Court of Justice EU, 6 September 2012, Kreussler v Sunstar

v

PHARMACEUTICAL LAW

Interpretation of 'pharmacological action' in Pharma Directive on the basis of guidance document

- **that Article 1(2)(b) of Directive 2001/83 must be interpreted as meaning that, for the purpose of defining the term 'pharmacological action' within the meaning of that provision, account may be taken of the definition of that term in the guidance document on the demarcation between the Cosmetic Products Directive and the Medicinal Products Directive.**

Pharmacological action: interaction between substance and cellular constituent within user's body is sufficient; interaction on molecular level not necessary

- **that, for a substance to be regarded as exerting a 'pharmacological action' within the meaning of that provision, it is not necessary for there to be an interaction between the molecules of which it consists and a cellular constituent of the user's body, as an interaction between that substance and any cellular constituent present within the user's body may be sufficient.**

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Court of Justice EU, 6 September 2012

(M. Safjan, A. Borg Barthet (Rapporteur) and M. Ilešič)

JUDGMENT OF THE COURT (Fifth Chamber)

6 September 2012 (*)

(Directive 2001/83/EC – Medicinal products for human use – Article 1(2)(b) – Meaning of 'medicinal product by function' – Definition of the term 'pharmacological action')

In Case C-308/11,

REFERENCE for a preliminary ruling under Article 267 TFEU from the Oberlandesgericht Frankfurt am Main (Germany), made by decision of 14 June 2011, received at the Court on 20 June 2011, in the proceedings

Chemische Fabrik Kreussler & Co. GmbH

v

Sunstar Deutschland GmbH, formerly John O. Butler GmbH,

THE COURT (Fifth Chamber),

composed of M. Safjan, President of the Chamber, A. Borg Barthet (Rapporteur) and M. Ilešič, Judges, Advocate General: N. Jääskinen, Registrar: A. Impellizzeri, Administrator, having regard to the written procedure and further to the hearing on 26 April 2012,

after considering the observations submitted on behalf of:

– Chemische Fabrik Kreussler & Co. GmbH, by U. Grundmann, Rechtsanwalt,

– Sunstar Deutschland GmbH, by C. Krüger and M. Runge, Rechtsanwälte,

– the Belgian Government, by T. Materne, acting as Agent,

– the Czech Government, by D. Hadroušek, acting as Agent,

– the Polish Government, by M. Szpunar, acting as Agent,

– the Portuguese Government, by L. Inez Fernandes and P.A. Antunes, acting as Agents,

– the United Kingdom Government, by H. Walker, acting as Agent,

– the European Commission, by M. Šimerdová and B.-R. Killmann, acting as Agents,

having decided, after hearing the Advocate General, to proceed to judgment without an Opinion,

gives the following

Judgment

1 This reference for a preliminary ruling concerns the interpretation of Article 1(2)(b) of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code

relating to medicinal products for human use (OJ 2001 L 311, p. 67), as amended by Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 (OJ 2004 L 136, p. 34) ('Directive 2001/83').

2 The reference has been made in proceedings between Chemische Fabrik Kreussler & Co. GmbH ('Chemische Fabrik Kreussler') and Sunstar Deutschland GmbH, formerly John O. Butler GmbH ('John O. Butler'), concerning the classification of a mouthwash solution called 'PAROEX 0,12%', which is marketed in German territory.

Legal context

European Union law

Directive 2001/83

3 Under Article 1(2)(b) of Directive 2001/83, 'medicinal product' means:

'any 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.'

Directive 76/768/EEC

4 Under Article 1(1) of Council Directive 76/768/EEC of 27 July 1976 on the approximation of the laws of the Member States relating to cosmetic products (OJ 1976 L 262, p. 169), as amended by Commission Directive 2005/42/EC of 20 June 2005 (OJ 2005 L 158, p. 17) ('Directive 76/768'), a 'cosmetic product' means:

'... any substance or preparation intended to be placed in contact with the various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance and/or correcting body odours and/or protecting them or keeping them in good condition.'

5 Annex VI to Directive 76/768, headed 'List of preservatives which cosmetic products may contain', mentions among those preservatives chlorhexidine with a maximum authorised concentration of 0.3%.

6 According to the preamble to Annex VI to Directive 76/768, 'preservatives' are substances which may be added to cosmetic products for the primary purpose of inhibiting the development of microorganisms in such products.

German law

7 The term 'medicinal product' is defined in Paragraph 2(1) of the Law on the marketing of medicinal products (Gesetz über den Verkehr mit Arzneimitteln), in its version of 12 December 2005 (BGBl. 2005 I, p. 3394).

8 Under point 2 of that provision, medicinal products are substances or preparations consisting of substances:

'... which may be used in or administered to human beings or animals either with a view to (a) restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or (b) making a medical diagnosis.'

The dispute in the main proceedings and the questions referred for a preliminary ruling

9 Chemische Fabrik Kreussler and John O. Butler are competitors on the German market for the marketing of mouthwash solutions containing chlorhexidine.

10 On that market John O. Butler markets as a cosmetic product a mouthwash solution called 'PAROEX 0,12%' in which chlorhexidine, an antiseptic, accounts for 0.12% of the product contents. The following is stated on the packaging, namely 'Mouthrinse for oral care – Helps reduce dental plaque accumulation – Protects gums and maintains oral health'. The information leaflet provided with the product states that users should rinse their mouth with 10 ml of undiluted solution for 30 seconds twice daily.

11 In the main proceedings, Chemische Fabrik Kreussler is of the view that the mouthwash marketed by John O. Butler is a medicinal product within the meaning of Paragraph 2 of the Law on the marketing of medicinal products inasmuch as it has a pharmacological action. It is apparent from a monograph dating from 1994, on the properties, effects and possible applications of chlorhexidine, that mouthwash solutions containing a chlorhexidine solution of 0.2% reduce salivary bacteria and, in this way, have a therapeutic or clinical effect in cases of gingivitis.

12 Consequently, Chemische Fabrik Kreussler brought an action before the Landgericht Frankfurt am Main (Regional Court, Frankfurt am Main) on 14 September 2006 seeking an injunction requiring John O. Butler to desist from advertising the product PAROEX 0,12% on bottles and/or folding boxes and/or instructions for use and/or from marketing that product for as long as it had not been authorised as a medicinal product.

13 The Landgericht Frankfurt am Main dismissed the action on the ground that PAROEX 0,12% does not exert a pharmacological action because the interaction between the molecules of chlorhexidine and a cellular constituent of the user required for such an action had not been established.

14 Ruling on the appeal, the Oberlandesgericht Frankfurt am Main (Higher Regional Court, Frankfurt am Main) also held that the product at issue did not exert a pharmacological action. It took the view that it could, for the purpose of defining that term, rely on the guidance document adopted by the European Commission's Directorate-General for Enterprise and Industry and entitled '*MEDICAL DEVICES: Guidance document – Borderline products, drug-delivery products and medical devices incorporating, as an integral part, an ancillary medicinal substance or an ancillary human blood derivative'* ('the guidance document on medical devices').

15 According to that court, it is apparent from that document that, for a substance to be recognised as exerting a pharmacological action within the meaning of Article 1(2)(b) of Directive 2001/83, there must be an interaction between the molecules of the substance in question and a cellular constituent of the user's body, which there is not as regards the product at issue.

16 Chemische Fabrik Kreussler appealed on a point of law against that judgment to the Bundesgerichtshof

(Federal Court of Justice), which overturned the judgment of the Oberlandesgericht Frankfurt am Main and referred the case back to it for a fresh hearing and decision. The Bundesgerichtshof also based its decision on the definition contained in the guidance document on medical devices and took the view that it is not necessary to establish that there is an interaction between the molecules of the substance in question and a cellular constituent of the human body for a product to be recognised as exerting a pharmacological action. It is sufficient to establish that the molecules of the substance in question interact in any way whatsoever with a cellular constituent. Inasmuch as chlorhexidine reacts with the bacterial cells in the user's mouth, the existence of a pharmacological action cannot be precluded from the outset.

17 Taking the view that the outcome of the proceedings before it is dependent upon the interpretation of Article 1(2)(b) of Directive 2001/83, the Oberlandesgericht Frankfurt am Main decided to stay the proceedings and to refer the following questions to the Court of Justice for a preliminary ruling:

'(1) For the purpose of defining the term "pharmacological action" in Article 1(2)(b) of Directive 2001/83 ..., can recourse be had to [the guidance document on medical devices], which states that there must be an interaction between the molecules of the substance in question and a cellular constituent, usually referred to as a receptor, which either results in a direct response or blocks the response of another agent?

(2) If the first question is answered in the affirmative, does the term "pharmacological action" require that there should be an interaction between the molecules of the substance in question and cellular constituents of the user, or is it sufficient if there is an interaction between the substance in question and a cellular constituent which does not form part of the human body?

(3) In the event that the first question is answered in the negative or that neither of the two definitions proposed in the second question is appropriate, which alternative definition should be used instead?'

Consideration of the questions referred

The first question

18 By its first question, the national court asks, in essence, whether Article 1(2)(b) of Directive 2001/83 is to be interpreted as meaning that, for the purpose of defining the term 'pharmacological action' within the meaning of that provision, account may be taken of the definition of 'pharmacological means' in the guidance document on medical devices.

19 In that regard, it must be pointed out that, as indicated by its title, that guidance document was drawn up for the purposes of the application of European Union directives on medical devices and is intended inter alia to aid the competent authorities to distinguish such devices from medicinal products.

20 It is apparent from the order for reference that the origin of the dispute in the main proceedings is the parties' disagreement regarding the classification of the product at issue as a cosmetic product or as a medicinal product.

21 Against that background, it is necessary to point out the existence of the Guidance Document on the demarcation between the Cosmetic Products Directive 76/768 and the Medicinal Products Directive 2001/83 as agreed between the Commission services and the competent authorities of the Member States ('the guidance document on the demarcation between the Cosmetic Products Directive and the Medicinal Products Directive'), in which the term 'pharmacological action' is defined in an identical manner to that of 'pharmacological means' in the guidance document on medical devices.

22 Consequently, the first question must be reformulated as seeking to ascertain, in essence, whether Article 1(2)(b) of Directive 2001/83 is to be interpreted as meaning that, for the purpose of defining the term 'pharmacological action' within the meaning of that provision, account may be taken of the definition of that term in the guidance document on the demarcation between the Cosmetic Products Directive and the Medicinal Products Directive.

23 In that regard, it must be stated that, in itself, that guidance document drawn up by the Commission's services, which is not one of the legal acts of the European Union referred to in Article 288 TFEU, cannot be of a legally binding nature or enforceable against individuals.

24 That is moreover apparent from that document, which states that it is not legally binding since only the Court of Justice has the jurisdiction to give a binding interpretation of European Union law.

25 As stated by the guidance document on the demarcation between the Cosmetic Products Directive and the Medicinal Products Directive in its introduction, the fact remains that, inasmuch as that document was drawn up by group of experts from the national authorities, the Commission's services and professional associations from industry, it may provide useful information for the interpretation of the relevant provisions of European Union law and therefore contribute to ensuring that they are applied uniformly.

26 Consequently, the national court may, in order to apply the term 'pharmacological action' within the meaning of Article 1(2)(b) of Directive 2001/83, take account of that document. In doing so, it must nevertheless ensure that the interpretation thus derived was derived in a manner consistent with the criteria laid down by the case-law relating to the interpretation of European Union legal acts, including those concerning the division of jurisdiction between the national courts and the Court in the context of preliminary ruling proceedings.

27 It follows from the foregoing considerations that Article 1(2)(b) of Directive 2001/83 must be interpreted as meaning that, for the purpose of defining the term 'pharmacological action' within the meaning of that provision, account may be taken of the definition of that term in the guidance document on the

demarcation between the Cosmetic Products Directive and the Medicinal Products Directive.

The second question

28 By its second question, the national court asks, in essence, whether Article 1(2)(b) of Directive 2001/83 is to be interpreted as meaning that, for a substance to be regarded as exerting a 'pharmacological action' within the meaning of that provision, it is necessary for there to be an interaction between the molecules of which it consists and a cellular constituent of the user's body, or whether an interaction between that substance and any cellular constituent present within the user's body may be sufficient.

29 In that regard, it must be pointed out at the outset that it is not apparent either from Directive 2001/83 or from the guidance document on the demarcation between the Cosmetic Products Directive and the Medicinal Products Directive that the molecules of the substance in question must necessarily interact with a human cellular constituent in order for it to be regarded as a substance which exerts a 'pharmacological action'.

30 By contrast, it is apparent from Article 1(2)(b) of Directive 2001/83 that the substance in question must be capable of restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action and that capability must have been scientifically established (see, to that effect, **Case C- 140/07 Hecht- Pharma [2009] ECR I-41, paragraph 26**).

31 Against that background, it must be held, in the light of the observations submitted to the Court, that a substance the molecules of which do not interact with a human cellular constituent may nevertheless, by means of its interaction with other cellular constituents present within the user's organism, such as bacteria, viruses or parasites, have the effect of restoring, correcting or modifying physiological functions in human beings.

32 It follows that it is not a priori inconceivable that a substance the molecules of which do not interact with a human cellular constituent may constitute a medicinal product within the meaning of Article 1(2)(b) of Directive 2001/83.

33 Moreover, it must be pointed out that products containing a substance which has a physiological effect cannot automatically be classified as medicinal products 'by function', for the purposes of Article 1(2)(b) of Directive 2001/83, unless the competent administration has made an assessment, with due diligence, of each product individually, taking account, in particular, of that product's specific pharmacological, immunological or metabolic properties, to the extent to which they can be established in the present state of scientific knowledge (**Hecht-Pharma, paragraph 40**, and Case **C- 27/08 BIOS Naturprodukte [2009] ECR I- 3785, paragraph 19**).

34 It is also important to bear in mind that, as well as the pharmacological, immunological or metabolic properties of the product in question, which constitute the factor on the basis of which it must be ascertained, in the light of the potential capacities of the product, whether it may, for the purposes of Article 1(2)(b) of Directive 2001/83, be used in or administered to human beings with a view to restoring, correcting or modifying physiological functions, account must be taken, in determining whether a product falls within the definition of a medicinal product 'by function' for the purposes of that provision, of all the characteristics of the product, including, inter alia, its composition, the manner in which it is used, the extent of its distribution, its familiarity to consumers and the risks which its use may entail (see **BIOS Naturprodukte, paragraphs 18 and 20**).

35 Lastly, it must be added that, to be capable of being regarded as being a medicinal product by function, the product in question must, having regard to its composition – including its content in active substances – and if used as intended, be capable of appreciably restoring, correcting or modifying physiological functions in human beings (see **Hecht-Pharma, paragraph 42**, and **BIOS Naturprodukte, paragraph 23**), which it is for the national court to ascertain.

36 Having regard to all the foregoing considerations, the answer to the second question is that Article 1(2)(b) of Directive 2001/83 must be interpreted as meaning that, for a substance to be regarded as exerting a 'pharmacological action' within the meaning of that provision, it is not necessary for there to be an interaction between the molecules of which it consists and a cellular constituent of the user's body, as an interaction between that substance and any cellular constituent present within the user's body may be sufficient.

The third question

37 The third question was submitted in the alternative in case of a negative answer to the first question or in the event that neither of the two definitions proposed in the second question is conceivable.

38 Consequently, in view of the answer given to the first and second questions, it is not necessary to answer the third question.

Costs

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

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

1. Article 1(2)(b) of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, as amended by Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004, must be interpreted as meaning that, for the purpose of defining the term 'pharmacological action' within the meaning of that provision, account may be taken of the definition of that term in the Guidance Document on the demarcation between the Cosmetic Products Directive 76/768 and the Medicinal Products Directive 2001/83

as agreed between the Commission services and the competent authorities of the Member States.
2. Article 1(2)(b) of Directive 2001/83 must be interpreted as meaning that, for a substance to be regarded as exerting a 'pharmacological action' within the meaning of that provision, it is not necessary for there to be an interaction between the molecules of which it consists and a cellular constituent of the user's body, as an interaction between that substance and any cellular constituent present within the user's body may be sufficient.
* Language of the case: German.