disease, and fail to impose adequate requirements as to the monitoring of the efficacy and toxicity of deferiprone, with more particular regard to the causation and progression of liver fibrosis in patients taking the product.

115 As regards the second aspect, concerning the harm to her reputation, the applicant states that the results of her research into the efficacy and safety of deferiprone and the contacts which she established with the Agency formed the basis of the evaluation procedure. In particular, the applicant is concerned that the nature and conclusions of her research have been misrepresented to the Agency and Commission and/or have been misconstrued by them. She submits that if the results of her research had been properly communicated to the Agency or Commission, no authorisation would have been granted. The applicant considers that her research demonstrates that deferiprone cannot be considered safe until further satisfactory toxicity tests on animals have been conducted. Since her views are well known in the scientific community, the contested decision has an immediate impact on the perceived quality of her research and its credibility.

116 Alternatively, if the applicant's concerns over the safety and efficacy of deferiprone prove to be validated when the product is marketed, this will necessarily have a detrimental effect on her standing in the medical and scientific community given the natural and legitimate belief that market authorisation was, at least in part, based on the results of her work.

117 In either case, this is likely to have an impact in the future on her ability to obtain research funding.

118 Finally, any harm to her reputation would be permanent and irreversible.

119 The Commission, supported by Apotex, disputes the claim that the condition of urgency has been satisfied.

120 As regards the risk to human health, the Commission argues that the adoption of the contested decision with strict conditions attached is justified with regard to efficacy and safety of the medicinal product. The serious and irreparable damage alleged can be taken into account by the Court hearing an application for interim measures only in so far as it may be caused to the interests of the party seeking the interim relief (order in *Pfizer Animal Health* v *Council*, cited above, paragraph 136, and order of 18 November 1999 of the President of the Court of Justice in Case C-329/99 P(R) *Pfizer Animal Health* v *Council* [1999] ECR I-8343, paragraph 94). The applicant does not suffer from thalassemia. She has therefore no interest which could be endangered by the maintenance of the decision pending the outcome of the main proceedings.

121 Moreover, the risk for patients concerned if the operation of the decision were suspended is much greater than that linked to placing the product on the market,

since it would deny some of them their present treatment and deny others access to that product. Since these patients do not have any alternative therapy to deferoxamine, there would be a high risk of premature death.

122 As for the damage consisting in the harm to the applicant's reputation, the existence or imminence of such harm must be established with a certain degree of probability (order of the President of the Court of Justice in Joined Cases C-51/90 R and C-59/90 R *Comos Tank and Others* v *Commission* [1990] ECR I-2167, paragraph 29). No evidence has been submitted with regard to either non-material or financial harm.

123 The applicant's concern that authorisation of deferiprone may have grave implications for her peers' and patients' perception of her professional competence, standing and integrity and for her ability to obtain continued research funding in the future is neither substantiated enough nor conclusive enough to demonstrate a clear causal link between the contested decision and those alleged negative effects. As the applicant herself acknowledges, her views that deferiprone cannot be considered safe until the completion of further toxicity tests have been conducted are well known in the scientific community. In making public within the scientific community her disagreement with the contested decision, the applicant can easily prevent the feared impact upon the perceived quality of her research and the ability to rely on it. Moreover, even if her reputation were harmed through the contested decision, that harm would not be irreparable, inasmuch as annulment of that decision at the conclusion of the main proceedings would allow her to restore her reputation (order of the President in Case T-507/93 R *Branco* v *Court of Auditors* [1993] ECR II-1013, paragraphs 23 and 24).

124 Finally, any damage attributable to the 'likely impact on her ability to obtain continued research funding in the future' would be financial in nature; it would therefore be insufficient to establish urgency (order of the President in Case

T-260/97 R *Camar* v *Commission and Council* [1997] ECR II-2357, paragraph 42). Exceptions to this principle are granted only in special circumstances (order of the President in Case T-65/98 R *Van den Bergh Foods* v *Commission* [1998] ECR II-2641, paragraph 65 et seq.).

125 Thus, whatever interests are taken into account, whether those of the Commission, charged by the legislator with issuing the marketing authorisation on the basis of the work carried out by the CPMP and the Agency, or those of patients suffering from thalassemia, for whom treatment with deferiprone represents a potentially life-saving therapy, these interests outweigh any remote damage that might result for the applicant's reputation if the contested decision were left to stand pending the final outcome of the main proceedings.

Findings of the President

126 According to settled case-law, the urgency of an application for interim measures must be assessed in relation to the necessity for an interim order to prevent serious and irreparable damage to the party applying for those measures. It is for that party to prove that it cannot wait for the outcome of the main proceedings without suffering damage that would entail serious and irreparable consequences (see, in particular, the President's order of 30 April 1999 in Case T-44/98 R II *Emesa Sugar* v *Commission* [1999] ECR II-1427, paragraph 128).

127 In her application for interim measures, the applicant submits that failure to suspend operation of the contested decision will adversely affect her reputation, inasmuch as that decision authorises the marketing of Ferriprox, which in her view constitutes a danger to public health.

128 With regard to the harm constituted by the effect of the contested decision on her reputation, it cannot be discounted that suspension of operation may make good non-material harm of that kind. However, suspension could not remedy such harm any more than annulment of the contested decision at the conclusion of the main proceedings. In any event, the purpose of the procedure for interim measures is not to ensure that damage is made good but to ensure that the judgment on the substance of the case takes full effect (order of the President of the Court of Justice in Case C-65/99 P(R) *Willeme* v *Commission* [1999] ECR I-1857, paragraph 62).

129 Furthermore, no evidence of such non-material damage has been adduced. The applicant's critical views on deferiprone are, as she herself stresses, well known in the scientific community. Several documents on the case-file confirm that the applicant has publicly expressed her opinion that deferiprone is ineffective.

130 Thus, the 'acknowledgements' section of the article entitled 'A Multi-Center Safety Trial of the Oral Iron Chelator Deferiprone', published in the periodical *Annals New York Academy of Sciences*, states:

'This study was sponsored by Apotex Inc., Weston, Ontario, Canada. Doctors Nancy Olivieri and Garry Brittenham participated in the organisation and conduct of this trial but did not take part in the data analyses and manuscript preparation and do not agree with the conclusions.'

131 An article written by the applicant and other researchers, entitled 'Long-Term Safety and Effectiveness of Iron-Chelation Therapy with Deferiprone for Thalassemia Major' and published in 1998 in the periodical *The New England*

Journal of Medicine (Annex 18 to the application for interim measures), concludes that 'Deferiprone does not adequately control body iron burden in patients with thalassemia and may worsen hepatic fibrosis'.

132 In addition, since the applicant did not sign any of the reports on the clinical trials attached to the authorisation application submitted by Apotex, she cannot be criticised for having approved the submission of those reports to the Agency.

133 Finally, so far as concerns any difficulty in obtaining research funding as a result of the operation of the contested decision, suffice it to point out that such harm is hypothetical in nature.

134 As regards the danger to human health which may result from the marketing of Ferriprox, the Commission objects that a risk of serious and irreparable harm of this kind is not such as to affect the applicant's interests, so that she cannot invoke it for the purpose of establishing that the condition of urgency has been satisfied.

135 It is true that it has been held, on an application for interim measures, that damage which may be caused to third parties or to the environment, invoked by a party applying for interim measures, may be taken into account only in the balancing of the interests at stake (orders in *Pfizer Animal Health* v *Commission*, cited above, paragraph 136, and in *Alpharma* v *Council*, cited above, paragraph 146). However, because of the applicant's particular position as investigator in the clinical trials recorded in the reports attached to the application for authorisation, which involves her signing those reports, she cannot be denied the possibility of satisfying the condition for urgency by invoking the danger to human health which could result from a lack of efficacy and from toxicity of the medicinal product authorised.

136 If it should transpire that deferiprone does produce in patients to whom it is administered the consequences stated by the applicant, resulting from its inefficacy and its toxicity, the resultant effects would not be reparable if the applicant were to be successful in her application for annulment.

137 However, in order to determine whether the applicant has proved the need for the suspension sought, it is necessary to analyse the alleged harm in the light of all the interests involved (order of the Court of Justice in Case C-280/93 R *Germany* v *Council* [1993] ECR I-3667, paragraph 29; orders of the President of the Court of Justice in Joined Cases C-239/96 R and C-240/96 R *United Kingdom* v *Commission* [1996] ECR I-4475, paragraph 67, and in *Italy* v *Commission*, cited above, paragraph 89).

138 In that regard, an order granting the suspension sought would involve a risk, equivalent to that which would result from refusal of suspension, of having effects which would be irreversible should judgment on the substance be given in the Commission's favour. The category of patients to whom Ferriprox will be administered is that for which there is no substitute treatment with deferoxamine. Without treatment with deferiprone, the iron overload of patients in this category cannot be eliminated and exposes them to the danger of premature death.

139 It must be pointed out in this regard that the category of patients for whom deferiprone therapy can be prescribed by medical specialists is limited. As is clear from the document entitled 'European Public Assessment Report' (Annex 4 to the document drafted by the Agency):

'Deferiprone is used for the treatment of iron overload in patients with thalassemia major who cannot receive deferoxamine therapy. Deferiprone should

not be used if treatment with deferoxamine is possible' (section entitled 'Package Leaflet').

140 The same document also states the following in regard to the therapeutic indications:

'Treatment of iron overload in patients with thalassemia major for whom deferoxamine therapy is contra-indicated or who present serious toxicity with deferoxamine therapy' (sections entitled 'Product Information' and 'Summary of Product Characteristics').

141 In so far as deferiprone has the advantage of being administered orally, and not parenterally as in the case of deferoxamine, Ferriprox could be used by patients other than those indicated on the labelling and package leaflet. In this regard, it should be noted that the marketing authorisation has attached to it an undertaking to notify the Agency of the sales figures for Ferriprox in each Member State for a minimum period of one year (Agency document entitled 'Ferriprox — Overview of the Procedure' (annexed to the Commission's observations) and Apotex's letter of 23 June 1999 to the CPMP (Annex 19 to the Agency document)), which will evidently allow effective monitoring of the use made of the medicinal product.

142 The applicant contends that DTPA therapy and desensitisation to deferoxamine constitute substitute treatments to deferoxamine. On this point, the applicant's arguments must be held to be unconvincing. DTPA is not authorised as a medicinal product for that purpose. Consequently, recourse to DTPA constitutes an abusive and hazardous use of that medicinal product, the responsibility for

which would rest with each doctor. It cannot therefore be held in general that this treatment is a therapeutic method which has already been tried and tested.

143 With regard to desensitisation to deferoxamine, the applicant's arguments, which are also challenged by the Commission, equally do not allow the conclusion that this is an alternative therapeutic solution, since it consists, precisely, in the administration of deferoxamine in smaller doses, something which, moreover, necessarily involves an increase in iron overload and in the risks which this represents for patients' health, as the Commission has argued without being challenged on this point by the applicant.

144 It follows that the lack of any necessity for deferiprone, which would arise if a therapeutic solution to replace deferoxamine treatment actually existed, has not been proved in a sufficiently convincing manner by the applicant.

145 In those circumstances, the President cannot substitute his assessment for that of the Commission in regard to the balancing of the advantages and risks which the authorised medicinal product presents for the patients concerned.

146 It follows from all of the foregoing that the conditions necessary for granting the suspension requested have not been satisfied.

On those grounds,

THE PRESIDENT OF THE COURT OF FIRST INSTANCE

hereby orders:

1. **The application for interim relief is dismissed.**

2. **Costs are reserved.**

Luxembourg, 7 April 2000.

H. Jung

Registrar

B. Vesterdorf

President