JUDGMENT OF THE COURT (First Chamber)

16 October 2008 *

In Case C-452/06,

REFERENCE for a preliminary ruling under Article 234 EC from the High Court of Justice of England and Wales, Queen's Bench Division (Administrative Court), made by decision of 3 November 2006, received at the Court on 9 November 2006, in the proceedings

The Queen, on the application of:

Synthon BV,

v

Licensing Authority of the Department of Health,

* Language of the case: English.

Interested party:

SmithKline Beecham plc,

THE COURT (First Chamber),

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

Advocate General: Y. Bot,
Registrar: J. Swedenborg, Administrator,

having regard to the written procedure and further to the hearing on 25 October 2007,

after considering the observations submitted on behalf of:

— Synthon BV, by G. Barling QC, S. Kon and C. Firth, Solicitors, and S. Ford, Barrister,

— SmithKline Beecham plc, by I. Dodds-Smith and R. Hughes, Solicitors, and J. Stratford, Barrister,

— the United Kingdom Government, by T. Harris and V. Jackson, acting as Agents, and P. Sales QC, and J. Coppel, Barrister,

— the Netherlands Government, by M. de Grave, acting as Agent,

— the Polish Government, by E. Ośniecka-Tamecka, P. Dabrowski and T. Krawczyk, acting as Agents,

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

— the Norwegian Government, by L. Gåseide Røsås and I. Alvik, acting as Agents,

after hearing the Opinion of the Advocate General at the sitting on 10 July 2008,

gives the following

Judgment

1 This reference for a preliminary ruling concerns the interpretation of Article 28 of 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 (OJ 2001 L 311, p. 67).

2 The reference was made in the course of proceedings between Synthon BV ('Synthon'), a company incorporated under Netherlands law operating in the pharmaceutical sector, and the Licensing Authority of the Department of Health of the United Kingdom ('the Licensing Authority') regarding the lawfulness of the decision by which the Licensing Authority refused an application, submitted by Synthon, for mutual recognition of a marketing authorisation of a medicinal product.

Legislative framework

Community legislation

3 Directive 2001/83 codified and assembled 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 were Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to medicinal products (OJ, English Special Edition 1965-1966, p. 20), as amended by Council Directive 93/39/EEC of 14 June 1993 (OJ 2003 L 214, p. 22) ('Directive 65/65'), and Second Council Directive 75/319/EEC of 20 May 1975 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (OJ 1975 147, p. 13), as amended by Commission Directive 2000/38/EC of 5 June 2000 (OJ 2000 L 139, p. 28) ('Directive 75/319').

4 Title III of Directive 2001/83 lays down the conditions and the procedures for placing medicinal products for human use on the market. The conditions which an application for a marketing authorisation must meet are laid down in Chapter 1 of Title III.

5 In that regard, Article 6 of the directive provides:

'1. 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 [('the Member State concerned')] in accordance with this Directive or an authorisation has been granted in accordance with [Council] Regulation (EEC) No 2309/93 [of 22 July 1993 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products (OJ 1993 L 214, p. 1)].

…'

6 Article 8 of Directive 2001/83, reproducing, in essence, Article 4 of Directive 65/65, lays down the conditions connected with the content of an application for marketing authorisation and provides, inter alia:

'1. In order to obtain an authorisation to place a medicinal product on the market regardless of the procedure established by Regulation (EEC) No 2309/93, an application shall be made to the competent authority of the Member State concerned.

…

3. The application shall be accompanied by the following particulars and documents, submitted in accordance with Annex I:

…

(i) Results of:

— physico-chemical, biological or microbiological tests,

— toxicological and pharmacological tests,

— clinical trials.

…'

7 Article 10(1) of Directive 2001/83, replacing, in essence, Article 4.8 of Directive 65/65, provides for the possibility of submitting an abridged application ('the abridged procedure'). It states, inter alia:

'1. In derogation of Article 8(3)(i), and without prejudice to the law relating to the protection of industrial and commercial property:

(a) The applicant shall not be required to provide the results of toxicological and pharmacological tests or the results of clinical trials if he can demonstrate:

…

(iii) … that the medicinal product is essentially similar to a medicinal product which has been authorised [('the reference product')] 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 …'

8 Chapter 4 of Title III of Directive 2001/83 governs the procedure for mutual recognition of marketing authorisations. In particular, Article 28 of that directive, in essence reproducing Article 9 of Directive 75/319, states:

'…

2. In order to obtain the recognition according to the procedures laid down in this Chapter in one or more of the Member States of a marketing authorisation issued by a Member State [('the reference Member State')], the holder of the authorisation shall submit an application to the competent authorities of the Member State or Member States concerned, together with the information and particulars referred to in Articles 8, 10(1) and 11. He shall testify that the dossier is identical to that accepted by the reference Member State, or shall identify any additions or amendments it may contain. … Moreover, he shall certify that all the dossiers filed as part of the procedure are identical.

…

4. Save in the exceptional case provided for in Article 29(1), each Member State shall recognise the marketing authorisation granted by the reference Member State within 90 days of receipt of the application and the assessment report. It shall inform the reference Member State which granted the initial authorisation, the other Member

States concerned by the application, the [European] Agency [for the Evaluation of Medicinal Products], and the marketing authorisation holder.'

9 Article 29 of Directive 2001/83, reproducing, in essence, the wording of Article 10 of Directive 75/319, states:

'1. Where a Member State considers that there are grounds for supposing that the marketing authorisation of the medicinal product concerned may present a risk to public health, it shall forthwith inform the applicant, the reference Member State which granted the initial authorisation, any other Member States concerned by the application and the [European] Agency [for the Evaluation of Medicinal Products]. The Member State shall state its reasons in detail and shall indicate what action may be necessary to correct any defect in the application.

2. All the Member States concerned shall use their best endeavours to reach agreement on the action to be taken in respect of the application. They shall provide the applicant with the opportunity to make his point of view known orally or in writing. However, if the Member States have not reached agreement within the time-limit referred to in Article 28(4) they shall forthwith refer the matter to the Agency with regard to the Committee's reference for the application of the procedure laid down in Article 32.

3. Within the time-limit referred to in Article 28(4), the Member States concerned shall provide the Committee with a detailed statement of the matters on which they have been unable to reach agreement and the reasons for their disagreement. The applicant shall be provided with a copy of this information.

4. As soon as he is informed that the matter has been referred to the Committee, the applicant shall forthwith forward to the Committee a copy of the information and particulars referred to in Article 28(2).'

National legislation

10 Under section 6 of the Medicines Act 1968 and Regulation 2 of the Medicines for Human Use (Marketing Authorisations Etc.) Regulations 1994 ('the 1994 Regulations') the Licensing Authority is the competent authority for the grant of marketing authorisations for medicinal products for human use in the United Kingdom.

11 Regulation 4 of the 1994 Regulations states that '[e]very application for the grant, renewal or variation of a United Kingdom marketing authorisation for a relevant medicinal product shall be made in accordance with the relevant Community provisions, subject to any provision of Community law affecting parallel imports', and that 'the applicant shall comply with so much of the relevant Community provisions as impose obligations on applicants as are applicable to the application or the consideration of it'.

12 Regulation 5 of those regulations provides that the Licensing Authority is to consider every application for the grant of a marketing authorisation in accordance with the relevant Community provisions.

The main proceedings and the questions referred for a preliminary ruling

13 Wishing to obtain a Danish marketing authorisation for Varox, a medicinal product for human use, Synthon submitted an application in accordance with the abridged procedure to the Danish Medicines Agency ('the DMA').

14 With a view to obtaining such authorisation, Synthon had used Seroxat — a medicinal product for which the marketing authorisation was held by SmithKline Beecham plc ('SKB') — as reference product, given that both Seroxat and Varox contain the same active moiety, namely paroxetine. On that basis, the DMA found that the condition of essential similarity between the two medicinal products in question had been met and granted Synthon a marketing authorisation for Varox on 23 October 2000.

15 Synthon made an initial application to the Licensing Authority for mutual recognition of the marketing authorisation for Varox in the United Kingdom in accordance with Article 9 of Directive 75/319. Synthon submitted that application relying on the marketing authorisation for Varox in Denmark which had already been granted by the DMA.

16 By letter of 19 January 2001, the Licensing Authority informed Synthon that it would not accept its application for mutual recognition. That decision was based on the Licensing Authority's general policy pursuant to which medicinal products containing different salts from the same active moiety could not be considered to be essentially similar.

17 On 21 November 2002, Synthon submitted a second application for mutual recognition, on the basis of Article 28 of Directive 2001/83, which the defendant in the main

proceedings again refused to accept on the same grounds. On 28 February 2003, Synthon therefore brought an action before the High Court of Justice of England and Wales, Queen's Bench Division (Administrative Court) seeking annulment of that second decision by the Licensing Authority and claiming damages.

18 In addition, it is apparent from the order for reference that, in the course of 2003, following the amendments made to Annex I to Directive 2001/83 by Commission Directive 2003/63/EC of 25 June 2003 (OJ 2003 L 159, p. 46), the Licensing Authority amended its aforementioned general policy and announced that it would, from then on, accept applications claiming an essential similarity between products containing different salts from the same active moiety.

19 The Court, giving a preliminary ruling on a reference from the Østre Landsret (Denmark) in another dispute between SKB and Synthon concerning the lawfulness of the DMA's decision of 23 October 2000 authorising the marketing of Varox, held, in its judgment of 20 January 2005 in Case C-74/03 *SmithKline Beecham* [2005] ECR I-595, that Article 4.8(a)(iii) of Council Directive 65/65 must be interpreted as not preventing an application for marketing authorisation in respect of a medicinal product from being handled under the abridged procedure under that provision where that product contains the same therapeutic moiety as the reference product but combined with another salt.

20 On the basis of those new factors, Synthon submitted a third application for mutual recognition in April 2005, and on 6 February 2006 the Licensing Authority granted it a marketing authorisation for Varox in the United Kingdom.

21 Synthon nevertheless continued its action against the Licensing Authority's decision of 28 February 2003 in order to obtain a declaratory judgment and an order for damages against the Licensing Authority.

22 In the course of those proceedings, the High Court of Justice of England and Wales, Queen's Bench Division (Administrative Court) decided to stay the proceedings and refer the following questions to the Court for a preliminary ruling:

'(1) Where:

— a Member State ("the concerned Member State") receives an application pursuant to Article 28 of Directive [2001/83] for mutual recognition, in the concerned Member State of a marketing authorisation of a medicinal product ("the Product") granted by another Member State ("the reference Member State");

— such marketing authorisation was granted by the reference Member State pursuant to the abridged application procedure … on the grounds that the Product is essentially similar to another medicinal product which has already been authorised within the EU for the requisite period ("the Reference Product"); and

— the concerned Member State operates a procedure for validation of the application during which it checks that the application contains the particulars and documents required by Articles 8, 10(1)(a)(iii) and 28 of [Directive 2001/83], including that the particulars provided are compatible with the legal basis upon which the application is submitted;

(a) is it compatible with [Directive 2001/83] and in particular Article 28 for the concerned Member State to check that the Product is essentially similar to the Reference Product (without carrying out any substantive assessment), to refuse to accept and review the application and not proceed to recognise the marketing authorisation granted by the reference Member State on the grounds that in its opinion the Product is not essentially similar to the Reference Product, or

(b) is the concerned Member State obliged to recognise the marketing authorisation granted by the reference Member State within 90 days of receipt of the application and the assessment report pursuant to Article 28(4) of [Directive 2001/83] unless the concerned Member State invokes the procedure set out in Articles 29 to 34 of [Directive 2001/83] (which is applicable where there are grounds for supposing that the marketing authorisation of the Product may present a risk to public health within the meaning of Article 29 of [Directive 2001/83])?

(2) If the answer to question 1(a) is no and the answer to question 1(b) is yes, where the concerned Member State rejects the application at the validation stage on the grounds that the Product is not essentially similar to the Reference Product, and thereby fails to recognise the marketing authorisation granted by the reference Member State or to invoke the procedure set out in Articles 29 to 34 of [Directive 2001/83], does the failure by the concerned Member State to recognise the marketing authorisation granted by the reference Member State in the circumstances referred to above amount to a sufficiently serious breach of Community law within the meaning of the second condition in the judgment in Joined Cases C-46/93 and C-48/93 *Brasserie du Pêcheur and Factortame* [[1996] ECR I-1029]? Alternatively, what factors ought the national court to take into consideration when it comes to determine whether such failure amounts to a sufficiently serious breach?

(3) Where the failure of the concerned Member State to recognise the marketing authorisation granted by the reference Member State as set out in question 1 above is based on a general policy adopted by the concerned Member State that

different salts of the same active moiety cannot, as a matter of law, be considered essentially similar, does the failure by the concerned Member State to recognise the marketing authorisation granted by the reference Member State in the circumstances referred to above amount to a sufficiently serious breach of Community law within the meaning of the second condition in the judgment in … *Brasserie du Pêcheur and Factortame*? Alternatively what factors ought the national court to take into consideration when it comes to determine whether such failure amounts to a sufficiently serious breach?'

The first question

23 By its first question, the referring court asks, in essence, whether Article 28 of Directive 2001/83 precludes a Member State to which an application is made for mutual recognition of a marketing authorisation of a medicinal product for human use granted by another Member State under the abridged procedure provided for in Article 10(1)(a)(iii) of that directive from refusing that application on the ground that the medicinal product in question is not essentially similar to the reference product referred to in that marketing authorisation.

24 In order to reply to that question, it is necessary to observe at the outset, that, contrary to the contentions of SKB and the governments of the United Kingdom and Norway, Directive 2001/83 makes no distinction, as to the effect and scope of marketing authorisations, depending on whether they were granted following an ordinary procedure or an abridged procedure.

25 That is particularly true as regards the procedure for mutual recognition established by Article 28 of Directive 2001/83. In accordance with the objective of abolishing all

barriers to the free movement of medicinal products in the Community referred to in recitals 12 and 14 in the preamble to the directive, it is apparent from Article 28(4) that a marketing authorisation granted by a Member State must, in principle, be recognised by the competent authorities in other Member States within 90 days of receipt of the application and the assessment report from the reference Member State, and that that recognition is not dependant on the procedure followed by the reference Member State for granting that authorisation.

26 It must then be pointed out that such an obligation of mutual recognition is strictly delineated by Article 28 of Directive 2001/83.

27 First, an application for mutual recognition must be held to be valid where, in accordance with the requirements of Article 28(2), it is accompanied by the information and particulars referred to in Articles 8, 10(1) and 11 of that directive, the dossier submitted is identical to the dossier accepted by the reference Member State, and any additions or amendments contained in the file have been identified by the applicant.

28 Second, it is clear from the wording of Article 28(4) of Directive 2001/83 that the existence of a risk to public health, within the meaning of Article 29(1) of that directive, constitutes the only ground that a Member State is entitled to rely on to object to the recognition of a marketing authorisation granted by another Member State. In addition, Article 29 provides that a Member State wishing to rely on such a ground is required to comply with a specifically prescribed procedure for provision of information, concerted action, and arbitration.

29 It follows that, as Synthon, the Polish Government and the Commission of the European Communities point out, a Member State to which an application for mutual recognition is made pursuant to Article 28 of Directive 2001/83 cannot call into question, on grounds other than those relating to the risk to public health, the assessments carried out by the reference Member State's authorities in the context of the

procedure for evaluating the medicinal product, such as those concerning essential similarity within the meaning of Article 10(1) of the directive.

30 In the present case, it is sufficient to note, as the Netherlands Government pointed out in its oral submissions, that the Licensing Authority did not indicate in its decision to refuse Synthon's application that the analysis carried out by the DMA, on the essential similarity between Varox and Seroxat, gave grounds for believing that recognition of the marketing authorisation could present a risk to public health. A fortiori, it is not apparent from the case-file that the Licensing Authority initiated the procedure laid down in Article 29 of Directive 2001/83.

31 In those circumstances, it cannot be accepted, as submitted by SKB and the governments of the United Kingdom and Norway, that the Member State in receipt of an application for mutual recognition is entitled — outside of the situation where there is a risk to public health referred to in Article 29 — to carry out a fresh assessment of the data on essential similarity which the reference Member State relied on in accepting an abridged application.

32 As the Advocate General stated in points 100 and 101 of his Opinion, not only would such an interpretation run counter to the very wording of Articles 28 and 29 of Directive 2001/83, but it would render those provisions redundant. If a Member State which was asked to recognise an authorisation already granted by another Member State could make that recognition subject to a second assessment of all or part of the application for authorisation, that would deprive the mutual recognition procedure established by the Community legislature of all meaning and seriously compromise the attainment of the objectives of Directive 2001/83 such as, in particular, the free movement of medicinal products in the internal market, referred to in paragraph 25 above.

33 The reply to the first question must therefore be that Article 28 of Directive 2001/83 precludes a Member State to which an application is made for mutual recognition of

a marketing authorisation of a medicinal product for human use granted by another Member State under the abridged procedure provided for in Article 10(1)(a)(iii) of that directive from refusing that application on the ground that the medicinal product in question is not essentially similar to the reference product.

The second and third questions

34 By its second and third questions, which it is appropriate to examine together, the referring court asks the Court, in essence, whether the failure on the part of a Member State to recognise, pursuant to Article 28 of Directive 2001/83, a marketing authorisation of a medicinal product for human use granted by another Member State under the abridged procedure provided for in Article 10(1)(a)(iii) of that directive, on the ground that the relevant medicinal product either is not essentially similar to the reference product or belongs to a category of medicinal products for which the Member State concerned has a general policy which does not allow it to be considered as essentially similar, constitutes a sufficiently serious breach of Community law, capable of rendering that Member State liable in damages.

35 In that regard, it should be borne in mind that, according to settled case-law (see, inter alia, *Brasserie du Pêcheur and Factortame*, paragraph 51; Case C-5/94 *Hedley Lomas* [1996] ECR I-2553, paragraph 25; and Case C-278/05 *Robins and Others* [2007] ECR I-1053, paragraph 69), for a Member State to incur liability for damage caused to individuals by a breach of Community law it is necessary that:

— the rule of law infringed should be intended to confer rights on individuals;

— the breach should be sufficiently serious;

— there should be a direct causal link between the breach of the obligation incumbent on the State and the damage sustained by the injured parties.

36 Although, in principle, it is for the national courts to determine whether the conditions for State liability for breach of Community law are met, the Court of Justice may nevertheless indicate certain circumstances which the national courts may take into account in their evaluation (Case C-150/99 *Stockholm Lindöpark* [2001] ECR I-493, paragraph 38).

37 As regards the condition requiring a sufficiently serious breach of Community law, on which the referring court asks the Court for a preliminary ruling, the Court has had occasion to make clear that such a breach is established where it implies manifest and grave disregard by the Member State for the limits set on its discretion, the factors to be taken into consideration in this connection being, inter alia, the degree of clarity and precision of the rule infringed and the measure of discretion left by that rule to the national authorities (*Brasserie du Pêcheur and Factortame*, paragraphs 55 and 56, and *Robins and Others*, paragraph 70).

38 If, however, the Member State was not called upon to make any legislative choices and had only considerably reduced, or even no, discretion, the mere infringement of Community law may be sufficient to establish the existence of a sufficiently serious breach (*Hedley Lomas*, paragraph 28, and *Robins and Others*, paragraph 71).

39 It follows that the Member State's discretion, which is broadly dependent on the degree of clarity and precision of the rule infringed, constitutes an important criterion in determining whether there has been a sufficiently serious breach of Community law (see, to that effect, *Robins and Others*, paragraphs 72 and 73).

40 Therefore, it is in the light of the principles set out in the foregoing paragraphs of this judgment that the questions posed by the referring court must be examined.

41 As regards Article 28 of Directive 2001/83, it is apparent from paragraphs 27 to 29 above that that provision confers on the Member State in receipt of an application for mutual recognition only a very limited discretion in relation to the reasons for which that Member State is entitled to refuse to recognise the marketing authorisation in question. In particular, as regards any assessment going beyond the verification of the validity of the application with regard to the conditions laid down in Article 28, the Member State concerned, except where there is a risk to public health, must rely on the assessments and scientific evaluations carried out by the reference Member State.

42 In any event, as has been stated at paragraph 28 above, Article 29 of Directive 2001/83 clearly and precisely precludes any possibility for the Member State to refuse an application for mutual recognition without having first undertaken the procedure provided for in that provision.

43 In those circumstances, a breach of Article 28 of that directive, such as that committed by the Licensing Authority in the main proceedings, is enough to establish a sufficiently serious breach of Community law (see, by analogy, inter alia, *Stockholm Lindöpark*, paragraph 42, and Case C-470/03 *AGM-COS.MET* [2007] ECR I-2749, paragraph 86).

44 No doubt can be cast on that finding by the argument of the United Kingdom Government and the Commission that the concept of an essentially similar medicinal product is complex and has only been clarified by the Court, in respect of the question at issue in the main proceedings, by the decision in *SmithKline Beecham*.

45 As the Advocate General stated in point 130 of his Opinion, even assuming that Article 10(1)(a)(iii) of Directive 2001/83 might be difficult to interpret in relation to that concept in the context of the abridged procedure, the fact remains that that procedure is totally distinct from the mutual recognition procedure at issue in the main proceedings. Therefore, any possible difficulty in the interpretation of that concept has no bearing on the clear and precise nature of the obligations imposed on Member States in the context of the recognition of a marketing authorisation already granted by another Member State applying one of the procedures provided for that purpose in that directive.

46 The reply to the second and third questions must therefore be that the failure on the part of a Member State to recognise, pursuant to Article 28 of Directive 2001/83, a marketing authorisation of a medicinal product for human use granted by another Member State under the abridged procedure provided for in Article 10(1)(a)(iii) of that directive, on the ground that the relevant medicinal product either is not essentially similar to the reference product or belongs to a category of medicinal products for which the Member State concerned has a general policy which does not allow it to be considered as essentially similar, constitutes a sufficiently serious breach of Community law, capable of rendering that Member State liable in damages.

Costs

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

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

1. **Article 28 of 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 precludes a Member State to which an application is made for mutual recognition of a marketing authorisation of a medicinal product for human use granted by another Member State under the abridged procedure provided for in Article 10(1)(a)(iii) of that directive from refusing that application on the ground that the medicinal product in question is not essentially similar to the reference product.**

2. **The failure on the part of a Member State to recognise, pursuant to Article 28 of Directive 2001/83, a marketing authorisation of a medicinal product for human use granted by another Member State under the abridged procedure provided for in Article 10(1)(a)(iii) of that directive, on the ground that the relevant medicinal product either is not essentially similar to the reference product or belongs to a category of medicinal products for which the Member State concerned has a general policy which does not allow it to be considered as essentially similar, constitutes a sufficiently serious breach of Community law, capable of rendering that Member State liable in damages.**

[Signatures]