OPINION OF ADVOCATE GENERAL LÉGER

delivered on 9 February 1995 *

1. The Divisional Court of the Queen's Bench Division of the High Court of Justice (hereinafter 'the Divisional Court') requests the Court to interpret point 8(a)(ii) of the second paragraph of Article 4 of Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, [1] as amended by Council Directive 87/21/EEC of 22 December 1986. [2] In essence, it asks for a ruling on the requirements of Community law with regard to the granting of marketing authorization for medicinal products [3] in a specific instance involving the use of the abridged procedure.

2. This is an important question since even now marketing authorization constitutes the cornerstone of Community law in the field of proprietary medicinal products for human consumption. Directive 65/65, as amended on numerous occasions, [4] is still the measure on which all the others are based. Even today, no proprietary medicinal product may be put on the market in a Member State unless an authorization has been issued by the competent authority of that Member State. [5] Moreover, to put it in a very simplified way, that measure provides that an applicant for marketing authorization in respect of a proprietary medicinal product for human consumption may use two types of initial procedure: a standard procedure [6] and an abridged procedure. [7] Under the standard procedure, applicants are to provide the results of a whole series of tests and experts' reports in order to obtain marketing authorization, [8] whereas they are not required to do

* Original language: French.

1 — OJ English Special Edition 1965-1966, p. 20.

2 — OJ 1987 L 15, p. 36.

3 — I shall use the terms 'medicinal product' and 'proprietary medicinal product' interchangeably, even though the definition of the former is wider than that of the latter. The former includes not only medicinal products of industrial manufacture, especially generic products (that is to say, medicinal products similar to existing products no longer protected by patents), but also includes the latter (that is to say ready-prepared medicinal products placed on the market under a special name and in a special pack). In Council Directive 89/341/EEC of 3 May 1989 amending Directives 65/65/EEC, 75/318/EEC and 75/319/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (OJ 1989 L 142, p. 11), which is not applicable in this case, all references in the corpus of Community law on medicinal products for human consumption to 'proprietary medicinal product' have been replaced by 'medicinal product'.

4 — See in particular: P. Deboyser: 'Le Marché Unique des Produits Pharmaceutiques', *Revue du Marché Unique Européen*, 1991, No 3, pp 101 to 176, and also 'Développements Récents du Droit Communautaire relatif aux Médicaments', *Revue européenne de Droit de la Consommation*, 1994, pp. 39 to 47.

5 — Article 3 of Directive 65/65.

6 — Second paragraph of Article 4 of Directive 65/65, amended on numerous occasions, in particular by Council Directives 75/318/EEC on the approximation of the laws of the Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of proprietary medicinal products (OJ 1975 L 147, p. 1) and 75/319/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (OJ 1975 L 147, p. 13).

7 — Point 8(a) and (b) of Article 4, second paragraph, of Directive 65/65, as amended by Directive 87/21.

8 — Directives 75/318 and 75/319, as amended on numerous occasions, in particular by Council Directives 83/570/EEC of 26 October 1983 (OJ 1983 L 332, p. 1) and 87/19/EEC of 22 December 1986 (OJ 1987 L 15, p. 31).

so, on certain conditions, if the particulars are drawn up in accordance with the abridged procedure. [9]

3. As regards the United Kingdom legislation, the Medicines Act 1968 (hereinafter 'the 1968 Act') makes provision for the licensing authority (the Secretary of State for Health) and lays down rules for the procedure to be followed in the preliminary stages of an application for marketing authorization, [10] and for the grant, renewal or refusal of such authorization. [11]

4. The question whether those provisions are compatible with Community law has been raised in proceedings between Scotia Pharmaceuticals Limited (hereinafter 'Scotia'), the plaintiff in the main action, and the Medicines Control Agency (hereinafter 'the MCA'), [12] in which Scotia alleges that the MCA used the abridged procedure and unjustifiably relaxed the conditions for the grant of marketing authorization in favour of Norgine Limited (hereinafter 'Norgine'), a company in competition with Scotia.

5. In the United Kingdom, Scotia possesses authorization granted in 1988 in respect of a product named 'Epogam' which is indicated for the relief of atopic eczema. [13] It also possesses two authorizations granted in 1990 for Epogam in paediatric capsules and for a product called 'Efamast', indicated for the relief of mastalgia. [14] The normal procedure was followed in the applications for those three authorizations. Accordingly, Scotia had to satisfy all the requirements laid down by Community law. The tests and clinical trials began in 1979 and by 1990 a considerable amount had been spent on research (about £19 million). [15]

6. In 1992 the MCA granted Norgine authorization to put a medicinal product called 'Unigam' [16] on the United Kingdom market. The application was dealt with under the 'abridged procedure' by detailed references to published scientific literature. [17]

7. The Divisional Court suspended the operation of the decision to license-

9 — Similarly, Article 1, second paragraph, of Directive 75/318, Articles 1 and 2(c) of Directive 75/319, Articles 1 to 4 of Directive 83/570, Article 1 of Directive 87/19 and Article 1 of Directive 87/21.

10 — Section 19 of the 1968 Act.

11 — Section 20(1), as amended by Statutory Instrument 1977/1050, reg 4(3).

12 — Executive arm of the Secretary of State for Health.

13 — Skin condition marked in particular by red patches and the formation of scabs.

14 — Diffuse breast pain, most frequently in the outer upper quadrant, spreading to the armpit and generally occurring in the premenstrual stage (usually connected to progesterone deficiency, it is never symptomatic of serious disease).

15 — Order for reference, p. 2.

16 — This product is indicated for the symptomatic relief of mastalgia and atopic eczema.

17 — Point 8(a)(ii) of the second paragraph of Article 4 of Directive 65/65, as amended by Directive 87/21.

Unigam, [18] pending the decision of the Court of Justice, Scotia undertaking to make good any loss suffered by Norgine. [19]

8. In order to give a clear exposition of the case, I think it essential to set out first of all how the relevant Community legislation has developed as regards the grant of marketing authorization in respect of medicinal products for human consumption.

9. The essential aim of the Community legislature is still that set forth by Advocate General Mancini in his Opinion in Case 301/82 *Clin-Midy* v *Belgium* [1984] ECR 251. [20] I shall repeat it verbatim:

'The aim of the directive [65/65] is defined in the preamble. The first recital lays down the basic principle on which any rule concerning the production and distribution of proprietary medicinal products must be based: its "primary purpose ... must be to safeguard public health". That principle is then developed. In particular, the directive states that: (a) that objective must be attained by means which will not hinder the development of the pharmaceutical industry or trade in medicinal products within the Community (second recital); (b) "trade ... is hindered by disparities between certain national provisions ... relating to medicinal products" (third recital) and "such hindrances must accordingly be removed" (fourth recital); (c) this entails approximation of the national rules (fourth recital), to be achieved "progressively"; and (d) priority must be given to eliminating the disparities liable "to have the greatest effect on the functioning of the common market" (fifth and final recital)'. [21]

10. According to the plan drawn up as far back as 1965, the Community legislature has in successive stages [22] used legal procedures in pursuit of these various objectives:

— the social and economic context [23] of the medicinal product is taken into account by Directive 87/21;

18 — Observations of the United Kingdom, point 15, and Observations of the Commission, point 3.

19 — Observations of the Commission, point 3.

20 — See Opinion and paragraphs 5 to 7 of the judgment.

21 — Opinion, p. 262.

22 — The adverb 'progressively' suggests the idea of gradual development in stages and is continually referred to in subsequent Community measures: seventh recital in the preamble to Directive 75/318, fifth recital in the preamble to Directive 75/319 and first recital in the preamble to Directive 87/19.

23 — Referred to in the second recital in the preamble to Directive 65/65: '... this objective must be attained by means which will not hinder the development of the pharmaceutical industry ...'

— national legislation has been harmonized with a view to achieving an expanded common market in medicinal products [24] in Directive 75/318 [25] (hereinafter 'the standards and protocols directive'), reaffirmed in Directives 75/319 [26] and 87/19, [27] the essential aim always being to protect public health. [28]

11. Thus, from the start, the Community legislature has set out the framework of an ambitious and realistic plan: [29]

— the ultimate aim pursued is to achieve an expanded single market in high-quality, high-technology medicinal products for human consumption, with a view to ensuring that all Community nationals, whatever their nationality or the Member State where they live, may equally receive the best possible medical protection; [30]

— that ultimate aim is to be attained in stages, each consisting of the attainment of intermediate goals. Since those various objectives are of necessity complementary [31] to each other, they cannot themselves be detached from the primary objective and contribute to the attainment of the ultimate objective.

12. Year after year, therefore, the Community legislature has given itself further means, both specific and necessary, which are essential to the achievement of the ultimate objective.

13. Three main periods can be identified in the development of the legislation. The first covers the years from 1965 to 1975. During this period, the Community legislature endeavoured first and foremost to ensure a high level of public health in respect of medicinal products for human consumption. [32]

24 — Second recital in the preamble to Directive 65/65: '... or trade in medicinal products within the Community ...'

25 — Cited above at footnote 6, in particular the first and second recitals.

26 — Ibid. and see especially the first, second and third recitals.

27 — Cited above at footnote 8, see in particular the first and second recitals.

28 — That objective is constantly reaffirmed in subsequent legislation: first recital in the preamble to Directives 75/319, 87/19, 87/21, third recital in the preamble to the standards and protocols directive and fourth recital in the preamble to Directive 83/570.

29 — In particular, first and second recitals in the preamble to Directive 65/65.

30 — See *inter alia*: P. Deboyser: 'Le Marché Unique des Produits Pharmaceutiques' and 'Développements Récents du Droit Communautaire relatif aux Médicaments', op. cit.; Vanpe and Leguen: *La Construction de l'Europe Pharmaceutique — Le Mortier des Douze*, Ed. Masson, 1991; M. Cassan: *L'Europe Communautaire de la Santé*, Ed. Economica, Collection Coopération et Développement, p. 104; F. Dehousse: 'Le Marché Unique des Produits Pharmaceutiques', *Journal des Tribunaux*, 1992, No 5633, p. 383 to p. 386; Campion et Viala: 'Vers la Libre Circulation des Médicaments en Europe', *Revue de Droit Sanitaire et Social*, No 1, 1994, pp. 80 to 97.

31 — Sixth recital in the preamble to Directive 65/65.

32 — First recital in the preamble to Directive 65/65.

14. Between 1975 and 1985, while still pursuing the primary objective, the legislature took into consideration the aim of achieving the free movement of medicinal products. [33] That objective was treated as complementary to the first. [34]

15. From 1985 onwards, legislation has taken account of other aspects of medicinal products policy which had hitherto been ignored, such as consumer information, [35] or had merely been mentioned, [36] such as the social and economic context of the product. [37] Once again, those specific and intermediate aims are treated as being complementary, necessary and essential to the primary objective. [38]

16. The features which I have sketched in outline can be applied specifically to the case before the Court, namely with regard to the grant of marketing authorization under the abridged procedure by detailed references to published scientific literature.

17. That is well illustrated by Directive 87/21 which, in completing and amending the abridged procedure only, [39] is crucial to the case.

18. The Commission considered the application of the derogation system and found that some national authorities are very quick to allow use of the abridged procedure and hardly check the references to published data supplied by an applicant for marketing authorization in respect of a generic medicinal product. This seriously penalizes a firm granted marketing authorization in respect of an innovatory medicinal product, since the results of the tests it submits in connection with its original application constitute more often that not the basis of the dossier supplied by an applicant in respect of a generic medicinal product. That is apparent from the Explanatory Memorandum to the Commission's report. [40]

33 — First and second recitals in the preamble to the standards and protocols directive, first, second and third recitals in the preamble to Directive 75/319 and first and second recitals in the preamble to Directive 83/570.

34 — Third recital in the preamble to the standards and protocols directive, first recital in the preamble to Directive 75/319 and third recital in the preamble to Directive 83/570.

35 — See the completion of the internal market: Commission's White Paper for the attention of the Council [COM (85) 310 final version of 14 June 1985] .

36 — Second recital in the preamble to Directive 65/65: '... means which will not hinder the development of the pharmaceutical industry ...'

37 — Second recital in the preamble to Directive 87/21: '... experience has shown that it is advisable to stipulate more precisely the cases in which the results of pharmacological and toxicological tests or clinical trials do not have to be provided with a view to obtaining authorization for a proprietary medicinal product which is essentially similar to an authorized product, while ensuring that innovative firms are not placed at a disadvantage'.

38 — Second recital in the preamble to Directive 87/19: '... in order to achieve such optimum protection of health, the resources allocated to pharmaceutical research must not be squandered ...'

39 — Article 1 of Directive 87/21.

40 — Explanatory Memorandum [COM (84) 437 final version of 25 September 1984] concerning the proposal for a Council directive amending Directive 65/65/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, point 14.

19. The basis of the principle governing the grant of marketing authorization under the abridged procedure is equally clearly stated in the Commission's memorandum: [41]

'The proposed amendment of Article 4(8) of Directive 65/65/EEC is intended to reestablish the normal principle for exemption, i. e. that according to which the innovating firm consents to the second applicant referring to the tests described in the dossier of the original medicine'.

20. In this new stage, the Community legislature intends to carry its task of harmonization into an area in which the discretionary margin with regard to marketing authorization enjoyed by the various national authorities is still too wide. The means used to avoid any encouragement of disparities between national practices are, first, a stricter limitation on access to that type of procedure and, second, a highly specific and very strict definition of the conditions to be satisfied in order for the abridged procedure [42] to be used. However, the principal aim pursued in taking account of the social and economic context of the medicinal product is the same as that laid down in 1965, that is to safeguard the overriding requirement of public health:

'... point 8 of the second paragraph of Article 4 of Council Directive 65/65/EEC, as last amended by Directive 83/570/EEC, provides that various types of proof of the safety and efficacy of a proprietary medicinal product may be put forward in an application for marketing authorization depending on the objective situation of the proprietary medicinal product in question'. [43]

21. Since the Community legislature had allowed proof of the reliability of some tests and experts' reports to be provided by the submission of documents, it had to be seen to be exacting as to the contents of the scientific documents to be submitted.

22. In keeping with the realistic approach which had hitherto guided it, the legislature took account of certain specific and objective factors:

41 — Ibid., point 15.

42 — Second recital in the preamble to Directive 87/21: '... it is advisable to stipulate more precisely the cases in which the results of pharmacological and toxicological tests and clinical trials do not have to be provided ...'

43 — First recital in the preamble to Directive 87/21.

— the cost of the research and development needed to perfect a product of the kind in question; [44]

— the performance of tests, which delays the marketing of a medicinal product and shortens the period of exclusive rights granted by the patent. [45]

23. The pursuit of that specific intermediate objective (enabling innovative firms to make a profit on their investments), which was mentioned as early as 1965 [46] and developed in subsequent legislation, [47] by harmonizing the rules for drawing up dossiers and dealing with applications under the abridged procedure, must be regarded as being complementary, essential and necessary to the attainment of the ultimate objective. [48]

24. In the new measure, [49] the legislature reaffirms that an application for marketing authorization under the abridged procedure must fulfil an initial condition in order to be acceptable: the medicinal product concerned must be a generic one; [50] in embodying the principle that the abridged procedure is not to be used where that would prejudice the law relating to the protection of industrial and commercial property, [51] it adds a further condition for the application to be accepted.

25. The circumstances [52] in which the applicant for marketing authorization is not required to provide the results of pharmacological and toxicological tests [53] and clinical trials [54] are clearly, distinctly and restrictively regulated. [55] With respect to the abridged

44 — The pharmaceutical industry is almost completely self-financing in the field of research and development (see *L'EFPIA en chiffres — L'Industrie Pharmaceutique en Europe*, 1994 Edition (1993 figures)).

45 — Commission's Explanatory Memorandum, cited above at footnote 40, point 14.

46 — Second recital in the preamble to Directive 65/65.

47 — Two measures concerning certain economic aspects of medicinal products and intended particularly to meet the pharmaceutical industry's preoccupations have been adopted: Council Directive 89/105/EEC of 21 December 1988 relating to the transparency of measures regulating the pricing of medicinal products for human use and their inclusion in the scope of national health insurance systems (OJ 1989 L 40, p. 8) and Council Regulation (EEC) No 1768/92 of 18 June 1992 concerning the creation of a supplementary protection certificate for medicinal products (OJ 1992 L 182, p. 1).

48 — Commission's Explanatory Memorandum, cited above at footnote 40, point 14, and also the first recital in the preamble to Directives 87/19 and 87/21.

49 — Article 1 of Directive 87/21.

50 — That is to say, a medicinal product similar to an existing product no longer protected by patent. See point 8 of the second paragraph of Article 4 of Directive 65/65, as amended by Directive 87/21:

'(a) ...

(i) ... proprietary medicinal product (...) essentially similar to a product authorized ...;

(ii) ... the constituent or constituents of the proprietary medicinal product have a well-established medicinal use, with recognized efficacy and an acceptable level of safety;

(iii) ... proprietary medicinal product (...) essentially similar to a product authorized ...;

(b) ... new proprietary medicinal products containing known constituents ...'

51 — Article 1, Directive 87/21: 'However, and without prejudice to the law relating to the protection of industrial and commercial property ...'

52 — Point (a) of the first paragraph of Article 1 of Directive 87/21: 'The applicant shall not be required to provide the results of pharmacological and toxicological tests or the results of clinical trials if he can demonstrate ...'

53 — Second protocol to the annex to the standards and protocols directive concerning pharmacological and toxicological tests, that is to say the effects produced in animals, and pharmacodynamic tests, that is to say how the body disposes of drugs, as amended by Directives 87/19 and 83/570.

54 — The third protocol to the annex to the standards and protocols directive, as amended by Directives 83/570 and 87/19, introduces the concept of clinical trials and clinical pharmacology to be carried out on patients receiving the new therapy.

55 — Article 1, first paragraph, points (a)(1), (ii), (iii) and (b) of Directive 87/21.

procedure, whichever possibility is chosen, a qualified expert [56] must provide scientific evidence to justify the use of that type of procedure. [57] In accordance with the 1975 directives, [58] the role of that expert consists in performing the tests and drawing up the analytical reports, [59] in particular ascertaining whether it is a generic medicinal product, in compliance with the control methods laid down by the legislation in force, [60] and then, depending on the various possibilities provided for in Directive 87/21, in drawing up the documents and particulars required by Parts II and III of the annex to the standards and protocols directive, [61] in accordance with the control methods prescribed by the Community rules in force.

26. The documents to be supplied in connection with the first possibility [62] are in essence the dossier previously assembled by the innovating firm which holds the marketing authorization for the original medicinal product. The documents in that file may only be used with the consent of the holder of marketing authorization. The qualified expert must check that the control methods used are still up-to-date and were carried out taking account of technical and scientific progress. In the view of the Community legislature, this possibility constitutes, as it were, the normal principle governing exemption. [63] Furthermore, it possesses the advantage of complying with all the objectives specifically pursued by the various directives which are of necessity complementary to the ultimate objective.

27. In the case of the second possibility, [64] the legislature gives an extremely precise and highly restrictive definition of the conditions to be satisfied for the use of the abridged procedure by references to published scientific literature. Thus, only experts for the purposes of Directive 75/319 who are required to take account of scientific and technical progress [65] are entitled to:

'... demonstrate ... by detailed references to published scientific literature presented in accordance with the second paragraph of

56 — Within the meaning of Directive 75/319, as amended by Directive 83/570.

57 — Article 2(c) of Directive 75/319.

58 — Amended by Directives 87/19 and 83/570.

59 — First protocol to the annex to the standards and protocols directive, as amended by Directives 83/570 and 87/19. Tests to check and identify the chemical composition of the product.

60 — Article 9a of Directive 65/65, as amended by Directive 83/570: 'After an authorization has been issued, the person responsible for placing the product on the market must, in respect of the control methods provided for in Article 4(7), take account of technical and scientific progress and introduce any changes that may be required to enable the proprietary medicinal product to be checked by means of generally accepted scientific methods. These changes must be accepted by the competent authorities of the Member State concerned.'

61 — Point 8, second paragraph, Article 4, of Directive 65/65 as amended, pharmacological and toxicological tests and clinical trials.

62 — Point 8(a)(i), second paragraph, Article 4: 'either (...) the proprietary medicinal product is essentially similar to a product authorized in the country concerned by the application and ... the person responsible for the marketing of the original medicinal product has consented to the pharmacological, toxicological or clinical references contained in the file on the original proprietary medicinal product being used for the purpose of examining the application in question'.

63 — Explanatory Memorandum of the Commission, cited above at footnote 40, point 15.

64 — Point 8(a) (ii), second paragraph, Article 4: 'or by detailed references to published scientific literature presented in accordance with the second paragraph of Article 1 of Directive 75/318/EEC that the constituent or constituents of the proprietary medicinal product have a well-established medicinal use, with recognized efficacy and an acceptable level of safety'.

65 — Article 9a of Directive 65/65, as amended by Directive 83/570.

Article 1 of Directive 75/318/EEC that the constituent or constituents of the medicinal product have a well-established medicinal use, with recognized efficacy and an acceptable level of safety'. [66]

28. It is the legislature's intention that minimal use should be made of that possibility: [67]

'This possibility is, in practice, very limited, since, in accordance with the second paragraph of Article 1 of Directive 75/318/EEC, this bibliographical evidence must be submitted in order to correspond "in like manner" to the criteria of safety and efficacy in the annex to that directive.'

29. Accordingly, qualified experts [68] chosen by the applicant for marketing authorization on the basis of point 8(a)(ii) of the second paragraph of Article 4 must ascertain whether the scientific documents submitted in support of the application are reliable (the tests reported in the documents in question must have been carried out by qualified persons chosen by the holder of marketing authorization for the original medicinal product in accordance with still up-to-date control methods) and complete (the documents of that description must include all the toxicological and pharmacological tests and clinical trials required in the case in point).

30. In so far as in practice only a medicinal product which has been in use for decades, and whose constituent or constituents have been subjected to tests detailed at length and commented on in scientific literature, would in actual fact satisfy those requirements, [69] the various intermediate objectives complementary to the prime objective pursued by Community legislation have been complied with.

31. In the third situation, [70] the legislature provides for a period for protecting the data contained in the dossier submitted in the application for marketing authorization in respect of the original medicinal product. An applicant for marketing authorization for a generic medicinal product may use the

66 — Point 8(a)(ii), second paragraph, Article 4 of Directive 65/65, as amended by Directive 87/21.

67 — Explanatory Memorandum of the Commission, cited above at footnote 40, point 15.

68 — For the purposes of Directive 75/319, as amended by Directives 83/570 and 87/19.

69 — This possibility in practice plays an important part in testing existing medicinal products (Article 39 of Directive 75/319) (see P. Deboyser: 'Le Marché Unique des Produits Pharmaceutiques', op. cit., points 9 and 14).

70 — Point 8(a)(iii), second paragraph, Article 4: 'or that the proprietary medicinal product is essentially similar to a product which has been authorized within the Community, in accordance with Community provisions in force, for not less than six years and is marketed in the Member State for which the application is made; this period shall be extended to 10 years in the case of high-technology medicinal products within the meaning of Part A in the annex to Directive 87/22/EEC (OJ 1987 L 15, p. 38) or of a medicinal product within the meaning of Part B in the annex to that directive for which the procedure laid down in Article 2 thereof has been followed; furthermore, a Member State may also extend this period to 10 years by a single decision covering all the products marketed on its territory where it considers this necessary in the interest of public health. Member States are at liberty not to apply the abovementioned six-year period beyond the date of expiry of a patent protecting the original product. However, where the proprietary medicinal product is intended for a different therapeutic use from that of the other proprietary medicinal products marketed or is to be administered by different routes or in different doses, the results of appropriate pharmacological and toxicological tests and/or of appropriate clinical trials must be provided.'

documents assembled by the holder of authorization to market the original medicinal product once the qualified expert has checked that the methods used at the time are still in current use. Overriding economic requirements are satisfied, since the innovating firm is allowed time to recoup the costs attaching to the production of the original medicinal product and make a profit.

32. At the present stage in the development of the Community rules on the grant of marketing authorization under the abridged procedure, the Member States have only a very narrow discretionary margin.

33. That, in broad outline, is how the Community legislation relevant to this case now stands.

34. The Court is asked to reply to the following question:

'In Community law is Directive 65/65/EEC to be interpreted as permitting a national competent authority in the circumstances of a case such as the present to issue an authorization to place a medicinal product on the market pursuant to an application made under Article 4(8)(a)(ii) of Council Directive 65/65/EEC as replaced by Council Directive 87/21/EEC, notwithstanding the fact that the particulars and documents submitted in support of such an application do not contain:

(a) detailed references to published scientific literature presented in accordance with each of the requirements of Parts 2 and 3 of the Annex to Directive 75/318/EEC; or

(b) experts' reports complying with each of the requirements of Articles 1 and 2 of Directive 75/319/EEC?'

35. The national court restricts its request for a ruling to a very specific case and maintains that the MCA was correct in deciding to use the abridged procedure by detailed references to published scientific literature, in considering Norgine's application for marketing authorization in respect of the medicinal product Unigam. [71] *In so far as the legal framework set out above applies to this case,* Scotia's claim to have been the victim of

71 — Order for reference, p. 18: '... it would be pointless to remit the application [to the MCA] for a redetermination as to whether exemption (a)(ii) is applicable and in discretion I would refuse to do so'.

unequal treatment which favoured Norgine is entirely devoid of substance. Since 'the use of evening primrose oil for medicinal purposes (in the form of medicinal products Efamast and Epogam) was innovated by Scotia ...', [72] the applications for marketing authorization for those products had of necessity to be dealt with under the standard procedure. By contrast, it was possible to consider using the abridged procedure in the case of Unigam, because it is a generic medicinal product. [73] Two different situations were, therefore, properly dealt with in different ways. [74]

36. With regard to that specific point, I am doubtful whether the procedure followed by the MCA when considering an application for marketing authorization under the abridged procedure by detailed references to published scientific literature [75] is consistent with the requirements of Community law. I am not persuaded that the MCA made at most a mere error of fact in the case in point. [76] My misgivings are sustained by many unanswered questions. For example, although the national court classes Scotia as an innovative firm, [77] at no point is it stated that the MCA took account of the law concerning the industrial and commercial protection of such firms when it decided to use the abridged procedure. What is more, neither at the hearing nor in its written observations has the Commission, the United Kingdom or Norgine considered the objective specifically pursued by the Community legislature in Directive 87/21.

37. Contrary to what they contend, the protection of the innovative firm's interests — an overriding economic necessity — is not only quite compatible with the intermediate objectives but essential in order to attain the ultimate objective laid down by the Community legislature.

38. By contrast, the procedure followed by the MCA ignores the objective specifically pursued, favours a secondary objective as opposed to that specific and mandatory objective, has the effect of emulating the national procedures targeted by the Community legislature when it drew up Directive 87/21 [78] and, in a word, renders that measure ineffective.

39. However, for lack of additional information, and taking into account my terms of reference in the case before the Court, I shall confine myself to the question asked by the national court.

72 — Order of the Divisional Court, p. 3.

73 — The MCA justified its use of the abridged procedure as regards Unigam on the grounds that it had the same constituent or constituents as Epogam and Efamast (order for reference, p. 13, and Observations of the United Kingdom, point 28).

74 — The conditions for invoking the principle of non-discrimination have not been satisfied (consistent case-law of the Court, especially the judgment in Case 283/83 *Racke* v *Hauptzollamt Mainz* [1984] ECR 3971, paragraph 7).

75 — Point 8(a)(ii), second paragraph, Article 4 of Directive 65/65, as amended by Directive 87/21.

76 — Order of the Divisional Court, p. 18.

77 — Order for reference, p. 2.

78 — See above, footnote 40.

40. I must own that I was not surprised to hear the Commission's Agent inform the Court at the hearing of his doubts as to the position to be adopted in order to settle this case.

41. Contrary to his opinion, I maintain that the proper solution is to be found in the Community legislation itself.

42. The MCA necessarily enjoys a certain discretion in applying the procedures and conditions set out in Directives 65/65, 75/318, 75/319, 83/570 and 87/21 when considering an application for marketing authorization in respect of a proprietary medicinal product. The discretion given to the competent authority and its extent are defined by the Community legislation set out above.

43. The MCA decided to grant Norgine marketing authorization for the product Unigam according to the procedure laid down in point 8(a)(ii), second paragraph, Article 4, when the dossier contained no published material [79] referring to single-dose toxicity tests, [80] pharmacokinetic tests [81] or clinical trials. [82]

44. In order to justify that practice, the United Kingdom and the Commission claim that to oblige the licensing authority to comply with the letter of the law would render the abridged procedure by detailed references to published scientific literature quite ineffective. Therefore, and in pursuance of the objective described as essential by the legislature, it is enough for the constituent or constituents of the medicinal product to meet the criteria laid down by the first paragraph of Article 5 of Directive 65/65, namely safety, efficacy and quality of the product. That interpretation is said to be consistent with the reasoning underlying the legislation. [83] I note, however, that at the hearing the Commission's representative acknowledged that such an interpretation ran the risk of reintroducing disparities between the various practices pursued by the national authorities.

45. I maintain that it would be unacceptable to endorse that practice, which is contrary not only to the spirit but also to the letter of that legislation.

79 — Order for reference, p. 21, and Observations of the United Kingdom, point 30.

80 — Part II, Chapter I, point B, first paragraph of the annex to the standards and protocols directive, as amended by Directive 87/19: '... a qualitative and quantitative study of the toxic reactions which may result from a single administration of the active substance or substances contained in the proprietary medicinal product, in the proportions and physico-chemical state in which they are present in the actual product'.

81 — Part II, Chapter I, point G, first paragraph of the annex to the standards and protocols directive: '... the fate of the active substance within the organism'.

82 — Part III, annex to the standards and protocols directive, clinical trials on volunteers (whether well or ill).

83 — Observations of the United Kingdom, point 9, and Observations of the Commission, point 13.

46. The abridged procedure by detailed references to published scientific literature constitutes an exception to the normal principle for exemption. [84] Accordingly, it is imperative that Article 4, second paragraph, point (8)(a)(ii) should be strictly applied. The licensing authority must ascertain that evidence of the safety, efficacy and quality of the constituent or constituents of the medicinal product for which marketing authorization is sought has been adduced in compliance with the requirements laid down [85] (observance of minimum standards concerning control methods and qualifications of those carrying out the tests [86]).

47. The derogation from the common rules is to be strictly interpreted: the burden of proof lies on the person seeking to rely on the derogation. The Court's case-law is well established on this point. [87] In this case, the only basis for an exception is scientific evidence of progress in the development of control methods. [88]

48. Endorsement of that practice may, in the short term, risk reintroducing disparities between national practices and giving priority to a secondary rather than a specific objective and, in the long term, jeopardizing the attainment of the ultimate objective (expanded single market in quality medicinal products).

49. With regard to pharmacodynamic tests, Scotia appears not to have submitted the results. [89] If that is so, it does not mean that the United Kingdom's practice is valid. Only qualified experts, [90] acting in accordance with the legislation in force, [91] can demonstrate that the tests have not been carried out or have been carried out in a different manner, taking account of scientific progress; the MCA, for its part, is required to establish whether the scientific evidence adduced can be substantiated. [92]

50. Subsequently, in connection with the same possibility, was the national authority entitled to dispense with experts' reports complying with each of the requirements laid down in Articles 1 and 2 of Directive 75/319?

51. Once more the United Kingdom's practice is at variance with Community legislation.

84 — Explanatory Memorandum of the Commission, cited above at footnote 40, point 15.

85 — Article 11, second paragraph, of Directive 65/65, as amended by Directive 83/570: 'An authorization shall also be suspended or revoked where the particulars supporting the application as provided for in Articles 4 and 4a are incorrect or have not been amended in accordance with Article 9a, or when the controls referred to in Article 8 of this directive or in Article 27 of 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 have not been carried out.'

86 — Standards and protocols directive and Directive 75/319, as amended by Directives 83/570 and 87/19.

87 — For the concept of a strict interpretation applied to public contracts for the supply of pharmaceutical products and specialities, see in particular one of the most recent judgments, namely that in Case C-328/92 *Commission* v *Spain* [1994] ECR I-1569, paragraphs 15 to 17.

88 — Articles 9a and 11 of Directive 65/65, as amended by Directive 83/570.

89 — Observations of the national court, p. 21, of the United Kingdom, paragraph 37 and of Scotia and Norgine at the hearing.

90 — For the purposes of Directive 75/319, as amended.

91 — For the purposes of the standards and protocols directive, as amended.

92 — Article 11, second paragraph, of Directive 65/65, as amended by Directive 83/570.

52. It permits the abridged procedure to be used even where no expert has expressed an opinion as to whether recourse to it is justified [93] and where separate toxicological and pharmacological reports have not been submitted. [94]

53. The United Kingdom does not put forward any arguments concerning failure to comply with Article 2(c) of Directive 75/319; on the other hand, as regards Article 2(b) of that directive, it asserts [95] that the primary purpose of Directive 87/21 is to safeguard public health and avoid unnecessary tests. Accordingly, what is required is non-compliance with the substantive rules. [96]

54. The Commission, for its part, contends that the practice of not complying with Article 2(c) of Directive 75/319 must be deemed to be invalid. With respect to non-compliance with Article 2(b), it contends that the practice must, exceptionally, be upheld on account of Unigam's constituents; the Commission adds that under the abridged procedure, the experts do not perform tests but submit published references. In those circumstances, it is unnecessary to comply with the requirements of the 1975 directives. [97]

55. I shall not linger over the question whether or not the United Kingdom's practice of not complying with Article 2(c) is justifiable. The letter of the law is, to my mind, unequivocal. A qualified expert is to carry out tests and trials and produce analytical reports pursuant to the rules in force [98] in order to demonstrate that the medicinal product for which marketing authorization is sought is a generic one. That is one of the conditions governing the acceptability of an application for marketing authorization submitted under the abridged procedure.

56. As regards non-compliance with Article 2(b), I note that the original version [99] merely required experts with qualifications

93 — Article 2(c) of Directive 75/319.

94 — Article 2(b) of Directive 75/319.

95 — Observations of the United Kingdom, point 41.

96 — Article 5, first paragraph, of Directive 65/65.

97 — Observations of the Commission, p. 8.

98 — Point 8, second paragraph, Article 4 of Directive 65/65, as amended by Directive 87/21.

99 — Directive 75/319, Article 2(a) and (b): 'The duties of the experts according to their respective qualifications shall be:
(a) to perform tasks falling within their respective disciplines (analysis, pharmacology and similar experimental sciences, clinical trials) and to describe objectively the results obtained (qualitatively and quantitatively);
(b) to describe their observations in accordance with Council Directive 75/318/EEC of 20 May 1975 on the approximation of the laws of the Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of proprietary medicinal products, and to state, in particular:
— in the case of the analyst, whether the product is consistent with the declared composition, giving any substantiation of the control methods employed by the manufacturer;
— in the case of the pharmacologist or the specialist with similar experimental competence, the toxicity of the product and the pharmacological properties observed;
— in the case of the clinician, whether he has been able to ascertain effects on persons treated with the product which correspond to the particulars given by the applicant in accordance with Article 4 of Directive 65/65/EEC, whether the patient tolerates the product well, the posology the clinician advises and any contra-indications and side-effects.'

in their respective fields to report the results of analyses and tests in accordance with generally accepted control methods but did not require those results to be submitted separately. Since Articles 9a and 11, second paragraph, of Directive 65/65 [100] were amended, the competent authority, in this case the MCA, has been obliged, when granting marketing authorization, to ascertain whether the control methods used are consistent with current scientific knowledge. Derogations from the minimum rules laid down can be allowed only on that condition. Where, therefore, scientific progress requires those tests and reports to be submitted separately, an applicant for marketing authorization will have to comply with that further requirement.

57. To argue by analogy, still in the same connection, qualified experts must be responsible for submitting scientific documents stating that all the tests were carried out and reports drawn up by qualified staff on the basis of control methods consistent with medical rules and the state of scientific progress. Furthermore, the expert chosen by the applicant for marketing authorization under the abridged procedure, that is Norgine, must prove scientifically that those methods are still up-to-date and appropriate. The competent authority, that is the MCA, establishes whether or not that dossier is complete and reliable. Where a test has gone unpublished, or where a scientific publication refers to a test conducted otherwise than by the prescribed control methods, an application submitted on the basis of point 8(a)(ii), second paragraph, Article 4 must, unless scientifically justified, be refused.

100 — Article 1(4) and (6) of Directive 83/570.

58. At this stage, therefore, in the development of Community law concerning the grant of marketing authorization under the abridged procedure by references to published scientific literature, the Member States' discretion is limited: it is dependent on scientific and technical progress; moreover, the burden of proving that the derogation is justified falls on the person seeking to rely on it.

59. By adopting the solution I am proposing, the Court will be following its own line of decided cases. In two judgments, it held that the authority competent to issue marketing authorization may not refuse [101] or provide for the lapse of authorization, [102] except by reference to overriding requirements of public health.

60. Let me say by way of extrapolation that such a practice would have carried *a risk* as

101 — Judgment in *Clin-Midy*, cited above at footnote 20: 'Article 21 of Directive 65/65 must be interpreted as meaning that authorization to market a proprietary medicinal product may not be refused, suspended or revoked *save on the ground of the protection of public health as referred to in the directive*' (point 2, operative part, emphasis added).

102 — Judgment in Case C-83/92 *Pierrel* v *Ministero della Sanità* [1993] ECR I-6419:
'1. Article 21 of Council Directive 65/65/EEC ... must be interpreted as meaning that the suspension or revocation of an authorization to market medicinal products *may be decided only on the grounds laid down in that directive or other applicable provisions of Community law.*
2. Directive 65/65/EEC, as amended, precludes national authorities *not only from introducing grounds for suspension or revocation other than those laid down by Community law but also from providing for the lapse of authorizations to market medicinal products*' (operative part, emphasis added).

regards public health: that of not marketing a drug capable of bringing about an appreciable improvement in the patient.

61. In this case, the Court is being asked to uphold a practice which allows a medicinal product to be put on the market even where the minimal conditions laid down in Directive 65/65, as amended by Directives 75/318, 75/319, 83/570, 87/19 and 87/21, concerning the grant of marketing authorization have not been satisfied, and which does not fall within the scope of an amendment of or derogation from the principles set out in the aforesaid provisions.

62. If the Court were to uphold such a practice, it would permit the marketing of a medicinal product which falls short of the necessary standards of safety, without thereby guaranteeing the consumer any appreciable improvement in health. The effect would be to generate two risks in the field of public health.

63. Thus the reasons why the MCA's practice in respect of marketing authorization for medicinal products pursuant to Article 4, second paragraph, point 8(a)(ii) ought not to be upheld can be grouped together as follows:

— the rationale behind the legislation (compliance with an overriding economic requirement necessary for the production of a medicinal product providing optimal safety for the consumer; a medicinal product manufactured in accordance with identical common standards; the harmonization so achieved making it possible to attain the ultimate objective, namely an expanded single market in quality medicinal products); [103]

— the general principle that derogations are to be interpreted strictly; [104]

— the restrictions imposed by Directive 83/570 on the discretion granted to the competent authority in respect of marketing authorization; [105]

— the *Clin-Midy* and *Pierrel* cases which require strict compliance with the Community provisions applicable to marketing authorizations. [106]

103 — See points 18 to 23 above.
104 — See points 46 to 48 above.
105 — See points 24 to 26 and 27 to 30 above.
106 — See points 59 to 62 above.

64. In conclusion, in the light of the considerations set out above, I propose that the Court give the following answer to the question submitted by the Divisional Court:

Article 4, second paragraph, point (8)(a)(ii) of Council Directive 65/65/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to medicinal products, as amended by Council Directive 87/21/EEC of 22 December 1986 precludes a national competent authority in circumstances such as those of the present case from issuing an authorization to place a medicinal product on the market where the particulars and documents submitted in support of such an application do not contain:

(a) detailed references to published scientific literature presented in accordance with each of the requirements laid down in Parts 2 and 3 of the Annex to 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 proprietary medicinal products; or

(b) experts' reports complying with each of the requirements laid down in Articles 1 and 2 of 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.