Reports of Cases

OPINION OF ADVOCATE GENERAL
EMILIOU
delivered on 23 October 2025[1]

Case C-118/24

EG Labo Laboratoires Eurogenerics SAS,
Theramex France SAS
v
Agence nationale de sécurité du médicament et des produits de santé (ANSM),
Biogaran SAS,
joined parties:
Eli Lilly Nederland BV,
Lilly France SAS

(Request for a preliminary ruling from the Conseil d'État (Council of State, France))

(Reference for a preliminary ruling – Medicinal products for human use – Marketing authorisation for a generic medicinal product – Authorisation granted following a decentralised and abridged procedure – Biological medicinal product serving as a reference medicinal product for a chemical medicinal product – Directive 2001/83/EC – Jurisdiction of the national courts of a Member State concerned to review the conditions for granting the marketing authorisation)

I. Introduction

1. This case presents the Court with an opportunity to clarify certain aspects of the decentralised procedure for the authorisation of medicinal products. That procedure, governed by Directive 2001/83/EC,[2] allows a medicinal product to be placed on the market in several Member States and may be conducted in a simplified manner, thereby relieving the applicant of the obligation to conduct pre-clinical tests and clinical trials. This is so, in a nutshell, when the product in question meets the conditions of being a generic of a previously authorised medicinal product ('reference medicinal product').

2. The questions referred to the Court by the Conseil d'État (Council of State, France) concern two aspects of that authorisation procedure.

[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 (OJ 2001 L 311, p. 67), as amended.

3. The first aspect relates to the scope of the judicial review that may be exercised, in a Member State, over the (administrative) decision by which a marketing authorisation (MA) is granted. What makes that issue somewhat complex is the fact that, as I will explain in more detail, the decentralised procedure requires the cooperation of the administrative authorities of several Member States; the resulting national MAs are granted only after a common agreement on the medicinal product at issue is reached between those authorities. In the past, that aspect of the decentralised procedure raised questions concerning which courts were competent to review a particular MA issued under that procedure and the scope of such a review. The Court has partly elucidated that matter in its judgment in *Astellas Pharma*[3] and the present case invites it to develop that case-law further.

4. The second issue to be addressed concerns the concept of 'generic medicinal product'. The referring court enquires, specifically, whether the abridged procedure reserved for generics (also known as the 'simplified procedure') may apply to a product under consideration developed by *chemical* synthesis, while the reference medicinal product on which the applicant relies has been obtained *biologically*.

II. Legal framework

5. Recital 2 of Directive 2001/83 states that 'the essential aim of any rules governing the production, distribution and use of medicinal products must be to safeguard public health.'

6. Recital 3 adds that 'however, 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.'

7. Recital 9 of the same directive provides that 'it is advisable to stipulate more precisely the cases in which the results of toxicological and pharmacological tests or clinical trials do not have to be provided with a view to obtaining authorisation for a medicinal product which is essentially similar to an authorised product, while ensuring that innovative firms are not placed at a disadvantage'.

8. Recital 10 of that directive provides that 'there are reasons of public policy for not conducting repetitive tests on humans or animals without over-riding cause'.

9. Article 8(3)(i) of Directive 2001/83 states, in essence, that applications for MAs must be accompanied by the results of pharmaceutical (physico-chemical, biological or microbiological) tests, pre-clinical (toxicological and pharmacological) tests and clinical trials.

10. Article 10 of that directive provides:

'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 a Member State or in the Community.

[3] Judgment of 14 March 2018, *Astellas Pharma* (C-557/16, 'the judgment in *Astellas Pharma*', EU:C:2018:181).

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. The different salts, esters, ethers, isomers, mixtures of isomers, complexes or derivatives of an active substance shall be considered to be the same active substance, unless they differ significantly in properties with regard to safety and/or efficacy. In such cases, additional information providing proof of the safety and/or efficacy of the various salts, esters or derivatives of an authorised active substance must be supplied by the applicant. The various immediate-release oral pharmaceutical forms shall be considered to be one and the same pharmaceutical form. Bioavailability studies need not be required of the applicant if he can demonstrate that the generic medicinal product meets the relevant criteria as defined in the appropriate detailed guidelines.

…

4. Where a biological medicinal product which is similar to a reference biological product does not meet the conditions in the definition of generic medicinal products, owing to, in particular, differences relating to raw materials or differences in manufacturing processes of the biological medicinal product and the reference biological medicinal product, the results of appropriate pre-clinical tests or clinical trials relating to these conditions must be provided. …'

11. Article 28 relating to the mutual recognition and the decentralised procedure reads as follows:

'1. 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.

2. Where the medicinal product has already received a marketing authorisation at the time of application, the concerned Member States shall recognise the marketing authorisation granted by the reference Member State. To this end, the marketing authorisation holder shall request the reference Member State either to prepare an assessment report on the medicinal product or, if necessary, to update any existing assessment report. The reference Member State shall prepare or update the assessment report within 90 days of receipt of a valid application. The assessment report together with the approved summary of product characteristics, labelling and package leaflet shall be sent to the concerned Member States and to the applicant.

3. In cases where the medicinal product has not received a marketing authorisation at the time of application, the applicant shall request the reference Member State to prepare a draft assessment report, a draft summary of product characteristics and a draft of the labelling and package leaflet. The reference Member State shall prepare these draft documents within 120 days after receipt of a valid application and shall send them to the concerned Member States and to the applicant.

4. Within 90 days of receipt of the documents referred to in paragraphs 2 and 3, the Member States concerned shall approve the assessment report, the summary of product characteristics and the labelling and package leaflet and shall inform the reference Member State accordingly. The reference Member State shall record the agreement of all parties, close the procedure and inform the applicant accordingly.

5. Each Member State in which an application has been submitted in accordance with paragraph 1 shall adopt a decision in conformity with the approved assessment report, the summary of product characteristics and the labelling and package leaflet as approved, within 30 days after acknowledgement of the agreement.'

12. Article 29 governs the procedure applicable in cases where, because of a potential serious risk to public health, a Member State is unable to approve the assessment report, the summary of product characteristics, the labelling and the package leaflet within the period laid down in Article 28(4) of Directive 2001/83.

13. Part II.2(b) of Annex I to Directive 2001/83 states 'Applications based upon Article 10(1)(a)(iii) (essentially similar products i.e. generics) [now Article 10(1)] shall contain the data described in Modules 1, 2 and 3 of Part I of this Annex together with data showing bio-availability and bio-equivalence with the original medicinal product provided the latter is not a biological medicinal product (see Part II, 4 Similar biological medicinal products).'

14. Part II.4 of Annex I states: 'The provisions of Article 10(1)(a)(iii) may not be sufficient in the case of biological medicinal products. If the information required in the case of essentially similar products (generics) does not permit the demonstration of the similar nature of two biological medicinal products, additional data, in particular, the toxicological and clinical profile shall be provided.

…'

15. Pursuant to Article 3(3) of Regulation (EC) No 726/2004 (as applicable *ratione temporis*):[4]

'A generic medicinal product of a reference medicinal product authorised by the Community may be authorised by the competent authorities of the Member States in accordance with Directive [2001/83 …] under the following conditions:

(a) the application for authorisation is submitted in accordance with Article 10 of Directive [2001/83 …];

(b) the summary of the product characteristics is in all relevant respects consistent with that of the medicinal product authorised by the Community except for those parts of the summary of product characteristics referring to indications or dosage forms which were still covered by patent law at the time when the generic medicine was marketed; …

…'

III. Facts, procedure and the questions referred

16. On 10 June 2003, the European Commission granted an MA to Eli Lilly Nederland BV ('Lilly Nederland') for Forsteo, a biological medicinal product containing the active substance teriparatide for the treatment of osteoporosis, in the form of a solution for injection (20 micrograms/80 microlitres) in a pre-filled pen.

17. By decisions of 11 January 2017 and 27 August 2020, the Commission granted MAs to EG Labo Laboratoires Eurogenerics SAS ('Laboratoires Eurogenerics') and Theramex France SAS ('Theramex') for two biosimilar versions of Forsteo, namely Movymia and Livogiva. Like Forsteo, those two medicinal products contain the active substance teriparatide, produced from a biological source.

18. On 31 January 2019, Biogaran SAS ('Biogaran') submitted an application for an MA for a medicinal product Tériparatide Biogaran ('the medicinal product at issue in the main proceedings'), presented as a generic version of Forsteo, under Article 10(1) of Directive 2001/83 (which provides for the abridged procedure). Like Forsteo, Tériparatide Biogaran contains the active substance teriparatide in the form of a solution for injection (20 micrograms/80 microlitres) in a pre-filled pen. However, unlike Forsteo, the teriparatide used in Biogaran is derived from a chemical synthesis. That MA application was subject to the decentralised procedure, provided for in Article 28 of Directive 2001/83.

19. In that procedure, Biogaran designated the Federal Republic of Germany as the reference Member State and the French Republic as one of the Member States concerned.

[4] 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). The changes (which are immaterial for the present purposes) made to that provision by Article 1(8), point (b), of Regulation (EU) 2019/5 of the European Parliament and of the Council of 11 December 2018 amending Regulation No 726/2004, Regulation (EC) No 1901/2006 on medicinal products for paediatric use and Directive 2001/83 (OJ 2019 L 4, p. 24) do not seem to apply *ratione temporis*, in the light of Article 5 of the abovementioned amending regulation and given the date when the relevant application for an MA was filed (see point 18 of the present Opinion).

20. On the basis of the general agreement reached in that procedure, by decision of 1 September 2020, the Director-General of the Agence nationale de sécurité du medicament et des produits de santé (National Agency for the Safety of Medicinal Products and Health Products; 'ANSM') granted an MA for Tériparatide Biogaran and recognised it as a generic version of Forsteo.

21. Laboratoires Eurogenerics and Theramex filed an action before the Conseil d'État (Council of State), seeking annulment of that decision.

22. The applicants in the main proceedings ask the Conseil d'État (Council of State) to review whether the conditions laid down in Article 10(1) of Directive 2001/83 for eligibility for the abridged procedure were satisfied with respect to Tériparatide Biogaran in order to determine whether the use of such a procedure entailed a risk to public health. They argue, in essence, that Tériparatide Biogaran has been developed by means of a chemical synthesis, and it cannot therefore be considered as a generic version of Forsteo, which has been obtained biologically.

23. In that context, the referring court has doubts, first, whether it can carry out such a review. It is aware of the clarification that the Court provided in its judgment in *Astellas Pharma* concerning the scope of national judicial review of an MA granted at the end of a decentralised procedure, but explains that the circumstances of the case pending before it differ from those in the case that led to that judgment. [5]

24. Second, that court also entertains doubts as to whether the MA granted for Tériparatide Biogaran has a lawful basis. It notes that it was granted in the context of an abridged procedure reserved for generics. In that respect, it is uncertain whether such a procedure may apply to a *chemical* medicinal product where its reference medicinal product has been obtained *biologically*.

25. In those circumstances, the Conseil d'État (Council of State) decided to stay the proceedings and to refer the following questions to the Court of Justice for a preliminary ruling:

'(1) Should Articles 28 and 29 of Directive [2001/83] be interpreted as meaning that a court of a Member State involved in a decentralised [MA] procedure without being the reference Member State, which has jurisdiction to hear an action brought against that decision granting [an MA] taken by the competent authority of that Member State in accordance with what the Court held in its judgment [in *Astellas Pharma*], is competent, in such a case, to verify that the decentralised procedure was conducted in compliance with the provisions of Directive [2001/83] and that the placing of the medicinal product on the market does not present a potential serious risk to public health within the meaning of Article 29(1) of that directive?

(2) Should Article 10 of Directive [2001/83] be interpreted as meaning that it precludes [an MA] from being granted to a chemical medicinal product in accordance with the simplified procedure laid down in Article 10(1) of that directive where the reference medicinal product is a biological medicinal product?'

26. Laboratoires Eurogenerics, Biogaran, Lilly Nederland and Lilly France SAS (together, 'Lilly'), the French, Estonian and Netherlands Governments and the Commission submitted written observations. Those interested parties, with the exception of the Estonian Government, were represented during the hearing that took place on 7 May 2025.

[5] Due to reasons which I will elaborate on later in the present Opinion.

IV. Assessment

27. First of all, I will start my analysis by making preliminary comments about the applicable regulatory framework and the Court's judgment in *Astellas Pharma* (A). On the basis of those comments, I will then address the first question referred which concerns the scope of the judicial review of the outcome of a decentralised authorisation procedure. I will explain that the applicable rules of EU law do not prevent national courts, like the referring court in the present case, from reviewing whether the medicinal product for which an MA was granted in an abridged procedure has been correctly considered a generic medicinal product within the meaning of Directive 2001/83 (which is one of the conditions for the abridged procedure to apply) (B).

28. Next, I will turn to the second question referred and conclude that the fact that the reference medicinal product relied upon has been obtained biologically while the medicinal product under consideration for the abridged procedure was obtained by chemical synthesis does not, per se, preclude the latter from being considered a generic version of the former. Last, I will close my assessment of the present case with some remarks concerning Article 3(3) of Regulation No 726/2004 which is relevant in order to determine, in essence, whether it was correct for the 'mixed' situation described above to be assessed under a national (decentralised) procedure rather than the centralised procedure (C).

A. Preliminary remarks

29. In this section, I will describe the relevant features of the regulatory context of the decentralised procedure at issue in the main proceedings (1) and comment on the scope of the judicial review, which national courts can conduct, of the outcome of such a procedure, as clarified by the Court (2).

1. The relevant regulatory context

30. In brief, there are two main routes for obtaining an MA for a medicinal product within the European Union. One is a centralised procedure conducted before the EU institutions and governed, in essence, by Regulation No 726/2004. That procedure allows a product to be placed on the market throughout the European Union. For some categories of medicinal products that route is mandatory, such as in the case of the majority of so-called biological medicinal products.[6] That procedure was followed for Forsteo, the (biological) medicinal product relied on as 'reference' medicinal product by Biogaran, when it applied for the MA at issue in the main proceedings (for the medicinal product Tériparatide Biogaran). That procedure was also followed for the two biosimilars of Forsteo marketed by the applicants in the main proceedings.

31. The other main authorisation route consists in a 'horizontal' system governed by Directive 2001/83 in which the Member States' authorities take the relevant decisions to allow the marketing of a specific medicinal product in their territories.[7] That route allows a medicinal product to be placed on the market in one or more Member States.

6 As noted in EMA, 'Biosimilars in the EU – Information guide for healthcare professionals', 2019 ('Biosimilars in the EU – Information guide'), p. 12.

7 See also the first subparagraph of Article 6(1) of Directive 2001/83 under which 'no medicinal product may be placed on the market of a Member State unless [an MA] 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 No 726/2004].' For the description of those authorisation routes as being vertical and horizontal, respectively, see Opinion of Advocate General Bobek in *Astellas Pharma* (C-557/16, 'the Opinion in *Astellas Pharma*', EU:C:2017:957, point 24).

32. Where an applicant wishes to obtain more than one national MA for the same medicinal product, the horizontal route can, in particular, take the form of a decentralised procedure (as is the case in the main proceedings). In short, it is used to obtain more than one national MA when no MA has previously been granted for the same medicinal product in one of the Member States. [8]

33. The legal basis for the decentralised procedure is provided for in Article 28 of Directive 2001/83. [9] Its steps can be described as follows: the applicant submits an application, based on an identical dossier, in the Member States in which it wishes the medicinal product in question to be marketed. Those Member States act as the 'concerned Member States', to use the wording of Directive 2001/83. Moreover, the applicant selects one of those Member States as the 'reference Member State'.

34. The competent authority of the reference Member State has to prepare, within a prescribed period, several documents that serve as the basis for the subsequent decision-making process, namely a draft assessment report, a draft summary of the product characteristics and a draft of the labelling and package leaflet ('the product-related documents'). Once prepared, those documents are sent to the applicant and to the authorities of the Member States concerned to obtain their approval, within a specific time frame. When that approval is granted, the reference Member State acknowledges the general agreement, closes the procedure and informs the applicant accordingly. On that basis, each Member State in which an application under the decentralised procedure has been submitted (that is to say, the reference Member State and all the Member States concerned) adopts a decision which constitutes the actual MA allowing the medicinal product in question to be marketed.

35. However, an agreement on the product-related documents may not immediately be reached where one of the Member States concerned has raised an objection based on the ground of 'potential serious risk to public health' under Article 29 of Directive 2001/83. Such a step triggers a specific procedure set out in that provision. Its purpose is to solve the issues raised so that the entire authorisation procedure can be finalised.

36. To summarise, for a decentralised procedure to result in the grant of an MA for a medicinal product, general agreement on the product-related documents must be reached between the competent authorities of all the Member States involved (including the resolution of any possible objection raised under Article 29 of Directive 2001/83). As a second step, each of the Member States involved must adopt an MA which complies with the general agreement. [10]

37. Moreover, that procedure can take an abridged form which, pursuant to Article 10(1) of Directive 2001/83, relieves the MA applicant of the obligation to conduct two of three categories of tests or trials that would otherwise be required. Indeed, pursuant to Article 8(3)(i) of Directive 2001/83, applications for MAs must (in general) be accompanied by the results of pharmaceutical tests, pre-clinical tests and clinical trials. Article 10(1) of Directive 2001/83 waives the requirement to provide the results of pre-clinical tests and clinical trials (but the results of

[8] In that respect, the decentralised procedure differs from the mutual recognition procedure, which is the other form that the 'horizontal route' can take and which is used for a product whose sponsor has already obtained an MA in one of the Member States and wishes to obtain a new MA in another Member State. See also, Commission, 'Notice to Applicants – Volume 2A – Procedures for marketing authorisation – Chapter 1 – Marketing authorisation', 2019, pp. 17 and 18.

[9] I note that Article 28 of Directive 2001/83 contains elements which are common for the decentralised and mutual recognition procedures, while Article 28(2) thereof is relevant only for the latter procedure. For the sake of simplicity, I will refer to the decentralised procedure as governed by Article 28 of Directive 2001/83.

[10] In other words, the competent authorities that are to adopt the relevant MAs cannot question the outcome of the procedure once it has been closed (see paragraphs 25 and 26 of the judgment in *Astellas Pharma*).

pharmaceutical tests are still required) where the product, in respect of which an MA has been applied for, is a generic of a pre-existing medicinal product, already authorised in one or more Member States of the European Union (which is then considered the reference medicinal product, as already observed). The applicant for an MA for a generic medicinal product may, however, refer to the data relating to such a reference product (stemming from the pre-clinical tests and clinical trials) only after the expiration of the 'data exclusivity period', which is in principle eight years.[11] The *raison d'être* of that period is to reward innovation in the pharmaceutical industry by ensuring that pharmaceutical companies benefit, during a given period of time, from market exclusivity for the specific (new) medicinal product.[12]

38. The composite nature of the decentralised procedure (which comprises two stages, as described above) gave rise to a question concerning which national courts have jurisdiction to verify the legality of an MA resulting from that process and the scope of such a review. That matter was addressed in the judgment in *Astellas Pharma* to which I will now turn.

2. *The judgment in* Astellas Pharma

39. The Court delivered the judgment in *Astellas Pharma* in the context of national proceedings, brought by the holder of an MA for a reference medicinal product, seeking the annulment of the MA granted for a generic medicinal product, on the basis of the alleged miscalculation of the expiry of the data exclusivity period. The dispute arose following the approval of a national MA for a generic medicinal product in Finland, one of the Member States concerned in a decentralised procedure. In that context, the holder of an MA of a reference medicinal product claimed, in essence, that the data exclusivity period had not yet expired. One of the issues that the Court had to determine was whether the MA granted at the end of that procedure could be subject to judicial review in one of the Member States concerned in order for the courts of that Member State to verify, specifically, the correct determination of the data exclusivity period.

40. In answering that question in the affirmative, the Court explained that Directive 2001/83 does not provide for the adoption of any measure that the holder of an MA for a reference medicinal product can challenge, in the context of a decentralised procedure, other than the national MAs issued for the generic in question. Consequently, when the holder of an MA for a reference medicinal product wishes to challenge the outcome of a decentralised procedure and allege miscalculation of the data exclusivity period, it can (only) challenge the national MA granted for the relevant generic medicinal product and can only proceed so before the courts of the Member State whose authorities granted that MA.[13]

41. At the same time, it follows from that judgment that the possibility of taking legal action *must* be made available as a matter of EU law. Indeed, the Court observed that the holder of an MA for a reference medicinal product has a right to ensure the respect of the data exclusivity period by an

[11] Article 10(1) of Directive 2001/83 provides for the '8 + 2 formula', which comprises eight years of data protection (during which the applicant for a generic product cannot cross-refer to the relevant data) and two years of marketing protection during which the generic cannot yet be placed on the market, as was also explained in footnote 9 in point 19 of the Opinion in *Astellas Pharma*. The period of 10 years may be extended to 11 years under the conditions set out in the last sub-paragraph of Article 10(1) of Directive 2001/83.

[12] It was observed that 'the length of the regulatory data protection period and the possibility to resort to the abridged procedure for marketing authorisation reflects a balance that the EU legislature decided to strike between protection of innovative companies and their investment, the general interest in an open market, and the desire to avoid unnecessary testing on animals and humans.' Opinion of Advocate General Bobek in Joined Cases *Novartis Europharm* v *Commission* (C-629/15 P and C-630/15 P, 'the Opinion in *Novartis*', EU:C:2016:1003, point 61). See also recitals 9 and 10 of Directive 2001/83, and judgments of 16 October 2003, *AstraZeneca* (C-223/01, EU:C:2003:546, paragraphs 42 and 43), and of 28 June 2017, *Novartis Europharm* v *Commission* (C-629/15 P and C-630/15 P, EU:C:2017:498, paragraph 78).

[13] The judgment in *Astellas Pharma*, paragraphs 38 and 39.

applicant (for a generic medicinal product) who wishes to rely on the data compiled for that reference medicinal product. The Court explained that that right is derived from Article 10(1) of Directive 2001/83, which sets out the details of that period. The obligation to provide that right with judicial protection, as a matter of EU law, then stems from Article 47 of the Charter of Fundamental Rights of the European Union ('the Charter'). [14]

42. In reaching that conclusion, the Court relied on its previous judgment in *Olainfarm*. [15] In that judgment, the Court confirmed the existence of the right of a holder of an MA for a reference medicinal product to challenge, in a different procedural and factual context, the conditions under which an MA for a generic product was granted (that right, and consequently the holder's standing, had *in casu* been denied by the relevant national authorities).

43. In contrast to the aforementioned judgments, the question regarding the scope of the judicial review is different in the present case.

44. The judgment in *Astellas Pharma* concerned the question whether the national courts could verify the determination of the data exclusivity period. However, in the present case, the referring court is asking whether the scope of judicial review carried out in a Member State (which is involved in a decentralised procedure without being the reference Member State) extends to verifying whether the medicinal product in respect of which an MA has been applied for is a 'generic medicinal product' within the meaning of Directive 2001/83 and, consequently, whether the abridged procedure (which only applies to the authorisation of generic medicinal products) could be lawfully relied on.

45. The answer to the first question referred therefore requires it to be ascertained whether the conclusion reached in the judgement in *Astellas Pharma* – about the national courts' competence to review the determination of the data exclusivity period – extends to cases where judicial review concerns a different question of law.

B. The judicial review at issue in the circumstances in the main proceedings

46. In order to address the question as summarised above (2), it is necessary, first, to clarify a preliminary issue discussed in depth during the hearing. To explain, the findings of the Court in its judgments in *Astellas Pharma*, and previously in *Olainfarm*, concerning access to judicial review, were based on the *right* that the applicants in those cases derived from Directive 2001/83 (right to ensure respect of the data exclusivity period). That led to a discussion, in the present proceedings, as to whether Directive 2001/83 actually allows for the judicial review of the outcome of a decentralised procedure when the applicants do not seek to protect any right arising from it (irrespective of the substantive scope of such judicial review) (1).

1. A preliminary issue: Can there be judicial review in the absence of a right arising from Directive 2001/83?

47. I observe that, contrary to the situation having led to the judgment in *Astellas Pharma*, the applicants in the main proceedings are not holders of the MA for the relevant reference medicinal product. Nor are they holders of the MA the legality of which is at issue in the main proceedings.

[14] *Ibidem*, paragraphs 35 to 38.

[15] Judgment of 23 October 2014, *Olainfarm* (C-104/13, 'the judgment in *Olainfarm*', EU:C:2014:2316, paragraphs 38 to 40).

Rather, they hold two MAs for medicinal products that compete with the medicinal product at issue in the main proceedings (because, as I have already explained, those MAs concern two biosimilars of the same reference product as that relied on for the medicinal product at issue in the main proceedings). [16]

48. The reasons which prompted those applicants to bring proceedings include the economic disadvantage that they claim to have suffered due to the approval of the MA at issue. They refer, in particular, to the conditions provided for in national law concerning the substitutability of the medicinal products at issue which, according to them, means that, in pharmacies, the medicinal product at issue in the main proceedings may substitute its reference medicinal product, while that is not the case as far as the biosimilars that they market are concerned. They claim that that results in unfair competition.

49. In that light, it is admittedly difficult to understand which right under EU law, and more specifically Directive 2001/83, akin to the right derived from Article 10(1) of that directive which is discussed in the judgments in *Astellas Pharma* and in *Olainfarm*, the applicants in the main proceedings would or could seek to protect in the present circumstances. Indeed, the authorisation procedure at issue in the main proceedings concerns primarily Biogaran (as the party who initiated it to obtain an MA for the medicinal product at issue). It also concerns Lilly Nederland as the holder of the MA for the reference medicinal product relied on by Biogaran for the purposes of the abridged procedure.

50. Biogaran and the Commission argue that since there is no right (under EU law) that the applicants in the main proceedings can seek to protect, Directive 2001/83 precludes their access to judicial review. Laboratoires Eurogenerics, Lilly and the French Government take the opposite view, arguing, in essence, that the existence of such a right is not a prerequisite for judicial review to be available.

51. I agree with the second position.

52. It is true that the emphasis put by the Court, in its judgments in *Astellas Pharma* and in *Olainfarm*, on the existence of the applicants' right (derived from Article 10(1) of Directive 2001/83) in reaching its conclusion on access to judicial review may indeed lead one to form the impression that, in the present circumstances, access to the courts is likewise conditioned upon the existence of such a (or other similar) right arising from Directive 2001/83. However, such a conclusion would be misplaced because the relevance of the existence of a right under that directive for the conclusion reached in those judgments has to be assessed in the light of the specific issues addressed by the Court.

53. I recall that, in the judgment in *Olainfarm*, the Court made it clear that Article 10(1) of Directive 2001/83, read in conjunction with Article 47 of the Charter, *precludes* the Member States from barring the holder of an MA for a reference medicinal product from accessing the national courts by denying him or her standing. Similarly, what follows from the judgment in *Astellas Pharma* is that the right to judicial protection cannot be precluded, essentially, by the complexity of the decentralised procedure (namely by the fact that a given national MA constitutes the second step in that procedure, the content of which is predetermined by the general agreement reached by competent bodies of the relevant Member States).

[16] I will turn to the concept of biosimilar medicinal products in more detail later.

54. However, the obligation, under EU law, to ensure the judicial protection of the right referred to above does not mean that the absence of a right arising under EU law automatically precludes the Member States from granting access to the courts, in the context of a decentralised procedure, to parties such as the applicants in the main proceedings. That conclusion could only be reached on the basis of the provisions of Directive 2001/83 or of the inference that some specific aspect of judicial review provided in a given Member State hampers the effectiveness of the decentralised procedure as such.

55. First, Directive 2001/83 is silent on that question. It contains no provision concerning judicial remedies, let alone their nature, which the Member States would be obliged (or only allowed) to put in place in connection with the decisions adopted as a result of the procedures governed by that directive. Consequently, in the absence of rules of EU law on that subject, it is for the Member States, in the framework of their procedural autonomy, to decide on the rules of standing in annulment actions, as the French Government has, in essence, observed. [17]

56. I note that a variety of legitimate interests may exist and be acknowledged in that regard, ranging from economic interests to public health considerations. [18] The French Government explained that the admissibility of the claim in the main proceedings (which appears to be uncontested in those proceedings) is based on the direct and individual effect of the MA at issue on the holders of the MA for the biosimilars in their capacity as competitors of the holder of the MA of the medicinal product at issue in the main proceedings.

57. I fail to identify any reason for considering that such a procedural solution hampers the effectiveness of the authorisation system introduced by Directive 2001/83 and the decentralised procedure in particular. [19]

58. That conclusion remains unaffected by the argument of the Commission calling essentially for coherence of the rules for standing that ought to exist, in its view, within the centralised authorisation procedure, on the one hand, and within 'horizontal' authorisation procedures, on the other. More specifically, the Commission has argued that had the medicinal product at issue in the main proceedings been subject to a centralised procedure under Regulation No 726/2004, the resulting decision could have been challenged before the EU Courts (only) in the context of annulment proceedings under Article 263 TFEU. The Commission further expressed the view that, in such circumstances, the parties, such as the applicants in the main proceedings, would be unlikely to meet the test of direct concern which, inter alia, applies in that context for private parties other than the addressees of the contested act. [20]

59. Without prejudice to the question of *locus standi* under Article 263 TFEU, I certainly acknowledge the difference in the conditions of standing that may appear when both of the main types of authorisation procedure (centralised and national) are compared (depending on the

[17] In the same vein, Advocate General Wahl started his analysis in his Opinion in *Olainfarm* (C-104/13, EU:C:2014:342, point 43) by determining whether the right to challenge the MA granted for a generic could be inferred from EU law or whether that matter remained within the sphere of national law.

[18] I refer, by analogy, to my observations, regarding the term 'legitimate interest' under EU law, in my Opinion in *Nicoventures Trading and Others* v *Commission* (C-731/23 P, EU:C:2025:435, point 30). I explained that that term does not refer to subjective rights *stricto sensu*, but 'corresponds to situations in which EU law guarantees the applicant a freedom (or liberty) or grants him or her a power or an immunity', thus also including economic interests.

[19] That aspect differs, of course, from the question whether the system of the decentralised procedure allows for a national *administrative* review of the outcome of that procedure. The Court addressed that question in the judgment in *Astellas Pharma* (paragraphs 25 to 32), concluding in the negative.

[20] I recall that pursuant to the fourth paragraph of Article 263 TFEU, 'any natural or legal person may … institute proceedings against an act addressed to that person *or which is of direct and individual concern to them* …'. Emphasis added.

national procedural rules under consideration). However, as already observed, the rules of standing governing access to national courts are, in the absence of EU rules, a matter of national law. That may of course lead to discrepancies, but those discrepancies are simply the consequence of the current state of EU law and can, at best, serve as consideration *de lege ferenda* for the European Union legislature's potential future action. By contrast, however laudable the objective of coherence may be, it does not constitute a sufficient reason to limit the Member States' competence in matters in relation to which the EU legislature has not acted so far.

60. To summarise, when, on the one hand, an applicant seeks to enforce a right derived from, in the present context, Directive 2001/83, EU law requires the Member States to provide such an applicant with access to the relevant remedy before the national courts (the right to seek annulment of the MA). When, on the other hand, an applicant does not seek to enforce any right derived from EU law, it is for the Member States to decide whether a right to challenge an MA exists.

61. Having set out those considerations, I will now turn to the first question referred, seeking a clarification of the possible limits to the substantive scope of the judicial review of the outcome of a decentralised procedure.

2. The scope of judicial review

62. By the first question referred, the referring court seeks to clarify whether a court of a Member State involved in a decentralised procedure governed by Articles 28 and 29 of Directive 2001/83, without being the reference Member State, may review whether the decentralised procedure has been conducted in compliance with the provisions of that directive and whether placing the medicinal product at issue on the market presents a potential serious risk to public health, within the meaning of Article 29(1) of that directive.

63. The parties and other interested persons in the present proceedings took rather divergent positions on that matter.

64. On the one hand, Biogaran argues, in essence, that the national judicial review cannot extend beyond the non-scientific elements of the matter, such as the expiry of the data exclusivity period (at issue in the judgment in *Astellas Pharma*).

65. According to the French Government, besides the formal aspects, the national court must also be able to verify whether placing the medicinal product in question on the market constitutes a potential serious risk to public health within the meaning of Article 29 of Directive 2001/83.

66. On the other hand, Laboratoires Eurogenerics, Lilly, the Estonian Government and the Commission take the view that, in essence, the scope of judicial review that can be carried out by the national courts encompasses the conditions for the decentralised procedure to apply (as set out in particular in Article 10 of Directive 2001/83). Laboratoires Eurogenerics states, moreover, that the scope of judicial review extends to all elements of a decentralised procedure that can concern a potential serious risk to public health, within the meaning of Article 29 of Directive 2001/83. By contrast, the Commission takes the view that it could be considered that judicial review regarding that question is excluded given the specific mechanism that Article 29 introduces for the resolution of any such issue.

67. In the light of those diverse positions, I wish to explain the precise issue in relation to which the referring court seeks clarification.

68. Although the first question is couched in general terms (in that it enquires about the possibility to review the compliance of the procedure at issue with the provisions of Directive 2001/83) and although it singles out the possibility to review whether placing the medicinal product on the market presents a potential serious risk to public health, it is clear to me that, as Lilly points out, in essence, the issue before the referring court is narrower and simpler.

69. First, the circumstances of the case reveal that the issue to be clarified is whether the national court can review the application of the concept of a 'generic medicinal product' within a decentralised and abridged procedure in order to determine whether that condition for the application of the abridged procedure has been satisfied. Second, it follows from the order for reference that it is the very eventuality that that may not have been the case that brings about, in the referring court's view, a potential serious risk to public health. Indeed, as previously explained, when an applicant wishes to place on the market a generic medicinal product, he or she does not have to conduct pre-clinical tests and clinical trials, but may instead refer to existing results of such tests and trials relating to the relevant reference medicinal product. Therefore, should it appear that a medicinal product was incorrectly considered a generic, that means that it was placed on the market (at the end of the abridged procedure) while some of the required elements to prove its efficacy and safety were unlawfully omitted.

70. It follows that the question to be clarified is whether Directive 2001/83 allows a national court of a Member State concerned to review the legality of an MA that has been granted for a medicinal product following the conclusion of a decentralised and abridged procedure, inasmuch as it is claimed that the conditions for a medicinal product to be considered a generic medicinal product under Directive 2001/83 were not satisfied.

71. In agreement with Laboratoires Eurogenerics, Lilly, the intervening governments having adopted a position on that matter and the Commission, I consider that that question must be answered in the affirmative.

72. In the same vein as my observations concerning the national rules on *standing* in annulment actions, the silence of the applicable rules of EU law, that is, in the present context, of Articles 28 and 29 of Directive 2001/83, on the matter of judicial remedies to be available to review an MA adopted at the end of a decentralised authorisation procedure means that the *scope* of those remedies comes within the ambit of the procedural autonomy that the Member States are recognised as having in such circumstances. That conclusion applies a fortiori in a case such as the present one, where the applicants do not seek to enforce any specific right derived from EU law (which would render the availability of judicial review mandatory).

73. That position is not affected by the various arguments raised in the present proceedings.

74. *First*, Biogaran puts forward, in essence, a risk of conflicting judgments.

75. To reply to that argument, I have to recall that the Court has made clear in the judgment in *Astellas Pharma* that the applicant may contest (successfully), before the courts of a given Member State, only the MA adopted by the authorities of *the same* Member State. By contrast, it

cannot challenge an MA issued by another Member State.[21] Hence, the judicial review of the outcome of a decentralised procedure must, or can, be available (depending on the circumstances) in each of the Member States involved in a decentralised procedure and may only extend to the MA adopted by the authorities of the given Member State.

76. That admittedly creates a risk of divergent outcomes (regarding whether the validity of different national MAs issued under the same decentralised procedure will be upheld by the courts).[22] It is also true that that risk is greater where national law provides for less stringent conditions in relation to standing. However, that risk is the necessary corollary of the system as currently designed. It cannot serve as an argument that would limit, in the absence of harmonised rules, the competence of the Member States to provide for such rules on standing in annulment actions as they deem necessary (provided, of course, that other more general rules of EU law are complied with).

77. *Second*, I am not convinced by the arguments to the effect, in short, that 'a parallelism' should exist between the scope of administrative review 'inbuilt' in the decentralised procedure and the subsequent judicial review, put forward by the French Government. Administrative review and judicial review are different. The fact that any objection in the framework of the decentralised procedure is limited to the ground of a 'potential serious risk to public health' within the meaning of Article 29 of Directive 2001/83 does not mean that judicial review must have the same scope.[23]

78. Moreover, the Court has made it clear in *Astellas Pharma*, as recalled by Lilly, that the competence of the national authorities in the decentralised procedure is not limited to a consideration of a 'potential serious risk to public health' but extends to verifying that the requisite pre-conditions for the use of the abridged procedure are satisfied.[24]

79. As the Commission points out, there are essentially two such pre-conditions, as set out under Article 10(1) of Directive 2001/83: (i) the expiry of the data exclusivity period and (ii) the existence of a generic medicinal product. Therefore, even if the argument on the 'parallelism' between the scope of administrative review and judicial review (that has to mirror but cannot go beyond the scope of verification by the administrative authorities in the decentralised procedure) were to be accepted, it would lead to the conclusion that access to judicial review should be granted, given that the judicial review applied for, in the main proceedings, concerns the verification of the second of those two pre-conditions.

80. *Third*, I am also not convinced by another argument, put forward by the French Government, to the effect that judicial review should respect the outcome of the decentralised procedure on the grounds of mutual recognition and mutual trust. Without it being necessary to address the question of the extent to which the existing system of the decentralised procedure actually relies on those two principles at the *administrative stage*,[25] I do not think that any such principle imposes any limits on the scope of national judicial review of the outcome of that stage. The technical character of the matters to be determined in the course of the decentralised procedure can certainly imply a lesser degree of intensity of judicial review (which may be limited to

21 The judgment in *Astellas Pharma*, paragraphs 40 and 41.

22 That aspect was analysed in the Opinion in *Astellas Pharma*, points 91 to 109.

23 Irrespective of how the scope of that ground is understood. See, on that issue, the Opinion in *Astellas Pharma*, points 74 and 75.

24 The judgment in *Astellas Pharma*, paragraphs 28 and 29.

25 For a sceptical view on that issue (in the light of the specific features of the decentralised procedure), see the Opinion in *Astellas Pharma*, points 50 to 54.

manifest errors and so on).[26] Nevertheless, it can hardly lead to a conclusion that some of the elements of the administrative decision-making should remain beyond the purview of judicial review.

81. *Fourth*, rather than undermining the effectiveness of the decentralised procedure, judicial review extending to the question at issue here contributes to one of the objectives of Directive 2001/83, that is, public health protection, as the Estonian Government points out. That objective is, pursuant to recital 2 thereof, the 'essential aim' of any rule governing the production, distribution and use of medicinal products.

82. I recall that reliance on the abridged procedure relieves the applicant of the obligation to submit the results of pre-clinical tests and clinical trials. However, as previously stated, if it was wrongly assumed that the medicinal product concerned constitutes a generic of a reference medicinal product, this will lead to a situation where a medicinal product is placed on the market without sufficient pre-clinical and clinical studies. Hence, the possibility for national courts to review whether the concept of a generic medicinal product was correctly applied should further the aim of protecting public health.

83. *Last*, I note that by the first question the referring court also enquires whether such a review may be carried out by the courts of a Member State that has not acted as the *reference* Member State, within the framework of a given decentralised procedure. I understand, as the Netherlands Government observed, that the referring court essentially asks whether judicial review, in the above context, should be reserved to the courts of the reference Member State (given the specific role played by that State in preparing the product-related documents) or whether the courts of the Member States concerned may also be seised in that respect.

84. I consider that the reply to that question follows from the judgment in *Astellas Pharma*.

85. As noted above, the Court, in that judgment, ruled that judicial review (of the determination of the data exclusivity period) should be available in the Member State concerned. At the same time, it excluded the possibility for the same applicant to contest, before the courts of the Member State concerned, an MA granted by the authorities of another Member State.[27] Thus, where an EU right is at stake, judicial review must be available in each of the Member States involved in a given decentralised procedure. A fortiori, where no such right is at stake and where the matter falls within the procedural autonomy of the Member States, Directive 2001/83 does not reserve the possibility of judicial review to the courts of the reference Member State.

86. That examination leads me to conclude that Articles 28 and 29 of Directive 2001/83 must be interpreted as meaning that they do not preclude a court of a Member State, involved in a decentralised marketing authorisation procedure, without being the reference Member State, which has jurisdiction to hear an action brought against the decision granting an MA adopted by the competent authority of that Member State, from verifying whether the medicinal product whose marketing was authorised can be considered a 'generic medicinal product' within the meaning of Article 10(2)(b) of Directive 2001/83.

[26] See, by analogy and in general, on the standard (intensity) of judicial review, my Opinion in *ECB* v *Crédit lyonnais* (C-389/21 P, EU:C:2022:844, points 42 to 45).

[27] The judgment in *Astellas Pharma*, paragraph 40.

87. I will now turn to the question whether that concept may apply to a chemical medicinal product, where the applicant for the abridged procedure relies on a reference medicinal product that was developed biologically.

C. Can a chemical medicinal product be a generic of a biological medicinal product?

88. By its second question, the referring court asks whether the abridged procedure (which is reserved for generics) may apply when the medicinal product in respect of which an MA has been applied for has been obtained by chemical synthesis, while the relevant reference medicinal product has been obtained biologically.

89. I recall that, in the main proceedings, it is argued that the MA granted for the medicinal product at issue relies on an unlawful basis because one of the conditions for the use of the abridged procedure, at the end of which that MA was issued, was not satisfied (given that it is argued that that medicinal product cannot be considered to be a generic of the reference medicinal product relied on). That makes it necessary to set out what differentiates, in general, the chemical and biological medicinal products (1) before assessing whether, in the light of the rules provided for in Directive 2001/83, those differences prevent the abridged procedure from applying to a 'mixed situation' such as the one in the main proceedings (that is a situation that involves a chemical medicinal product presented as a generic of a biological reference medicinal product) (2).

1. Biological versus chemical medicinal products

90. It is worth pointing out that, as Lilly explained at the hearing, medicinal products can generally be divided into those that are obtained by chemical synthesis (chemical medicinal products), on the one hand, and those that are from biological sources, namely biological medicinal products, on the other hand.[28] That said, Directive 2001/83 uses, in principle, the general term 'medicinal product'[29] while singling out (and defining) only the category of 'biological medicinal products' as products 'the active substance of which is a biological substance.'[30]

91. It follows from the discussion in the present proceedings that when compared to products containing chemically produced active substances (sometimes referred to as 'small-molecule' medicines[31]), biological active substances typically consist of larger, more complex molecular structures. More sophisticated methods are required to study their properties for the purpose of obtaining an authorisation for the medicinal products that contain them.[32] Moreover, biological

[28] See, to that effect, EMA, 'Guideline on good pharmacovigilance practices (GVP) – Product- or population-specific considerations II: Biological medicinal products', 4 August 2016, EMA/168402/2014 Corr, p. 5, Section P.II.A.1.

[29] Defined in Article 1(2) of Directive 2001/83 as '(a) any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or (b) [a]ny substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis'.

[30] See Section 3.2.1.1.(b) in Module 3 of Part I of Annex I to that directive. See also Biosimilars in the EU – Information guide, p. 5.

[31] Commission, 'What you need to know about biosimilar medicinal products – Process on corporate responsibility in the field of pharmaceuticals – Access to medicines in Europe – A consensus information document', 2013, pp. 5 and 8 ('Biosimilar medicinal products – A consensus information document').

[32] Biosimilars in the EU – Information guide, p. 6.

substances are manufactured using living organisms, which by definition vary. The resulting biological active substance is therefore often characterised by a certain degree of inherent variability, referred to as 'microheterogeneity'. [33]

92. That term describes, in simple terms, slight changes in the molecular structure, which prevent biological medicinal products from being reproduced identically. [34] Those minor differences may exist within or between batches of the same biological medicinal product. [35] As I understand it, they correspond to an 'impurity' which can, however, be accepted provided that it remains within an acceptable range to ensure constant safety and efficacy of the medicinal product concerned and is, thus, 'not clinically meaningful'. [36]

93. Nevertheless, Lilly observed during the hearing that the microheterogeneity inherent in biological medicinal products may contribute to the tolerability of the medicinal products when administered. While that matter is of course for the experts to determine in each individual case, it seems that microheterogeneity does not, in principle, occur in respect of chemical medicinal products because chemical synthesis can result in the same identical molecule being reproduced, in terms of both its composition and its spatial structure. [37]

94. That said, the discussion during the hearing indicates that that (typical) difference between biological medicinal products and chemical medicinal products may not be relevant in the case in the main proceedings. Indeed, the Netherlands Government observed that the molecule of teriparatide (the active substance at issue in the main proceedings) is homogeneous. Accordingly, in the view of that government, no microheterogeneity occurs and, irrespective of whether teriparatide is obtained by chemical synthesis or by biological process, its molecular structure is the same. That seems to be consistent with Biogaran's observation that teriparatide is a simple biological molecule which can be synthetised by a chemical process. Those elements of the discussion therefore indicate that the case of teriparatide is rather peculiar (which may be the reason why its chemical synthesis was in fact possible). [38]

95. Whether the above description and understanding are correct is, of course, for the referring court to verify. I note that the order for reference does not contain any information to that effect and the referring court's concerns are expressed in general terms, while the inherent variability (in general) of biological medicinal products is referred to in order to describe the argument that the applicants in the main proceedings made before that court.

96. In that light, I will approach the second question referred on the understanding that it asks about the implication of the differences in the manufacturing process on the possibility of applying the abridged procedure to an MA application for a medicinal product presented as a generic that has been produced chemically, where the reference medicinal product relied on is biological (irrespective of any concrete microheterogeneity being observed).

[33] *Ibidem.*

[34] Their variability is exemplified by glycosylated proteins. Those proteins contain sugar or carbohydrate groups attached to the protein backbone, which can differ between individual molecules of the same protein. See Biosimilar medicinal products – A consensus information document, p. 8. For graphic examples, see Biosimilars in the EU – Information guide, p. 6.

[35] See, for a more detailed explanation, Biosimilars in the EU – Information guide, p. 6.

[36] *Ibidem*, pp. 6 and 8.

[37] See, to that effect, Biosimilar medicinal products – Consensus information document, p. 8 et seq.; Biosimilars in the EU – Information guide, p. 10. The Commission observed at the hearing that a slight variability may occur also in the case of chemical medicinal products.

[38] See also Mrozovski, J.-M., 'Tériparatide, l'exception générique des biosimilaires – Teriparatide, the generic exception for biosimilars', *Actualités Pharmaceutiques*, Vol. 61, Issue 617, 2022, pp. 45 and 46.

2. Manufacturing process of the relevant medicinal products and applicability of the abridged procedure

97. To examine the issue summarised above, I will consider the text of the relevant provisions of Directive 2001/83 (a), the context in which they arise (b) and the objectives of Directive 2001/83 (c).

(a) Textual analysis

98. As Biogaran, the French, Netherlands and Estonian Governments and the Commission observe, in essence, the relevant provisions of Directive 2001/83 do not impose any requirement concerning the manufacturing process in which the medicinal products have been obtained and, therefore, as to the nature of the active substance – chemical or biological – that the reference and generic medicinal product must contain for the abridged procedure to apply.

99. First, I recall that according to Article 10(1) of Directive 2001/83, the applicant for the abridged procedure has to 'demonstrate that the medicinal product is a generic of a reference medicinal product', without there being any reference to the manufacturing process for the products involved.

100. Second, the same observation must be made concerning the definition of a 'reference medicinal product' in Article 10(2)(a) of Directive 2001/83, according to which it is a medicinal product authorised under Article 6, in accordance with the provisions of Article 8 of Directive 2001/83. [39]

101. Finally, the same applies in respect of the definition of a 'generic medicinal product', in Article 10(2)(b) of Directive 2001/83, which states that it is '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'. [40]

102. I will address those three components in the order of the complexity that they bring to the present proceedings, starting with the least complex one.

103. As regards, first, the condition relating to *pharmaceutical form*, for the purpose of determining whether the abridged procedure applies, the Court held that account must be taken of the form in which the medicinal product is presented and the form in which it is administered, including its physical form. [41] The above position, in my view, gives no indication that it would exclude the satisfaction of that condition in a 'mixed situation' such as the present one. I also note that there is no claim to the contrary in these proceedings.

[39] I recall that those are general provisions setting out, in short, the conditions under which medicinal products may be placed on the market.

[40] Emphasis added. That provision contains further elements detailing those three main components and I will turn to them in more detail below.

[41] See judgment of 29 April 2004, *Novartis Pharmaceuticals* (C-106/01, EU:C:2004:245, paragraph 40).

104. As regards, second, the condition relating to *bioequivalence*, I note that that condition is considered to be met when the 'generic and the reference medicine release the active substance into the body at the same rate and to the same extent under similar conditions'. [42]

105. Given the above and the general terms in which the condition at issue is expressed ('whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies'), I fail to see any reason, in the law, why that bioequivalence cannot be demonstrated, per se, in a 'mixed' situation such as the present one.

106. I note that Lilly observes that no studies on bioequivalence have been provided by Biogaran on the medicinal product at issue in the main proceedings. On that same point, Biogaran observed that, in the decentralised procedure at issue, it was indeed concluded that the requirement to provide such a study could be waived, due to the parenteral administration of the medicinal product at issue. [43]

107. In that respect, pursuant to the last sentence of Article 10(2)(b) of Directive 2001/83, bioavailability studies indeed need not be required if the applicant 'can demonstrate that the generic medicinal product meets the relevant criteria as defined in the appropriate detailed guidelines'.

108. I observe, further, that pursuant to the relevant guidelines adopted by the European Medicines Agency (EMA), bioequivalence studies are generally not required for medicinal products that are injected, [44] which seems to be the case for the medicinal product at issue. At the same time, the existing EMA guidelines seem to concern either bioequivalence between two chemical products or, in the case of biosimilars, the comparability of two biological medicinal products. [45] A mixed scenario, such as the one in the present case, does not seem to have been explicitly envisaged, as Biogaran also observed.

109. That said, I have already explained that the issue addressed by the referring court in the present case does not concern any circumstances specific to the authorisation procedure at issue, beyond the difference in the manufacturing process of the medicinal products involved. Accordingly, and in the absence of any doubts expressed by the referring court concerning the compatibility of the conditions under which the requirement to provide those studies was (it would seem) waived, that aspect of the case cannot, in my view, be usefully analysed in more detail.

[42] Biosimilars in the EU – Information guide, pp. 11 and 34. EMA, 'Questions and answers on generic medicines', 2012, p. 2. A similar definition, given in the respective soft-law documents authored by the Commission, was referred to in the judgment of 3 December 1998, *Generics (UK) and Others* (C-368/96, 'the judgment in *Generics*', EU:C:1998:583, paragraph 31).

[43] Parenteral drug administration refers to the delivery of medications through routes other than the digestive tract, typically via injection. See Soar, J. and Standing, J., 'Parenteral drug administration', in: *Medication Safety – An Essential Guide*, Courtenay, M. and Griffiths, M. (eds), Cambridge University Press, 2009, pp. 97 to 112.

[44] EMA, 'Guideline on the investigation of bioequivalence', CPMP/EWP/QWP/1401/98 Rev. 1/Corr, 2010, p. 23.

[45] *Ibidem*, p. 4: 'The scope is limited to chemical entities. Recommendation for the comparison of biologicals to reference medicinal products can be found in guidelines on similar biological medicinal products.' See also, to that effect, EMA, 'Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: Non-clinical and clinical issues', EMEA/CHMP/BMWP/42832/2005 Rev1, 2013; EMA, 'Guideline on non-clinical and clinical development of similar biological medicinal products containing low-molecular-weight-heparins', EMEA/CHMP/BMWP/118264/2007 Rev. 1, 2016.

110. Turning, finally, to the condition of *the same qualitative and quantitative composition in active substances*, Laboratoires Eurogenerics and Lilly understand it, in essence, as requiring molecular identity of the active substances which, according to them, is not possible in a mixed situation, such as the present one, because of the differences in the production process and the inherent variability of biological medicinal products.

111. First, as already noted, while inherent variability is a typical feature of biological medicinal products, it may not have occurred in the present case (which, again, is for the referring court to verify).

112. Second, I understand that where it exists, the aforementioned microheterogeneity affects the molecular structure of the biological medicinal product. Because such microheterogeneity will not be present, in principle, in a chemical product, there will be a difference of molecular structure between the products under comparison.

113. Third, I do not think that such a difference precludes the condition of the 'same qualitative and quantitative composition in active substances' being met.

114. In that respect, I note that the Court ruled in the judgment in *SmithKline*[46] that the possibility for the abridged procedure to apply did not require an exact molecular correspondence between active substances of the products at issue, but should rather be based on the therapeutic action of the two medicinal products under comparison.

115. In the judgment *in casu*, the Court concluded that the condition referred to above was met, even though the composition of the active substances of the two products at issue was different in relation to the salts used. The Court relied on the fact that the salt differed with respect to its negative part, which was an inert element and consequently irrelevant for the therapeutic action.[47]

116. I also note that the definition in Article 10(2)(b) of Directive 2001/83 (subsequent to the judgment in that case) contains the clarification that 'the different salts, esters, ethers, isomers, mixtures of isomers, complexes or derivatives of an active substance shall be considered to be the same active substance, unless they differ significantly in properties with regard to safety and/or efficacy.' In such a case, 'additional information providing proof of the safety and/or efficacy of the various salts, esters or derivatives of an authorised active substance must be supplied by the applicant'.

117. As I understand it, a difference in salts, esters, ethers or isomers which, in fact, seems to be relevant, especially for chemically manufactured medicinal products,[48] will lead to differences in the precise molecular structure. Yet, the legislature considers that that does not preclude, in principle, the condition of 'the same qualitative and quantitative composition in active

[46] Judgment of 20 January 2005, *SmithKline Beecham* (C-74/03, 'the judgment in *SmithKline*', EU:C:2005:39).

[47] It is true that Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by Law, Regulation or Administrative Action relating to proprietary medicinal products (OJ, English Special Edition: Series I Volume 1965, p. 20), the legal predecessor of Directive 2001/83 that applied *ratione temporis* to the facts at issue in that judgment, did not contain the concept of 'generic medicinal product' but referred to 'essentially similar product'. However, the Court's conclusion is fully relevant under the current rules because the concept of 'essential similarity' was explained by the Court in its judgment in *Generics* in terms that were subsequently adopted by the legislature to become the first part of the current definition of the 'generic medicinal product' (as regards the conditions related to the active substance, pharmaceutical form and bioequivalence).

[48] See to that effect, EMA, 'Reflection paper on the chemical structure and properties criteria to be considered for the evaluation of new active substance (NAS) status of chemical substances', EMA/CHMP/QWP/104223/2015, 2015, p. 4.

substances' being met. Rather, it is an aspect that may lead to the need for additional proof of the safety and efficacy, but does not preclude a given medicinal product from being considered a generic.

118. That element in my view further indicates that the legislature does not require the generic in respect of which an MA has been applied for and its reference medicinal product to have an identical molecular structure. Hence, a possible difference, should it be established, due to the microheterogeneity of the biological product, relied on as a reference medicinal product, does not automatically preclude the applicability of the abridged procedure in a situation such as the present one.

119. That conclusion is not precluded by certain elements of the relevant normative context. Indeed, in the present proceedings, two specific provisions of Directive 2001/83 have been invoked, to which I will turn next.

(b) Context

120. One of the main reasons why the second question has been referred relates to Article 10(4) of Directive 2001/83. That provision concerns the category of 'biosimilar medicinal products', namely biological products that are similar to an already authorised biological medicinal product. [49]

121. I observe that under that provision 'where a biological medicinal product which is similar to a reference biological product *does not meet the conditions in the definition of generic medicinal products*, owing to, in particular, differences relating to raw materials or differences in manufacturing processes of the biological medicinal product and the reference biological medicinal product, the results of appropriate pre-clinical tests or clinical trials relating to these conditions must be provided' [50] (in view of obtaining an authorisation to place a medicinal product on the market).

122. That provision thus concerns an authorisation mechanism that applies specifically in the case of a biological medicinal product, in respect of which an MA has been applied for that is similar to another reference biological medicinal product. Laboratoires Eurogenerics and Lilly understand that provision to mean that, by contrast, the abridged procedure in Article 10(1) of Directive 2001/83 only applies to chemical medicinal products (acting both as reference and as candidate generic products). It follows, in their view, that a mixed scenario, such as the one in the present case, is excluded from that provision's scope, because the two procedures set out in Article 10(1) and (4) of Directive 2001/83 respectively are mutually exclusive (with the result that the first one can never apply when a proposed generic relies on a reference biological medicinal product).

123. In agreement with the French and Netherlands Governments and the Commission, I disagree with that argument.

[49] As Lilly observes, the introduction of Article 10(4) of Directive 2001/83 by Directive 2004/27 appears to have been a response to the then new development of biosimilars. Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83 (OJ 2004 L 136, p. 34). The first MA for a biosimilar was granted in the European Union in 2006. Biosimilar Medicinal Products – A Consensus Information Document, p. 9 and footnote 11.

[50] Emphasis added.

124. The text of Article 10(4) of Directive 2001/83 runs, in fact, counter to the suggestion made by Laboratoires Eurogenerics and Lilly because it implies that biological medicinal products *may* satisfy the conditions for authorisation as generics of a reference biological medicinal product. Indeed, Article 10(4) is quite clear about the fact that the additional testing and trials to which it refers are required when the proposed biological product 'does not meet the conditions in the definition of generic medicinal products'.

125. Accordingly, rather than excluding the interpretation that the abridged procedure under Article 10(1) of Directive 2001/83 is reserved to chemical products, Article 10(4) of Directive 2001/83 acknowledges the particular difficulty of a biological product in 'copying' – in an identical manner – another biological product, while not excluding that possibility in absolute terms. [51]

126. That position is not affected by Part II.2(b) of Annex I to Directive 2001/83, referred to by Laboratoires Eurogenerics. That provision lists the data to be submitted in an abridged procedure 'provided the [reference medicinal product] is not a biological medicinal product'.

127. Similarly to what I observed in respect of Article 10(4) of Directive 2001/83, that provision of Annex I can hardly be understood as excluding biological medicinal products from being considered reference medicinal products. Indeed, it simply refers the reader to another part of the same annex, which deals with the specific situation of biosimilars, stating that 'if the information required in the case of essentially similar products (generics) does not permit the demonstration of the similar nature of two biological medicinal products, additional data, in particular, the toxicological and clinical profile shall be provided.'

128. In summary, the special procedure for biosimilars was established to respond to the specific nature of biological medicinal products, where the proposed medicinal product does not usually meet the conditions set out in Article 10(1) of Directive 2001/83 due to the intrinsic variabilities of molecular structure. However, this was not meant to exclude, in an absolute manner, the possibility that a biological medicinal product could act as reference medicinal product in the abridged procedure.

129. Moreover, that conclusion may also be seen to confirm my previous finding that the abridged procedure does not presuppose the molecular identity of the medicinal products concerned. Indeed, I have already explained that biological products are typically characterised by slight variations in their molecular structure, which may occur even between or within the batches of a given medicinal product and therefore, as I understand it, between a given biological medicinal product and its biosimilar. Yet, that fact did not lead to the authorisation of those products to be confined to the procedure set out in Article 10(4) of Directive 2001/83. If the possibility of such molecular variations does not preclude the abridged procedure set out in Article 10(1) of that directive from applying under those circumstances, it is difficult to see why it should be otherwise in a mixed situation such as the present one.

[51] Recital 15 of Directive 2004/27, which amended Directive 2001/83 to introduce both provisions discussed here (Article 10(1) and (4)), states that 'biological medicinal products similar to a reference medicinal product *do not usually* meet all the conditions to be considered as a generic medicinal product mainly due to manufacturing process characteristics, raw materials used, molecular characteristics and therapeutic modes of action. …' Emphasis added. That statement seems to reflect the discussion held on that matter during the legislative process in which the idea of a blanket exclusion of biological products from the abridged procedure was rejected. See, in particular, Amended proposal for a directive of the European Parliament and of the Council amending Directive [2001/83], COM(2003) 163 final, pp. 19 to 21.

130. Irrespective of the latter point, the conclusion that the abridged procedure may apply to a mixed situation, such as the present one, is supported by the objectives pursued by Directive 2001/83.

(c) Consideration of the objectives pursued by Directive 2001/83

131. *First*, in establishing a harmonised framework for the authorisation of medicinal products for human use on the European market, Directive 2001/83 pursues, in particular, the essential aim of safeguarding public health (referred to in recital 2 thereof).

132. It is with that in mind that the Court held, in its judgment in *Generics*, that the (then applicable) conditions governing the use of the abridged procedure aimed at guaranteeing that there would not be a significant difference between the reference medicinal product and the proposed generic medicinal product (then designated as an 'essentially similar product'), in terms of safety and efficacy. [52] It is also that overarching aim that led the Court in that judgment to conclude, in essence, that the absence of a significant difference in terms of safety and efficacy was to be verified through the criteria of the same composition in active substances, pharmaceutical form and bioequivalence (which were later adopted by the legislature in the current Article 10(2)(b) of Directive 2001/83). [53]

133. Thus, contrary to what is argued, in essence, by Laboratoires Eurogenerics and Lilly, the conclusion that the abridged procedure may apply in circumstances such as the present one does not hamper the aim of safeguarding public health because, irrespective of the manufacturing process involved and of the chemical or biological nature of the products at issue, the condition relating to safety and efficacy of the proposed product will be examined under the three criteria referred to above.

134. I have already explained that those criteria do not refer to the manufacturing process or the nature (chemical or biological) of the resulting medicinal products. Those aspects are therefore not decisive per se in determining whether a medicinal product can be considered a generic of a given reference medicinal product. It is my view that only the characteristics of the proposed medicinal product, once tested under the criteria referred to above, may lead to the conclusion that its safety and efficacy is not comparable to the safety and efficacy of the reference medicinal product, with the result that the applicant will not be allowed to rely on the results of pre-clinical tests and clinical trials obtained in respect of the latter.

135. *Second*, Directive 2001/83 also aims at avoiding any obstacles to the development of the pharmaceutical industry and trade in medicinal products within the European Union. [54]

136. Laboratoires Eurogenerics and Lilly argue that allowing the abridged procedure to apply in a mixed situation, such as the present one, would go against that objective.

137. I disagree.

[52] The judgments in *Generics*, paragraph 36, and in *SmithKline*, paragraph 39.

[53] For the description of the evolution of the legal framework see, in particular, Opinion of Advocate General Ruiz-Jarabo Colomer in *Generics (UK) and Others* (C-368/96, EU:C:1998:21, points 5 to 8), or of Advocate General Jacobs in *SmithKline Beecham* (C-74/03, EU:C:2004:541, points 5 to 11).

[54] See recitals 2 and 3 of Directive 2001/83.

138. It is undeniable that the development of new medicinal products takes many years and involves a lot of scientific research and investment. Directive 2011/83 rewards those innovation efforts by means of the exclusive data period, which I have discussed in the context of the first question referred. Indeed, the use of the abridged procedure and the possibility for the applicant for an MA for a generic to rely on the relevant data, gathered in respect of a previously authorised product, is possible only once that period has expired (without prejudice to the law relating to the protection of industrial and commercial property).

139. *Third*, the possibility of resorting to the abridged procedure reflects a balance that the EU legislature decided to strike between the protection of innovative companies and their investments, the general interest in an open market, and the desire to avoid unnecessary testing on animals and humans,[55] which are also objectives of the regulatory framework under Directive 2001/83. A balanced approach to the attainment of those aims implies that, once the data exclusivity period has expired, the rationale of the applicable rules stemming therefrom shifts in principle from the objective of rewarding the research to the other two abovementioned objectives (that is, ensuring an open market and avoiding unnecessary testing on animals and humans).

140. Allowing a chemical generic of a biological medicinal product to be placed on the market, following an abridged procedure, where all the applicable conditions are met, fosters the promotion of both of those objectives. Indeed, it relieves the applicants of the requirement to conduct tests, where the relevant data can be relied on to draw the necessary conclusions concerning the safety and efficacy of the proposed product. Furthermore, it provides patients (and State social security systems) with a cheaper alternative. By contrast, preventing the MA of a chemical generic despite the fact that all the applicable conditions are met would mean that the achievement of the objectives referred to above would be hampered. Indeed, the applicant will be required to conduct pre-clinical tests and clinical trials *de novo*, which could either result in depriving the market of an alternative product or would negatively affect its price.

141. The last question for me to examine is whether the mixed scenario *in casu* could have been lawfully assessed in the national (decentralised) procedure, rather than in the centralised one. In that connection, I will now turn to Article 3(3) of Regulation No 726/2004.

D. Article 3(3) of Regulation No 726/2004

142. I recall that Forsteo, the reference medicinal product of Biogaran Tériparatide, has been authorised under the centralised authorisation procedure. That brings into play Article 3(3) of Regulation No 726/2004, to which the referring court draws attention and pursuant to which a generic of such a product may be authorised by the competent authorities of the Member States, in accordance with Directive 2001/83. That is, however, only the case, when, in particular, the application for authorisation is submitted in accordance with Article 10 of that directive and when, under Article 3(3)(b) of Regulation No 726/2004, 'the summary of the product characteristics is *in all relevant respects consistent* with that of the medicinal product authorised by the [Union …].'[56]

[55] The Opinion in *Novartis*, point 61. Pursuant to recital 10 of Directive 2001/83, 'there are reasons of public policy for not conducting repetitive tests on humans or animals without over-riding cause'. Also, pursuant to recital 14 of Directive 2004/27 (which amended the provisions of Directive 2001/83 of relevance here), 'since generic medicines account for a major part of the market in medicinal products, their access to the Community market should be facilitated in the light of the experience acquired.'

[56] Emphasis added.

143. Lilly relies on Article 3(3)(b) of that regulation to argue, in essence, that the second condition was not satisfied because such summaries have to be identical, including as regards the manufacturing process. Because that condition was not (and could not be) met, that party argues that the MA for the medicinal product at issue in the main proceedings was wrongly granted under a decentralised procedure and should have been subject to a centralised one.

144. I note, first, that the summary of the product characteristics ('the SmPC') is 'a document describing the properties and the officially approved conditions of use of a medicine.' [57] It provides 'the basis of information for healthcare professionals on how to use the medicine safely and effectively'. [58] It should be submitted together with the application for the MA [59] and the competent authority adopts a position on it. Thus, that document 'forms an intrinsic and integral part of the [MA]'. [60]

145. Its mandatory components are defined in Article 11 of Directive 2001/83 and include, in particular, pursuant to paragraph 2 of that provision, the 'qualitative and quantitative composition in terms of the active substances and constituents of the excipient, knowledge of which is essential for proper administration of the medicinal product. …'.

146. It is true that, according to the relevant guideline, in the case of biological medicinal products, the SmPC shall indicate the biological origin of the active substance, namely 'the nature of any cellular system(s) used for production and, if relevant, the use of recombinant DNA technology should be specified'. [61] Such information cannot be provided, by definition, for the relevant chemical 'copy' of such a product.

147. However, Article 3(3)(b) of Regulation No 726/2004 provides that the SmPC has to be 'in all relevant respects consistent', and not identical. Where, in the assessment process, the difference in the manufacturing process and, therefore, the resulting difference in the nature of the product (chemical versus biological) are found not to have any bearing on the efficacy and safety of the proposed generic medicinal product, I do not see how that difference may lead to the conclusion that the SmPC of such a generic medicinal product is not 'in all relevant respects consistent' with the SmPC of its reference biological medicinal product. Hence, I take the view that Article 3(3)(b) of Regulation No 726/2004 does not affect the conclusion that I have reached previously.

148. In the light of the foregoing, I am of the view that Article 10(2)(b) of Directive 2001/83 must be interpreted as meaning that it does not preclude an MA from being granted for a chemical medicinal product, in accordance with the abridged procedure laid down in Article 10(1) of that directive, where the reference medicinal product is a biological medicinal product, provided that the conditions under which the former can be considered a generic of the latter laid down in Article 10(2)(b) of Directive 2001/83 are satisfied.

[57] See the definition of that term in the glossary developed by the EMA, available at https://www.ema.europa.eu/en/glossary-terms/summary-product-characteristics.

[58] *Ibidem* and European Commission, 'Notice to Applicants – A guideline on summary of products characteristics (SmPC)', September 2009 ('Notice to Applicants – A guideline on SmPC'), p. 2.

[59] See Article 8(3)(j) and Article 11 of Directive 2001/83 and Article 6(1) and Article 10 of Regulation No 726/2004.

[60] Notice to Applicants – A guideline on SmPC, p. 2.

[61] *Ibidem*, p. 6.

V. Conclusion

149. In the light of all the foregoing considerations, I propose that the Court answer the questions referred by the Conseil d'État (Council of State, France) as follows:

(1) Articles 28 and 29 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

must be interpreted as meaning that they do not preclude a court of a Member State, involved in a decentralised marketing authorisation procedure, without being the reference Member State, which has jurisdiction to hear an action brought against the decision granting a marketing authorisation adopted by the competent authority of that Member State, from verifying whether the medicinal product whose marketing was authorised can be considered a 'generic medicinal product' within the meaning of Article 10(2)(b) of Directive 2001/83.

(2) Article 10(2)(b) of Directive 2001/83

must be interpreted as meaning that it does not preclude a marketing authorisation from being granted for a chemical medicinal product, in accordance with the abridged procedure laid down in Article 10(1) of that directive, where the reference medicinal product is a biological medicinal product, provided that the conditions under which the former can be considered a generic of the latter laid down in Article 10(2)(b) of Directive 2001/83 are satisfied.