OPINION OF ADVOCATE GENERAL MAZÁK

delivered on 26 March 2009 [1]

1. In the present reference for a preliminary ruling, the High Court of Justice of England and Wales, Queen's Bench Division (Administrative Court) (United Kingdom) has referred two questions to the Court on the interpretation of, respectively, Article 10 of Directive 2001/83/EC on the Community code relating to medicinal products for human use, [2] and the conditions for establishing a sufficiently serious breach of Community law to render a Member State liable in damages.

I — Legal framework

2. Directive 2001/83 codified and merged into a single text the directives on the approximation of provisions laid down by law, regulation or administrative action relating to medicinal products for human use, among which figure Directive 65/65/EEC, [3] Directive 75/318/EEC, [4] and Directive 75/319/EEC. [5]

3. Article 6(1) of Directive 2001/83 provides as follows:

'No medicinal product may be placed on the market of a Member State unless a marketing authorisation has been issued by the competent authorities of that Member State in accordance with this Directive or an authorisation has been granted in accordance with Regulation (EEC) No 2309/93.'

1 — Original language: English.

2 — Directive of the European Parliament and of the Council of 6 November 2001 (OJ 2001 L 311, p. 67), as amended by Directive 2004/27/EC of 31 March 2004 (OJ 2004 L 136, p. 34) ('Directive 2001/83' or 'the Directive').

3 — Council Directive 65/65 of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (OJ, English Special Edition 1965-1966(I) p. 24), as amended by Council Directive 93/39/EEC of 14 June 1993 (OJ 1993 L 214, p. 22) ('Directive 65/65').

4 — Council Directive 75/318 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 (OJ 1975 L 147, p. 1), as amended by Commission Directive 1999/83/EC of 8 September 1999 (OJ 1999 L 243, p. 9) ('Directive 75/318').

5 — Second Council Directive 75/319 of 20 May 1975 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (OJ 1975 L 147, p. 13), as amended most recently by Commission Directive 2000/38/EC of 5 June 2000 (OJ 2000 L 139, p. 28) ('Directive 75/319').

4. Article 88 of Regulation (EC) No 726/2004 [6] provided for the repeal of Regulation No 2309/93 and went on to state that references to that regulation are to be construed as references to Regulation No 726/2004.

5. Article 8 of Directive 2001/83, which corresponds, in essence, to Article 4 of Directive 65/65, states in paragraph 3:

'The application [for authorisation to place a medicinal product on the market] shall be accompanied by the following particulars and documents, submitted in accordance with Annex I:

…

(i) Results of:

— pharmaceutical (physico-chemical, biological or microbiological) tests,

— pre-clinical (toxicological and pharmacological) tests,

— clinical trials.

…'

6. Article 10(1) and (2) of Directive 2001/83 states:

'1. By way of derogation from Article 8(3)(i), and without prejudice to the law relating to the protection of industrial and commercial property, the applicant shall not be required to provide the results of pre-clinical tests and of clinical trials if he can demonstrate that the medicinal product is a generic of a reference

6 — Regulation of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (OJ 2004 L 136, p. 1), Article 88 of which provided for the repeal 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. l).

medicinal product which is or has been authorised under Article 6 for not less than eight years in a Member State or in the Community ["the period of protection"].

…

2. For the purposes of this Article:

(a) "reference medicinal product" shall mean a medicinal product authorised under Article 6, in accordance with the provisions of Article 8;

(b) "generic medicinal product" shall mean a medicinal product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies …'

7. According to Articles 2 and 3 of Directive 2004/27, where the application for authorisation was made before 30 October 2005, the applicable period of protection is that laid down in Article 10 of Directive 2001/83 prior to its amendment by Directive 2004/27. The original wording of Article 10 provided that the period of protection was to be at least 6 years, but that it was open to each Member State to extend that period of protection up to 10 years.

8. Article 28(1) of Directive 2001/83 states as follows:

'With a view to the granting of a marketing authorisation for a medicinal product in more than one Member State, an applicant shall submit an application based on an identical dossier in these Member States. The dossier shall contain the information and documents referred to in Articles 8, 10, 10a, 10b, 10c and 11. The documents submitted shall include a list of Member States concerned by the application.

The applicant shall request one Member State to act as "reference Member State" and to prepare an assessment report on the medicinal product in accordance with paragraphs 2 or 3.'

9. According to the Agreement on the European Economic Area ('the EEA Agree-

ment'), to which the Republic of Austria was a party before its accession to the EU, Directive 65/65 and Directive 75/319 were applicable in Austria from 1 January 1994.

II — Factual and procedural background and the questions referred

10. In 1963, the competent Austrian authorities granted to the Waldheim company, in accordance with the Austrian law in force at the time, authorisation to place the medicinal product galantamine, under the brand name 'Nivalin', on the market for the treatment of polio.

11. Although, in 1995, the authorisation of Nivalin was amended to include its experimental use in the treatment of Alzheimer's disease and later on to include the 'symptomatic treatment' of Alzheimer's disease, the original Nivalin dossier per se was never brought up-to-date in accordance with the requirements of Directive 65/65 and Directive 75/319, which had been applicable in Austria since 1 January 1994 by virtue of the EEA Agreement. Waldheim withdrew Nivalin from the market in 2001.

12. Meanwhile, as a result of cooperation agreements with Waldheim, in 1999 Janssen-Cilag AB submitted a full application to the competent Swedish authority (the Swedish Medicinal Products Agency, 'the Swedish MPA'), pursuant to Article 4 of Directive 65/65 (now Article 8 of Directive 2001/83), for marketing authorisation for galantamine, under the brand name 'Reminyl', for the treatment of Alzheimer's disease (in particular, an Alzheimer-type dementia).

13. After having obtained, on 1 March 2000, marketing authorisation for Reminyl in Sweden, Janssen-Cilag also obtained mutual recognition of its authorisation in Austria on 22 August 2000. In the United Kingdom, Shire Pharmaceuticals Ltd ('Shire') has been the holder of the marketing authorisation for galantamine since 14 September 2000.

14. On 14 December 2005, in the context of a decentralised procedure pursuant to Article 28(1) of Directive 2001/83, Generics (UK) Ltd ('Generics'), a British distributor of medicinal products, submitted an application for marketing authorisation for a generic form of galantamine to the Licensing Authority, the competent national body for granting authorisations in the United Kingdom, which was designated as the reference Member State. Simultaneous applications were lodged in 17 other Member States.

15. The application was submitted on the basis of the generic product exception in Article 10(1) of Directive 2001/83. Nivalin, which was the subject of an authorisation from Austria, was specified as the reference medicinal product authorised for a period of not less than 10 years in the EEA. The application also mentioned the British authorisation of Reminyl as the reference medicinal product in the United Kingdom, and as the product used for the bioavailability study necessary to show that the Generics's product was, in fact, a generic of Nivalin/Reminyl.

16. The Licensing Authority rejected Generics's application. It considered that Nivalin, covered by the Austrian authorisation, could not be used as the reference medicinal product for an application for marketing authorisation for a generic medicinal product within the meaning of Article 10(1) of Directive 2001/83, since its dossier had not been updated since 1 January 1994 to comply with the requirements of Community legislation, applicable in Austria following the entry into force of the EEA Agreement. As regards Reminyl, the 10-year period of protection referred to in Article 10 of Directive 2001/83 in its original version had not yet expired and, therefore, the authorisation could not be granted on that basis.

17. Generics thereupon brought an action against the Licensing Authority's decision before the High Court, which referred the following questions to the Court for a preliminary ruling:

'1. Where a medicinal product falling outside of the scope of the Annex to Regulation [No] 2309/93 has been placed on the market in a Member State (Austria) under its national authorisation procedure prior to the accession of that Member State to the EEA or the EC and:

(a) that Member State has subsequently acceded to the EEA and then the EC, and as part of the conditions of its accession it has transposed into its national law the authorisation provisions of Directive 65/65 (now Directive 2001/83), no transitional provisions applying in this respect;

(b) the product in question has remained on the market in that Member State for some years after its accession to the EEA and the EC;

(c) following the accession of that Member State to the EEA and the EC, the marketing authorisation for the product in question has been varied by adding a new indication, and the variation was considered by the authorities of that Member State to be consistent with the requirements of Community law;

(d) the dossier of the product in question was not updated in accordance with Directive 65/65 (now Directive 2001/83) after that Member State's accession to the EEA and the EC; and

(e) a product containing the same active ingredient has subsequently been authorised under Article 6 of Directive 2001/83 and placed on the market in the EC;

is the medicinal product to be considered to be "a reference medicinal product which is or has been authorised under Article 6 … in a Member State" within the meaning of Article 10(1) of Directive 2001/83, and if so which of the above conditions is/are decisive in this respect?

2. In circumstances where the competent authority of a reference Member State erroneously refuses an application for a marketing authorisation made under Article 10(1) of Directive 2001/83 in the context of the decentralised procedure provided for in that directive, on the ground that the medicinal product referred to in Question 1 above was not a "reference medicinal product" within the meaning of Article 10(1), what guidance, if any, does the Court of Justice think it appropriate to provide as to which circumstances the national court ought to take into consideration when it comes to determine whether the breach of Community law is a sufficiently serious breach within the meaning of the judgment in *Brasserie du Pêcheur and Factortame*[7]?'

18. Observations have been submitted by Generics, Shire and Janssen-Cilag (the two interested parties in the main proceedings who were jointly represented before the Court), the United Kingdom Government, the Government of the Republic of Poland and the Commission. The hearing took place on 27 November 2008.

7 — Joined Cases C-46/93 and C-48/93 [1996] ECR I-1029.

III — Assessment

19. I shall first of all set out Generics's principal arguments in overview. As regards the submissions of the other parties, where appropriate, I shall generally refer to them during my analysis.

20. As regards the first question, Generics maintains that it is possible for a medicinal product such as Nivalin to be considered as 'a reference medicinal product' within the meaning of Article 10(2)(a) of Directive 2001/83. First, Generics submits that, according to the case-law, [8] minor differences in strength and/or pharmaceutical form between a medicinal product already authorised and a medicinal product for which authorisation is sought under the abridged procedure in accordance with Article 10(1) of Directive 2001/83 do not prevent the former from being considered as 'a reference medicinal product'.

21. Furthermore, Generics considers that the rationale for the abridged procedure is to strike a balance between two sets of competing interests, namely: (i) to facilitate the entry onto the market of generic products, by relieving generic applicants from the obligation of carrying out repetitive pharmacological and toxicological tests and clinical trials (which is linked to the aim of avoiding the repetition of tests on humans or animals unless absolutely necessary [9]); and (ii) to safeguard the interests of innovative firms [10] (by way of granting them a period of data and market exclusivity during which they may recoup their investment in the development of the product). Thus, according to Generics, the essential question is whether the reference product has been authorised within the Community for the relevant period of time. It argues that, in this case, the distributors of Reminyl have attempted to use a new marketing authorisation as a procedural device to prolong the 10-year period of data exclusivity for Nivalin [11] (and for Reminyl which, according to Generics, is the same product). To permit that strategy to succeed would be inimical to the objectives of Directive 2001/83 and the Treaty.

22. In addition, such an interpretation of Article 10(1) of Directive 2001/83 is: neither (i) justified by the quality, safety or efficacy of the medicinal product for which authorisation is sought, because the latter have to be evaluated by the competent authority pursuant to other provisions of the Directive, nor (ii) justified by the requirement to safeguard the interests of innovative firms, because the abovementioned case-law clearly established limits to that protection.

8 — Case C-368/96 *Generics (UK) and Others* [1998] ECR I-7967; Case C-106/01 *Novartis Pharmaceuticals* [2004] ECR I-4403; and Case C-36/03 *Approved Prescription Services* [2004] ECR I-11583.

9 — This essentially corresponds to the 10th recital in the preamble to the Directive.

10 — This corresponds in essence with the ninth recital in the preamble to the Directive.

11 — Which has been on the market since 1963.

23. Moreover, Generics submits that Article 10(1) of the Directive does not permit an inquiry into the compatibility of national legislation or of a given authorisation with the requirements of Directive 2001/83. In so far as national legislation is not compatible with Community law there are other means by which that should be addressed, namely Articles 226 EC and 227 EC.

24. As the United Kingdom and Polish Governments, together with Shire and Janssen-Cilag, also argue in essence, the Commission considers that the crucial fact remains that the dossier for Nivalin for its original use (treatment of polio) was not updated in accordance with Directive 65/65 (now Directive 2001/83) following Austria's accession to the EEA and the EC. Accordingly, that product was never authorised under Article 6 of the Directive or under the previous Community legislation. Therefore, it cannot constitute a reference medicinal product for the purposes of Article 10 of Directive 2001/83.

25. According to Shire and Janssen-Cilag, Article 10(1) does not simply require that a product should have been marketed, within the EEA, for the requisite number of years. Rather, it is intended to ensure that the innovative firm is able to achieve some return on the investment required to generate a data package that complies with the requirements of both Article 6 and Article 8 of the Directive, whilst at the same time ensuring that the competent authorities have access to sufficient pre-clinical and clinical data to protect public health.

A — *Appraisal*

26. By its first question, the referring court seeks to know whether or not, in circumstances such as those at issue in the main proceedings, the product in question (Nivalin) is to be considered 'a reference medicinal product which is or has been authorised under Article 6 … in a Member State' (Austria) within the meaning of Article 10(1) of Directive 2001/83.

27. It should be noted at the outset that it is apparent from the order for reference, and from the documents before the Court in general, that while Nivalin was granted national authorisations in Austria in the 1960s, those authorisations were not renewed after Austria acceded to the EEA and the Community under either Directive 2001/83 or the earlier Community legislation, and the Nivalin dossier was never updated to comply with the Community *acquis*. Thus, the national authorisations of Nivalin were never converted into authorisations under Article 6 of the Directive.

28. It is apparent from a reading of Articles 6(1), 8, 10(1) and 10(2)(a) of the Directive ('the provisions at issue') that for a product to be a 'reference medicinal product' it must be authorised under Article 6 in accordance with the conditions enumerated in Article 8. At the same time, it is clear that these articles cannot be interpreted in a manner which allows for a continuing form of authorisation of a reference medicinal product other than one which complies with Article 6 and satisfies the requirements of Article 8, not least that the full dossier of particulars and documents be provided.

29. In other words, what is required is solely an authorisation of a reference medicinal product in accordance with Community provisions. [12]

30. Of course, it is true that Article 10(1), and in particular the phrase 'authorised under Article 6', should be interpreted in such a way that it is of no consequence whether a medicinal product has been authorised within the meaning of Directive 2001/83 per se or within the meaning of the earlier Community legislation.

31. Furthermore, neither the provisions at issue, the directive as a whole nor any other Community provision contain an exception which would justify following the procedure in Article 6(1) otherwise than in full or would allow for alternative procedures, for instance in accordance with other Community provisions or with national law.

32. Therefore, it is necessary to emphasise that it does not follow from Generics's submissions or from the documents before the Court that Nivalin was authorised in accordance with Article 6(1) of the Directive or within the meaning of the earlier Community legislation.

33. In that connection, it is of no consequence that Nivalin was authorised in a Member State (Austria) under its national authorisation procedures [13] prior to the accession of that Member State to the EEA or the Community. This is because there is no Community provision which would recognise such an authorisation as having the same status as one granted in accordance with Community provisions.

34. Equally, it is of no consequence that Nivalin was used in that Member State before its accession to the EEA and the

12 — That is why Generics may not rely on the case-law referred to in point 20 above. The reason is that, contrary to the present case, in those cases the reference medicinal product was duly authorised in accordance with Community provisions in force.

13 — Which did not correspond to the Community provisions.

Community and/or, for that matter, that it remained on the market in that Member State for some years after accession. [14] The reason is that the relevant Community law does not attach to those circumstances anything which would have the effect of substituting an authorisation granted in accordance with Article 6 of the Directive or the earlier Community legislation.

35. I consider that the above interpretation of the provisions at issue follows from the second recital in the preamble to Directive 2001/83, which corresponds to the first recital in the preamble to Directive 65/65 and states that 'the essential aim of any rules governing the production, distribution and use of medicinal products must be to safeguard public health'.

36. Therefore, a reference medicinal product may be 'authorised in accordance with Community provisions in force', in particular Article 8 of the Directive, only if it is supported by a complete dossier establishing inter alia that all the requisite tests have been carried out, [15] which it appears is not the case here.

37. The above interpretation of the provisions at issue is also confirmed by the guidelines published by the Commission in *The rules governing medicinal products in the European Community, Volume II: Notice to applicants for marketing authorisations for medicinal products for human use in the Member States of the European Community*, commonly referred to as the Notice to Applicants. [16] In the same way as Advocate General Jacobs, I consider that while the Notice to Applicants lacks legal force in the sense that it is not legally binding, it must be accorded some weight in the interpretation of the directive. [17] The Court has had regard to

14 — Even where, as part of the conditions of its accession, the Member State has transposed into its national law the authorisation provisions of Directive 65/65 (now Directive 2001/83), without any transitional provisions applying in this regard.

15 — In this respect, I agree with the Opinion of Advocate General La Pergola in Case C-94/98 *Rhône-Poulenc Rorer and May & Baker* [1999] ECR I-8789, footnote 26, where he refers to the specific nature of 'a paradoxical product in the sense that although its essential function is clearly therapeutic it may also give rise to pathological conditions if it is defective or misused (see Cadeau, E., and Richeux, J.-Y., "Le Juge Communautaire et le Médicament. Libre Circulation des Marchandises et Protection de la Santé Publique" in *Les Petites Affiches* No 7/1996, p. 4)'.

16 — As Advocate General Jacobs pointed out in his Opinion in Case C-223/01 *AstraZeneca* [2003] ECR I-11809, point 63, '[t]hat guide reflects the consensus of the Member State representatives on the Committee for Proprietary Medicinal Products and the European Agency for the Evaluation of Medicinal Products established by Regulation No 2309/93'.

17 — See his Opinion in Case C-74/03 *SmithKline Beecham* [2005] ECR I-595, point 92. In his Opinion in *Approved Prescription Services*, cited in footnote 8, points 70 to 72, Advocate General Jacobs aptly noted that 'in a technically complex field, it seems reasonable to give careful consideration to a document which represents the harmonised views of the Commission and the competent authorities of the Member States as to how the Community legislation might workably be put into effect. The Directive itself requires that applications be presented in a way which takes account of the Notice … Moreover, the Court has emphasised the importance of ensuring a uniform administration of the marketing authorisation regime across the Member States [referring to *Generics (UK) and Others*, cited in footnote 8, paragraphs 48 and 50]. The Notice to Applicants has an obvious and important role to play in that regard'.

that Notice in its reasoning in a number of judgments. [18]

38. Volume 2A of the Notice to Applicants, entitled Procedures for marketing authorisation, in the version of November 2005 reads as follows: 'reference must be made to the dossier of a reference product for which a marketing authorisation has been granted in the Community on the basis of *a complete dossier in accordance with Articles 8(3)*, 10a, 10b or 10c of Directive 2001/83'. [19]

39. Then, under reference to the Act of Accession of 2003 [20] and, in particular, in relation to existing marketing authorisations of the acceding Member States, the Notice to Applicants states: 'because *they have not been authorised in accordance with the [Community] acquis*, these products, until their marketing authorisations are renewed in compliance with the *acquis*, cannot be used as reference products'. [21] I do not see why a different approach should apply to pre-accession authorisations that existed in the States that acceded to the EU in 1995.

40. Apart from the Notice to Applicants, my interpretation of the provisions at issue is also consistent with guidance issued by the Co-ordination Group for Mutual Recognition and Decentralised Procedures (Human) ('the CMD(h)') established under Article 27 of Directive 2001/83. In that guidance, the CMD(h) addresses the situation with which this case is concerned.

41. It is apparent from the order for reference that, following discussion of the specific case of galantamine, the CMD(h) published a statement on its website (part of the website of Heads of the EU Medicines Agencies) that a medicinal product can be used as a reference medicinal product for the purpose of the data exclusivity period as of the date of accession of the Member State to the EU only if the medicinal product is in compliance with the Community *acquis*. [22]

18 — See *Generics (UK) and Others*, cited in footnote 8, paragraph 28; *AstraZeneca*, cited in footnote 16, paragraph 28; *Novartis Pharmaceuticals*, cited in footnote 8, paragraph 53; *Approved Prescription Services*, cited in footnote 8, paragraph 27; and *SmithKline Beecham*, cited in footnote 17, paragraph 42.

19 — Chapter 1, section 5.3.1. My emphasis.

20 — The Treaty of Accession 2003 of the Czech Republic, Estonia, Cyprus, Latvia, Lithuania, Hungary, Malta, Poland, Slovenia and Slovakia, signed in Athens on 16 April 2003.

21 — My emphasis.

22 — See the CMD(h) Best Practice Guide on the compilation of the dossier for new applications submitted in mutual recognition & decentralised procedures (March 2008), page 2, which also refers to the Frequently Asked Questions on the Community acquis and data exclusivity for the reference product, available at the Heads of Member States Medicines Agencies website: http://www.hma.eu/20.html#ir-faq_2_4b8e8. According to the mission statement, the Heads of Medicines Agencies meet regularly to provide a focus for leadership within the Community System of Medicines Regulation, and to provide a forum for the exchange of views on issues of Community interest.

42. Besides the above guidance, I agree with Shire and Janssen-Cilag that it is possible to infer the importance of a complete dossier of particulars and documents in relation to a reference medicinal product from the judgment in *AstraZeneca* [23] where the Court held that 'in order to be able to grant a marketing authorisation for a generic medicinal product on the basis of the abridged procedure … *what matters is that all the particulars and documents* relating to the reference medicinal product *remain available* to the competent authority for the Member State where the application for the marketing authorisation is made and not that the reference medicinal product has in fact been placed on the market'. [24]

43. In addition, my interpretation of the provisions at issue is also supported by the Swedish MPA's exchange with the competent Austrian authority (the Ministry of Labour, Health and Social Affairs, in particular the Federal Institute for Medicines) in the context of Reminyl's full application of 1999. It is apparent from the documents before the Court that in a fax of 10 February 1999 the Austrian Ministry made clear that the Nivalin 'marketing authorisation was granted before the Austrian regulations, implementing the relevant EC Directives, have come into force [and] an update of this existing authorisation is more or less a complete new assessment of a complete new dossier'.

44. Notwithstanding the fact that in my view the strict rules in the provisions at issue do not allow a different conclusion to be reached to the one I have set out above, in view of the sensitivity of the present subject, I will also deal with certain of Generics's arguments and approaches to interpretation in respect of the provisions at issue, in conjunction with the contents of the question referred.

45. First, as regards the argument according to which Generics is relying on Nivalin's two variations of 1995, introduced after Austria acceded to the EU, Shire and Janssen-Cilag, the United Kingdom Government and the Commission correctly point out that such

23 — Cited in footnote 16, paragraph 27. See also the Opinion of Advocate General Jacobs in that case, point 70: 'the safeguarding of public health … is ensured not by evidence that the reference product is in fact traded but by the comprehensive particulars and documents provided by the applicant for authorisation to market that product pursuant to … Directive 65/65. Those particulars and documents, updated by that applicant in accordance with the Annex to Directive 75/318 … remain available to the competent authority for the Member State where the application for the generic authorisation is made.'

24 — My emphasis. See also Case C-201/94 *Smith & Nephew and Primecrown* [1996] ECR I-5819, paragraph 30, where the Court held that '[t]he discretion enjoyed by the competent authority of the Member State under [Directive 65/65] is very limited. It cannot, on any view, extend to the possibility of issuing a marketing authorisation under Article 3 of Directive 65/65 when the information referred to in Article 4 of that directive has not been supplied in full and the tests referred to therein have not been performed. Such a marketing authorisation may be issued only when it is shown that all the obligations set out in Article 4 have been complied with', referring to Case C-440/93 *Scotia Pharmaceuticals* [1995] ECR I-2851.

variations in and of themselves do not demonstrate that the entire package of data in the dossier for Nivalin conformed with the Community provisions in force. This is because the dossier relating to Nivalin for its original use (treatment of polio) was never updated and brought into compliance with the Community legislation.

46. In that connection, it should be noted that the first question referred mentions that 'the marketing authorisation [for Nivalin] has been varied by adding a new indication, and the variation was considered by the authorities of [Austria] to be consistent with the requirements of Community law'. However, it would appear that at the time there were no Community rules concerning variation of national marketing authorisations that would be applicable in Nivalin's case. [25]

47. Therefore, it follows from the two preceding paragraphs that Nivalin's two variations of 1995 do not assist Generics's case.

48. Secondly, Generics also argues that Nivalin and Reminyl ought to be covered by the same global marketing authorisation in terms of Article 6(1) of the Directive. That provision states, however, that 'any additional strengths, pharmaceutical forms, administration routes, presentations, as well as any variations and extensions shall also be granted an authorisation … or be included in the initial marketing authorisation'; in my view it is clear that such an authorisation would fall to be granted only, in cases involving the same global marketing authorisation, where the initial marketing authorisation (Nivalin) had been granted in accordance with the first subparagraph of Article 6(1) of the Directive. That is not the case here.

49. Thirdly, Generics considers that its interpretation of Article 10(1) is also consistent with the application of Council Regulation (EEC) No 1768/92 concerning the creation of a supplementary protection certificate ['SPC'] for medicinal products [26] (interpreted by the Court in *Novartis and Others* [27]). According to Article 3(b) of that regulation, an authorisation to place the product on the market

25 — Commission Regulation (EC) No 541/95 of 10 March 1995 concerning the examination of variations to the terms of a marketing authorisation granted by a competent authority of a Member State (OJ 1995 L 55, p. 7) essentially applied to medicinal products which had benefited from the procedures of mutual recognition or those which had been authorised following consideration by the Committee for Proprietary Medicinal Products.

26 — Regulation of 18 June 1992 (OJ 1992 L 182, p. 1).

27 — Joined Cases C-207/03 and C-252/03 [2005] ECR I-3209.

granted in accordance with the national legislation of Austria should, for certain purposes, be treated as an authorisation granted in accordance with Directive 65/65.

50. However, I agree with Shire and Janssen-Cilag and the United Kingdom Government that that regulation has entirely different objectives to the Directive, [28] the SPC acting as a kind of extension of the period of patent protection. Furthermore, Regulation No 1768/92 adopts a rule in relation to Austria, Sweden and Finland which is different from the general rule under the Directive. I concur with the United Kingdom Government's analysis: the fact that express provisions were provided for in the regulation so as to deem that a pre-accession authorisation should be considered to be an authorisation in accordance with the Directive merely shows that no such implication can be drawn from the Directive itself, from which such provision is absent.

28 — The objective of that regulation being, in part at least, to compensate pharmaceutical companies for the delay which occurs between filing a patent application and the grant of authorisation to place the product on the market.

51. Fourthly, Generics maintains that it follows from the case-law that the refusal to issue a marketing authorisation for a medicinal product for which the active ingredient is imported from another Member State (in this case, Belgium, where Generics sources galantamine hydrobromide), while that product was issued a marketing authorisation in both the Member State of export (Belgium) and the Member State of import (the United Kingdom), constitutes a restriction on the free movement of goods which is contrary to Article 28 EC. Moreover, such a restriction is not warranted by the protection of public health, because galantamine has been used within Europe for decades and within the EEA since 1994.

52. In that connection, I consider that it is sufficient to point out the following. While according to the second recital in the preamble to the Directive the latter's 'essential aim [is] to safeguard public health', the third recital states that 'this objective must be attained by means which will not hinder the development of the pharmaceutical industry or trade in medicinal products within the Community'. The procedure for mutual recognition is based on mutual confidence between the Member States, which requires the conditions for issuing marketing authorisations of medicinal products to be fully

harmonised by the Community pharmaceutical legislation. [29] That means that the Community provisions, and in this case in particular Article 10 of the Directive, need to be applied strictly and in the way in which I argue above. Otherwise, one would undermine the harmonised system as a whole and, as a result, the free movement of medicinal products within the Community.

53. Having dealt with Generics's arguments, I would like to point out that the interpretation of the provisions at issue I proffer in this Opinion [30] is also supported by a consideration of the relevant legislative history, in particular the original wording of Article 10, before its amendment by Directive 2004/27. Article 10(1)(a)(iii) provided that 'the proprietary medicinal product is essentially similar to a product which has been authorised 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'. [31] I hasten to add that, as has been pointed out by the Commission, no indication can be found that, in enacting Directive 2004/27, the Community legislature intended to alter this aspect of the scheme.

54. To elucidate somewhat on the circumstances in the main proceedings, as noted by Shire and Janssen-Cilag, it may also be pointed out that Article 39(2) of Directive 75/319 required Member States to validate or upgrade old approvals systematically, before they could be considered to be authorisations granted in accordance with Directive 65/65.

55. It is clear from the order for reference that the Austrian Arzneimittelgesetz (Law on medicinal products) of 1983, as amended in 1988, allowed for the continued validity of old authorisations granted under previous national legislation, but did not require formal 'validation' of these authorisations. However, the 1993 amendment to the Arzneimittelgesetz envisaged a review of old authorisations. In respect of such products, the transitional provision envisaged a regulation by the Minister for Health specifying the applicable time limits for the submission of documents. Nonetheless, no regulation was ever issued. [32]

29 — See the Opinion of Advocate General Bot in Case C-452/06 *Synthon* [2008] ECR I-7681, points 65 and 66.

30 — See, in particular, points 28 to 36 above.

31 — My emphasis.

32 — The provision for review of old approvals was subsequently amended in 2004, after the Austrian authorisation for Nivalin had been withdrawn.

56. Furthermore, the issue of pre-existing dossiers that did not conform to the requirements of Article 4 of Directive 65/65 was addressed by the 1993 amendments to that directive. Directive 93/39 added the following subparagraph between the first and second subparagraphs of Article 4 of Directive 65/65: 'in respect of medicinal products authorised on the date of implementation of this Directive, the Member State shall if necessary apply this provision at the time of the five-yearly renewal of the marketing authorisation provided for in Article 10'. In effect, the authorisation holder was obliged to demonstrate at the time of renewal that the authorisation and its dossier conformed to the then current Community requirements for the approval of a medicinal product. This requirement was implemented in Austrian law by the 1993 amendments to the Arzneimittelgesetz. The Nivalin authorisations were, however, never renewed and the dossier was therefore never upgraded to comply with the requirements of Article 4 of Directive 65/65.

57. Finally, while none of Generics's arguments referred to above proved helpful to its case, I consider that one issue may well come to its aid and that is an issue which is referred to in question 1(e), concerning Reminyl. In that part of the question referred, the national court queries whether it would assist Generics if 'a product containing the same active ingredient has subsequently been authorised under Article 6 of Directive 2001/83 and placed on the market in the EC'.

58. In my view, the Commission is undoubtedly correct in its submission that the authorisation of Reminyl in Sweden would indeed enable that product to be used as the reference medicinal product for generic products, but only provided that (the two products are bioequivalent [33] and) the applicable period of protection has expired. While that condition was not fulfilled at the material time, Shire and Janssen-Cilag confirmed at the hearing that the period of exclusivity has already expired in those Member States in which it is protected for six years and will expire in the United Kingdom as well on 1 March 2010.

59. In view of the answer to the first question, there is no need to answer the second question. [34]

33 — On the question when medicinal products are 'essentially similar', see the *Generics* line of case-law, and recently, for instance, *Approved Prescription Services*, cited in footnote 8, at paragraph 17. Two products are bioequivalent to one another when they have the same bioavailability, that is, they are absorbed into the body and transferred to the site of action at the same rate and to the same extent. See the Opinion of Advocate General Jacobs in *Approved Prescription Services*, cited in footnote 8. See also the Opinion of Advocate General Bot in *Synthon*, cited in footnote 29, at footnote 35.

34 — That is also the reason for not presenting the parties' submissions concerning the second question.

IV — Conclusion

60. I am therefore of the opinion that the Court should answer the questions referred by the High Court of Justice of England and Wales (United Kingdom) as follows:

Where a medicinal product falling outside of the scope of the Annex to 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 has been placed on the market in a Member State (Austria) under its national authorisation procedure prior to the accession of that Member State to the European Economic Area (EEA) or the Community and the dossier of the product in question was not updated in accordance with Directive 65/65/EEC (now Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use) after that Member State's accession to the EEA and the Community, that product is not to be considered to be 'a reference medicinal product which is or has been authorised under Article 6 … in a Member State' within the meaning of Article 10(1) of Directive 2001/83.

However, where a product containing the same active ingredient has subsequently been authorised under Article 6 of Directive 2001/83 and placed on the market in the Community, that product may constitute a reference medicinal product for the purposes of Article 10 of Directive 2001/83, provided that the period of protection has expired and the bioequivalence of the generic product with this product has been demonstrated.