Reports of Cases

OPINION OF ADVOCATE GENERAL
WAHL
delivered on 20 May 2014[1]

Case C-104/13

AS "Olainfarm"
v
Latvijas Republikas Veselības ministrija
Zāļu valsts aģentūra

(Request for a preliminary ruling from the Augstākās tiesas Senāts (Latvia))

(Industrial policy — Directive 2001/83/EC — Medicinal products for human use — Authorisation to place on the market — Article 10 — Generic medicinal products — Concept of 'reference medicinal product' — Article 10a — Medicinal product based on active substances that have been in well-established medicinal use — Right of the holder of a marketing authorisation for a reference product to challenge the authorisation of a generic)

1. A pharmaceutical company has obtained marketing authorisation for a medicinal product which is based on active substances that have been in well-established medicinal use for at least ten years in the EU (also referred to as a 'well-established medicinal product'). The competent national authorities have subsequently granted a marketing authorisation for a generic which employs that product as its reference product.

2. Can a well-established medicinal product even be employed as a reference product? And furthermore, does the manufacturer of such a reference product enjoy, as a matter of EU law, a right to challenge the decision of the national authorities to register the generic? Those are the questions on which the Augstākās tiesas Senāts (the Supreme Court of the Republic of Latvia) seeks guidance in the present case.

I – **Legal framework**

A – *Directive 2001/83/EC*[2]

3. It follows from recital 2 in the preamble to Directive 2001/83 that the overarching aim of rules governing the production, distribution and use of medicinal products must be to safeguard public health. However, according to recital 3, this objective must nonetheless be reconciled with the need to ensure the development of the pharmaceutical industry and trade in medicinal products within the European Union.

1 — Original language: English.

2 — Directive of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, as amended by Directive 2004/27/EC of 31 March 2004 (OJ 2001 L 311, p. 67).

4. According to recital 9, obtaining authorisation for a medicinal product which is essentially similar to an authorised product must not place innovative firms at a disadvantage. Recital 10 further states that reasons of public policy justify avoiding repetitive tests on humans or animals without overriding cause.

5. Article 6 concerns the authorisation of medicinal products that are to be placed on the market. It provides as follows:

'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 in accordance with this Directive …'

6. Article 8 lays down the conditions for the authorisation of a medicinal product. It states:

'1. In order to obtain an authorisation to place a medicinal product on the market …, 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:

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

— pre-clinical (toxicological and pharmacological) tests,

— clinical trials.'

7. Article 10 concerns the procedure to be followed in relation to the placing on the market of generics. It provides as follows:

'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 medicinal product which is or has been authorised under Article 6 for not less than eight years in the Member State or in the [European Union].

A generic medicinal product authorised pursuant to this provision shall not be placed on the market until ten years have elapsed from the initial authorisation of the reference product.

…

The ten-year period referred to in the second subparagraph shall be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorisation holder obtains an authorisation for one or more new therapeutic indications which, during the scientific evaluation prior to their authorisation, are held to bring a significant clinical benefit in comparison with existing therapies.

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. …

…

5. In addition to the provisions laid down in paragraph 1, where an application is made for a new indication for a well-established substance, a non-cumulative period of one year of data exclusivity shall be granted, provided that significant pre-clinical or clinical studies were carried out in relation to the new indication.'

8. Article 10a provides for derogation from the requirement to submit the results of pre-clinical tests and clinical trials in the context of the authorisation of medicinal products based on well-established active substances. It states:

'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 or clinical trials if he can demonstrate that the active substances of the medicinal product have been in well-established medicinal use within the [European Union] for at least ten years, with recognised efficacy and an acceptable level of safety in terms of the conditions set out in Annex I. In that event, the test and trial results shall be replaced by appropriate scientific literature.'

B – *Latvian law*

9. The derogations set out in Article 10 of Directive 2001/83 have been incorporated into Latvian law by Article 28 of Ministru kabineta 2006.gada 9.maija noteikumu No 376 'Zāļu reģistrēšanas kārtība' (Decree No 376 of the Council of Ministers of 9 May 2006 on the procedure for registration of medicinal products; 'Decree No 376').

10. Article 28 of Decree No 376 provides as follows:

'An applicant for registration shall be authorised not to submit the results of pre-clinical tests or of clinical trials (by way of derogation from the requirements laid down in Article 17(10), without however infringing the provisions relating to the protection of industrial and commercial property), provided that he can demonstrate that:

1. the medicinal products are generics of reference medicinal products which have been registered in one of the Member States of the European Economic Area for at least eight years. When that is the case, registration of the generic medicinal products shall not enter into force until at least 10 years have elapsed since the reference medicinal product was registered in the States of the European Economic Area …;

2. the active substance or substances present in the composition of the medicinal products have been in well-established medicinal use in the composition of medicinal products already registered for at least 10 years in one of the Member States of the European Economic Area

with recognised efficacy and an acceptable level of safety, in accordance with Annex 4 to this decree. When that is the case, the results of tests and research shall be replaced by appropriate scientific literature.'

II – **Facts, procedure and the questions referred**

11. In 2003, AS Olainfarm ('Olainfarm') — a pharmaceutical company established in Latvia — applied for an authorisation to place a medicinal product called 'NEIROMIDIN' on the Latvian market. At that time the Republic of Latvia was not a Member State of the European Union. Thus the medicinal product was authorised under the national legislation then in force. That legislation corresponded only partly to EU-law provisions governing the authorisation of medicinal products.

12. In 2008, following the accession of Latvia to the European Union, Olainfarm applied for and received a marketing authorisation for NEIROMIDIN in accordance with Article 10a of Directive 2001/83 on the grounds that the medicinal product in question was based on active substances that had been in well-established medicinal use for at least ten years within the European Union. In 2011, another Latvian pharmaceutical company, AS Grindeks ('Grindeks'), applied for and received an authorisation to place on the market a generic called 'IPIDAKRINE-GRINDEKS'. In the application, NEIROMIDIN was indicated as the reference product.

13. Seeking annulment of the authorisation of the generic, Olainfarm brought an action before the Latvijas Republikas Veselības ministrija (National Ministry of Health, Latvia) ('the Ministry'). In essence, Olainfarm contended that the documents submitted for the reference medicinal product (that is, NEIROMIDIN) did not satisfy the requirements of EU law. However, the Ministry considered that Olainfarm — being the manufacturer of the reference medicinal product — did not enjoy an individual right to challenge the decision to authorise the generic.

14. To challenge that decision, Olainfarm first brought an action before the Administratīvā rajona tiesa (District Administrative Court), and later brought an appeal before the Administratīvā apgabaltiesa (Regional Administrative Court). Olainfarm justified its interest in bringing an action by the fact that Grindeks had been afforded unfounded advantages to the detriment of Olainfarm which was in the midst of performing lengthy and costly studies with a view to submitting its product for authorisation in accordance with Article 8 of Directive 2001/83 in order to benefit from the ten-year protection period laid down in the directive. Olainfarm also contended that the reference to a 'reference medicinal product' had to be consistent with the definition in Article 10(2)(a) of Directive 2001/83. In that context, Olainfarm considered that that definition was exhaustive and could not be interpreted extensively to include well-established medicinal products. Thus, a product such as NEIROMIDIN could not be employed as a reference medicinal product as such authorisation would be contrary to Article 8 of Directive 2001/83.

15. In the view of both Grindeks and the competent national authorities, the manufacturer of a reference product does not enjoy an individual right to challenge the decision of the Ministry by which the generic is registered. In addition, a medicinal product authorised under Article 10a of Directive 2001/83, could, in their view, serve as a reference medicinal product in the course of the authorisation procedure for generics. According to Grindeks, where the documentation required for the application for authorisation concerning a reference medicinal product has been updated after the accession of a Member State to the European Union, with the result that the authorisation requirements of Directive 2001/83 have been fulfilled, such a medicinal product may be used as reference medicinal product within the meaning of the directive. Grindeks also observed that a previously authorised medicinal product could not — contrary to what Olainfarm suggested — be authorised again and receive further protection. Nor could such a medicinal product benefit from an additional period of protection. What is more, Grindeks considered that the period of data exclusivity

under Article 10(1) of Directive 2001/83 covers only genuinely new substances that are registered for the first time. Therefore, Grindeks had not obtained any advantage in relation to Olainfarm as a consequence of the authorisation of the generic. This was so, in essence, because the period of protection for the data relating to the medicinal products registered by Olainfarm had already expired.

16. In those circumstances, the Augstākās tiesas Senāts decided to stay the proceedings and to refer the following questions to the Court for a preliminary ruling:

‘(1) On a proper construction of Article 10 or of any other provision of Directive 2001/83 has the manufacturer of a reference medicinal product an individual right to bring an action challenging the decision of a competent authority by which a generic medicinal product of another manufacturer of medicinal products was registered, using as the reference medicinal product the product registered by the manufacturer of the reference medicinal product? In other words, does that directive confer on the manufacturer of the reference medicinal product the right to a judicial remedy, the object of which is to determine whether the manufacturer of the generic medicinal product made lawful, well-founded reference to the product registered by the manufacturer of the reference medicinal product, relying on Article 10 of the directive?

(2) If the reply to the first question [is in the] affirmative, on a proper construction of Articles 10 and 10a of the directive, may a medicinal product registered in accordance with Article 10a of the directive as a well-established medicinal product be employed as a reference medicinal product for the purpose of Article 10(2)(a)?’

17. Written observations in the present proceedings have been submitted by Olainfarm and Grindeks, as well as by the Latvian, Estonian, and Italian Governments, and by the Commission, all of which — apart from the Estonian Government — presented oral argument at the hearing on 20 March 2014.

III – **Analysis**

A – *Preliminary issues*

18. In the present case, the referring court asks the Court to clarify the meaning and scope of Directive 2001/83 in relation to market authorisation for generics. In particular, what is at issue is whether a marketing authorisation for a well-established medicinal product affords the holder a right to challenge (the lawfulness of) the authorisation of a generic which has been granted by reference to that medicinal product (the first question referred). In that context, the referring court also wishes to know whether a well-established medicinal product may be employed as a reference medicinal product for the generic (the second question referred).

19. The referring court has framed its second question as being subordinate to the first and only to be answered if the first is answered in the affirmative. While the two questions are inevitably interlinked, the second clearly possesses value of its own. The second question seeks to clarify the meaning of ‘reference medicinal product’ in the context of the directive and should, in my view, be answered irrespective of the conclusion that is reached with regard to the first question. Furthermore, given that the answer to the second question has, in reality, implications for the reply to be given to the first, I will begin my assessment with the second question. Before turning to those questions, however, some preliminary remarks are in order.

20. Given that Directive 2001/83 does not provide a clear-cut answer to either of the two questions referred, it is necessary to look at the objectives underlying the directive. Those objectives — as expressed in recitals 2 and 3 — are essentially twofold. On the one hand, rules governing the production, distribution and use of medicinal products are to aim, first and foremost, at safeguarding public health within the European Union. On the other hand, it must be ensured that achieving the public health objective does not unduly hamper the development of the pharmaceutical industry or trade in medicinal products.

21. In keeping with the overarching objective pertaining to public health, all medicinal products that are placed on the market in a Member State in accordance with Article 6 of Directive 2001/83 must fulfil certain requirements which are specified in Article 8 of the directive. That provision contains the main rule, according to which the manufacturer of the medicinal product in question must prove the safety of the product in question by providing the competent national authorities with results of pre-clinical tests and clinical trials attesting to the safety and efficacy of the product in question.

22. There are, however, several exceptions to that rule. [3]

23. Firstly, under Article 10 of Directive 2001/83, where a manufacturer plans to launch the generic [4] of an already authorised medicinal product (referred to as a 'reference medicinal product' in the directive), it is not necessary to provide the results of such tests and trials when applying for a marketing authorisation. A mere reference to the dossier of the reference product is sufficient.

24. Secondly, a similar simplified procedure — which also omits the phase of clinical tests and trials and allows a mere reference to scientific literature — is provided for in Article 10a of Directive 2001/83. This procedure may be used where the manufacturer of a medicinal product can demonstrate that the active substances of the product have been in 'well-established' medicinal use within the European Union for a considerable period of time (that is, for at least ten years).

25. The rationale for those exceptions is, quite simply, the fact that additional tests and trials would not contribute to ensuring public health to the extent that safety and efficacy has already been proven in relation to the same substances. Depending on which of the above-mentioned simplified procedures is followed, that will be done either by demonstrating that the medicinal product is a generic of a specific reference medicinal product that has been authorised under Article 6 for not less than eight years (Article 10) or, alternatively, by demonstrating that the product is composed of active substances that have been in extensive use for at least ten years (Article 10a). [5] Indeed, given that unnecessary tests on humans and animals are to be avoided as far as possible, conducting repeated tests without any demonstrable benefit to public health would run counter to that public policy objective. [6]

3 — These exceptions are contained in Articles 10, 10a, 10b, and 10c of Directive 2001/83. Given that only the exceptions laid down in Articles 10 and 10a are relevant for the present case, I will consider only those exceptions in the following points.

4 — To qualify as a generic, the medicinal product in question must possess, in accordance with Article 10(2)(b), the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference product. In addition, the generic must be bioequivalent with the reference product. This must be demonstrated by appropriate bioavailability studies.

5 — The documentation that must be provided in relation to applications made under Article 10a is specified in Part II of Annex I to Directive 2001/83. It provides, inter alia, that '[t]he documentation submitted by the applicant should cover all aspects of the safety and/or efficacy assessment and must include or refer to a review of the relevant literature, taking into account pre- and post-marketing studies and published scientific literature concerning experience in the form of epidemiological studies and in particular of comparative epidemiological studies. All documentation, both favourable and unfavourable, must be communicated.'

6 — The legislature's intention that unnecessary tests should be avoided is clearly expressed in recital 10 to Directive 2001/83. See also Case T-321/05 *AstraZeneca* v *Commission* [2010] ECR II-2805, paragraph 666 and case-law cited.

26. However, an important proviso applies here. Recourse to the exception concerning generics in Article 10 of Directive 2001/83 should not place manufacturers that invest in research in order to develop new medicinal products at a competitive disadvantage as compared with companies producing generics. This is confirmed by recital 9 to the directive. To provide an incentive for innovation, a period of exclusivity is granted in Article 10 of Directive 2001/83 to manufacturers who place new medicinal products on the market.

27. Two points must be mentioned. Firstly, the results of pre-clinical tests and clinical trials enjoy special protection during a period of eight years (data exclusivity). It is only after the expiry of those eight years that an application for a marketing authorisation for a generic can be made on the basis of such data. Secondly, once a marketing authorisation has been granted to the generic, it cannot be placed on the market before the expiry of a two-year period (market exclusivity). As a whole, a ten-year protection period (or a maximum of eleven years in the circumstances referred to in Article 10(4) of Directive 2001/83) is granted to the reference product, which is calculated from the time when that product was granted its initial authorisation.

28. Accordingly, any interpretation of the provisions of Directive 2001/83 must strike an adequate balance between the objectives which underlie it (in particular, the need to safeguard public health and the need to promote innovation). Against this background, I will now move on to consider (in reverse order) the questions referred.

B – *Pinning down the meaning of a 'reference medicinal product'*

29. The second question turns on the concept of 'reference medicinal product' within the meaning of Article 10(2)(a) of Directive 2001/83. More particularly, the issue is whether a well-established medicinal product authorised under Article 10a of the directive, such as the one at issue in the main proceedings, may be employed as a reference medicinal product for a generic for which a marketing authorisation is sought under Article 10(1).

30. That question brings to the fore the different ways in which authorisation to place a medicinal product on the market can be obtained under Directive 2001/83. On the one hand, a marketing authorisation may be granted under the more onerous procedure provided for in Article 8 of Directive 2001/83. As mentioned, this procedure requires thorough documentation concerning the results of the pre-clinical tests and clinical trials which are to prove the safety and efficacy of the product concerned. On the other hand, authorisation may be granted through a simplified procedure under Article 10a of the directive (or indeed under Article 10 for generics). To prove the safety and efficacy of a medicinal product, it is sufficient for the purposes of that procedure to demonstrate that the product is composed of active substances that have themselves been in well-established medicinal use within the European Union for at least ten years. Under this scenario, tests and trials are replaced with detailed references to scientific literature, that is, to information already in the public domain.[7]

31. Therefore, the crux of the second question lies in determining whether — account being taken of the public health objective underlying the directive — a well-established medicinal product authorised under Article 10a of Directive 2001/83 can qualify as a reference product for a generic in the same way as a medicinal product which has been authorised under Article 8 and for which the results of relevant tests and trials have been submitted to the competent authorities. In other words, does a medicinal product based on well-established active substances carry the same value in terms of guaranteeing public health given that the safety of the product is guaranteed only 'indirectly'?

7 — See for the criteria of well-established medicinal use, Commission guidelines, *Notice to Applicants. Volume 2A: Procedures for marketing authorisation. Chapter 1. Marketing authorisation*, pp. 33 to 34. Available at: http://ec.europa.eu/health/files/eudralex/vol-2/a/vol2a_chap1_2013-06_en.pdf.

32. I am satisfied that that question can be answered in the affirmative.

33. I am aware of the fact that in defining the meaning of a 'reference medicinal product', Article 10(2)(a) of Directive 2001/83[8] makes express reference only to products authorised under Article 8 of the directive, but not to well-established medicinal products authorised in accordance with Article 10a.

34. However, I see no cogent reason why the use of well-established medicinal products as reference products for generics should not be accepted. This is for the following reasons.

35. As illustrated in point 25 above, both exceptions to Article 8 of Directive 2001/83 — that is, Article 10 for generics and Article 10a for well-established medicinal products — are designed to ensure that unnecessary tests on humans and animals are avoided. Where recourse is had to these procedures, the safety and efficacy of the product for which marketing authorisation is sought can be proven by other means.

36. Let us assume that — as is the case here — a well-established medicinal product authorised under Article 10a of Directive 2001/83 is used as a reference for a generic (that is, instead of a product authorised under Article 8). In such circumstances, the competent authorities would assess the safety and efficacy of the generic on the basis of the file on the well-established medicinal product. More specifically, that assessment would be based on the scientific literature considered to be sufficient in order to prove the safety and efficacy of the active substances on which that product is based. Could this run counter to the public health objective of Directive 2001/83?

37. I do not think so.

38. In fact, by providing for an exception in favour of well-established medicinal products under Directive 2001/83, the EU legislature has clearly accepted that the procedure under Article 10a adequately ensures the attainment of that objective (even without the submission of documentation concerning the results of pre-clinical tests and clinical trials). In such circumstances, I cannot see how the authorisation of a 'copy' (a generic) of such a product could — any more so than the placing on the market of the reference product itself — compromise the attainment of the public health objective underlying Directive 2001/83. On the contrary, allowing such reference to be made ensures that no unnecessary tests on humans or animals are carried out.

39. A further point that should not be overlooked is the content of the Commission guidelines on Procedures for marketing authorisation[9] to which a number of parties have referred in their written observations. Admittedly, these guidelines are not legally binding. As the Court has accepted, the guidelines can nonetheless provide a helpful reference point for a judicial assessment.[10] With regard to the issue at hand, those guidelines state that an application concerning a marketing authorisation for a generic can refer 'to the dossier of a medicinal product for which a marketing authorisation has been granted in the [European Union] in accordance with [A]rticles 8(3), 10a, 10b or 10c of Directive 2001/83'.[11] Indeed, the rationale for also accepting reference to well-established medicinal products is that the authorisation of such a product is based on actual documented use of the substances in question. Accordingly, their safety and efficacy have been verified by the national authorities who have granted the marketing authorisation under Article 10a of Directive 2001/83.

8 — This definition — in tandem with a comprehensive reorganisation of Article 10 of Directive 2001/83 which had originally listed all possible exceptions to the main rule in Article 8 — was introduced by Directive 2004/27.

9 — See footnote 7 above.

10 — See C-223/01 *AstraZeneca* [2003] ECR I-11809, paragraph 28. See also the Opinion of Advocate General Jacobs in Case C-74/03 *SmithKline Beecham* [2004] ECRI-595, point 92, and the Opinion of Advocate General Mazak in Case C-527/07 *Generics (UK)* [2009] ECR I-5259, point 37.

11 — Commission guidelines, *Notice to Applicants*, p. 29, cited in footnote 7 above.

40. Lastly, accepting the use of a well-established medicinal product as a reference product is (albeit implicitly) supported by the Court's judgment in *Generics (UK)*,[12] a case turning on the meaning of 'reference medicinal product'.[13] In that context, the Court held that only medicinal products authorised according to the provisions of Directive 2001/83 may serve as reference medicinal products for generics.[14] It is also particularly significant here that the idea that, as regards the authorisation of generics, Article 10 of Directive 2001/83 could be construed as relaxing the requirements of safety and efficacy arising from the directive was firmly rejected by the Court. In order not to jeopardise the standards of safety and efficacy which medicinal products placed on the market must imperatively satisfy, it was considered to be of paramount importance that all the details and documents concerning the reference medicinal product be available to the competent authority when the application concerning the generic is assessed.[15] The determinative criterion that allows for the departure from the general rule (requiring the results of pre-clinical tests and clinical trials to be provided) under Article 10 for generics is, therefore, that all the details and relevant documentation which demonstrate the safety and efficacy of the reference product must be available to the competent authorities.[16]

41. Applying that reasoning to the present context leads me to the following considerations. For a product to qualify as a reference medicinal product, two cumulative criteria must be fulfilled. Firstly, the reference product must have been granted a marketing authorisation under Directive 2001/83. And secondly, the competent authorities must be able to assess the safety and efficacy of the reference product. As explained above, both criteria are fulfilled also in circumstances where a well-established medicinal product is used as a reference product for a generic.

42. Accordingly, I take the view that a medicinal product registered under Article 10a of Directive 2001/83 may be employed as a reference medicinal product for the purposes of Article 10(2)(a) of the directive.

C – *The right to challenge a decision granting a marketing authorisation for a generic*

43. By its first question the referring court essentially asks whether the holder of a marketing authorisation for a reference product (also referred to as 'the holder') has, as a matter of EU law, the right to challenge the marketing authorisation for a generic which uses that medicinal product as the reference product and, if so, under what circumstances. The question thus turns on whether such a right can be inferred from EU law or whether, instead, this matter remains within the sphere of national law.

44. In my view, such a right can indeed be inferred from Directive 2001/83.

45. What is in dispute in the case before the referring court is not whether Latvian legislation provides for adequate safeguards in order to ensure that individuals enjoy effective procedural guarantees where EU law requires such guarantees to be put in place by the Member States. The issue is rather whether EU law provides for a right that would require Member States to ensure procedural guarantees within

12 — See footnote 10 above.

13 — In that case, at issue was whether or not a product, which had not been authorised in accordance with Directive 2001/83, could nonetheless be employed as a reference product. By reference to the overarching aim of the directive to ensure public health, such a possibility was excluded by the Court. See, in particular, paragraphs 26 and 37 of the judgment.

14 — See *Generics (UK)*, paragraphs 23 and 30. In order for an application for a generic to succeed, the applicant must be able to show that the reference medicinal product was authorised on the basis of EU law in force at the time of the application for marketing authorisation for the reference medicinal product. See also *AstraZeneca*, paragraph 23.

15 — See *Generics (UK)*, paragraphs 23 to 26 and case-law cited.

16 — Ibid., paragraph 27 and case-law cited. In other words, it is only possible to replace an applicant's obligation to provide results of the tests and trials referred to in Article 8(3)(i) of Directive 2001/83 where it can be demonstrated that the medicinal product in question is so similar to the reference medicinal product, which already benefits from marketing authorisation in conformity with EU law, that it does not differ significantly from that product as regards safety and efficacy.

their own legal system. Indeed, as both the Estonian and Italian Governments observe, the Court has previously dealt with cases [17] in which the holder had challenged the legality of the marketing authorisation for a generic of its product in the context of the national authorisation procedure. However, those cases did not expressly touch upon the issue of whether or not such a right could be derived directly from EU law.

46. As explained above, in addition to the public health concerns that are embodied in the provisions of Directive 2001/83 — and in particular Articles 8 and 10 thereof — the other key objective of that directive is to ensure that pharmaceutical companies contributing to innovation are not placed at a disadvantage as compared with the manufacturers of generic products. [18] Bearing this in mind, it is clearly important that adequate safeguards be put in place in order to enable those companies to protect themselves against generic competitors (provided that certain conditions are fulfilled). Seen in this light, an individual right for the holders to challenge the marketing authorisation of competing generics offers a means of doing precisely that.

47. Indeed, as the majority of the parties having submitted observations accept, the granting of an authorisation for a generic potentially affects the manufacturer of the reference medicinal product. However, there is disagreement as to what exactly the protection of commercial interests may entail in this context.

48. As argued by both the Commission and the Italian Government, it seems justified to assume that the placing on the market of a generic will have an impact on sales of the reference product and competitive conditions in its regard. This concern is, as explained in point 27 above, reflected in Article 10 of Directive 2001/83: generics cannot be placed on the market during the ten-year protection period afforded to the reference product in accordance with the second subparagraph of Article 10(1). That provision grants the reference product market exclusivity for ten years starting from the initial authorisation of that product.

49. Against that backdrop, let us assume that the competent national authorities nonetheless grant a marketing authorisation for a generic in circumstances where, for example, there is uncertainty as to whether the product for which authorisation is sought in accordance with Article 10 is in fact the generic of the reference product (or indeed, where doubts arise as to how the ten-year protection period ought to be calculated). If the holder did not have a right to challenge that decision — whatever the grounds invoked [19] — this would, in my view, clearly run counter to the objective of ensuring that no competing generics are placed on the market during the ten-year protection period provided for in Article 10 of Directive 2001/83. Indeed, any other conclusion would substantially limit the practical effect of that protection period. This would, consequently, be contrary to the underlying objective of the directive, that is, to promote innovation.

50. That said, I cannot read into Directive 2001/83 any more far-reaching right that would extend beyond that period of time. Once the ten-year protection period has expired, the holder no longer enjoys market exclusivity and is, accordingly, in the same position as any other third party. In fact, extending the right to challenge a decision to grant a marketing authorisation for a generic beyond the ten-year period expressly provided for in Article 10 of the directive would enable the holder to block the entry into the market of competitors by restricting the use of information already in the public domain.

17 — See, for example, Case C-440/93 *Scotia Pharmaceuticals* [1995] ECR I-2851; *AstraZeneca*; *SmithKline Beecham*; and *Generics (UK)*.

18 — *AstraZeneca* v *Commission*, paragraphs 667 and 668 and case-law cited.

19 — Those grounds can relate to public as well as private interests involved in the grant of a marketing authorisation for the generic.

51. However, one might ask whether the same reasoning applies where, as in the case before the referring court, the reference product is itself based on active substances that have been in well-established medicinal use within the European Union for at least ten years. In other words, does the holder of a marketing authorisation for such a medicinal product have the same right to market exclusivity?

52. I believe this to be the case.

53. Admittedly, it could be argued that no real need to protect the holder would exist in such circumstances. This would be so, in particular, because the development of well-established medicinal products does not require any innovative effort justifying special protection (as compared with products authorised under Article 8). Moreover one could argue — as Grindeks and the Latvian Government do — that the period of data exclusivity under Article 10 of Directive 2001/83 covers only genuinely new substances that are registered for the first time.

54. It is true that where the reference product has been approved under Article 10a of Directive 2001/83, there is no data to be protected and the level of innovation of such products is arguably lower than that of products approved under Article 8. The reason for this is, as illustrated above, that the reference product was approved on the basis of a file containing references to relevant scientific literature and not on the basis of extensive research from which a dossier containing detailed results of pre-clinical tests and clinical trials was compiled (as is the case under Article 8).

55. However, in so far as the use of a well-established medicinal product as a reference product for a generic is accepted as I have suggested above, I am unable to find convincing reasons that would justify not granting the ten-year protection period for these reference products as well. Indeed, the second subparagraph of Article 10(1) of Directive 2001/83 is unequivocal on this point: a ten-year period of market exclusivity is granted to reference products without distinction. [20]

56. It is true, as explained above, that the innovative input of a manufacturer of a well-established medicinal product under Article 10a of Directive 2001/83 is arguably lower than that of a company that has invested heavily in research to obtain a marketing authorisation for a new active substance. Furthermore, under this scenario, the period of data protection for the reference product has expired. From this perspective, the suggestion that the ten-year protection period should nonetheless equally apply to well-established medicinal products may doubtless seem excessive.

57. However, *not* affording market exclusivity (and accordingly, a right to challenge a decision allowing registration of a generic with a view to maintaining exclusivity) for well-established products when they are used as reference products for generics would give an unwarranted competitive advantage to manufacturers of generics who could make unlimited use of the file compiled by the holder. This point was clarified at the hearing: even though a manufacturer such as Grindeks could also apply for a marketing authorisation for its product under Article 10a (and compile the file itself), it is both cheaper and simpler to apply for a marketing authorisation under Article 10 for a generic of a well-established medicinal product. This is so because, as far as generics are concerned, a mere reference to the original file suffices. This undoubtedly saves the manufacturer both time and money.

20 — This is also supported by the Commission guidelines, *Notice for Applicants* (cited in footnote 7 above). See, in particular, p. 43.

58. Most fundamentally perhaps, where a company wishes to manufacture a generic of a medicinal product which has already been authorised, it can be assumed that the holder (irrespective of the procedure under which the reference product was approved) has had a degree of success in marketing that product. Consequently, if ten-year market exclusivity and the right to challenge decisions to allow generics to be placed on the market during that time were not granted to the holder, companies manufacturing generics would be able to benefit from and free ride on the marketing efforts already made in relation to the reference product.

59. Finally, as alluded to above, the protection afforded to a well-established medicinal product can no doubt seem disproportionate here. On the other hand, nothing prevents a manufacturer, such as Grindeks in the present case, from initially submitting an application on the basis of Article 10a for a well-established product, should it wish to avoid the ten-year protection period in question.

60. It is therefore my view that Article 10(1) of Directive 2001/83 must be interpreted as conferring on the holder of a marketing authorisation for a reference medicinal product the right to challenge the marketing authorisation for a generic which uses that medicinal product as the reference product during the ten-year protection period (or, as the case may be, eleven-year period) to which the holder is entitled under that directive.

IV – **Conclusion**

61. In the light of the foregoing I propose that the Court answer the questions referred for a preliminary ruling by the Augstākās tiesas Senāts (Latvia) as follows:

A medicinal product registered in accordance with Article 10a 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, as amended by Directive 2004/27/EC of 31 March 2004, may be employed as a reference medicinal product for the purposes of Article 10(2)(a) of the directive.

Article 10(1) of Directive 2001/83 must be interpreted as conferring on the holder of a marketing authorisation for a reference medicinal product the right to challenge the marketing authorisation for a generic which uses that medicinal product as the reference product during the ten-year protection period (or, as the case may be, eleven-year period) to which the holder is entitled under that directive.