Case C-589/23

Request for a preliminary ruling

Date lodged:

25 September 2023

Referring court:

Bundesgerichtshof (Germany)

Date of the decision to refer:

14 September 2023

Defendants and appellants in the appeal on a point of law:

Cassella-med GmbH & Co.KG

MCM Klosterfrau Vertriebsgesellschaft mbH

Applicant and respondent in the appeal on a point of law:

Verband Sozialer Wettbewerb e. V.

BUNDESGERICHTSHOF (FEDERAL COURT OF JUSTICE, GERMANY)

ORDER

[…]

In the case of

1. Cassella-med GmbH & Co. KG, […] Cologne,

2. MCM Klosterfrau Vertriebsgesellschaft mbH, […] Cologne,

Defendants and appellants in the appeal on a point of law,

[…]

v

Verband Sozialer Wettbewerb e. V., […] Berlin,

Applicant and respondent in the appeal on a point of law,

[…]

On 14 September 2023 […], the First Civil Chamber of the Federal Court of Justice

made the following order:

I. The proceedings are stayed.

II. The following question on the interpretation of the first case in 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) is referred to the Court of Justice of the European Union for a preliminary ruling:

Is there a pharmacological action within the meaning of the first case in Article 1(2)(b) of Directive 2001/83/EC where the substance in question (in this case: D-mannose), by means of a reversible binding to bacteria via hydrogen bonds, prevents the bacteria from adhering to human cells (in this case: the bladder wall)?

Grounds:

1 A. The applicant is a registered association whose statutory duties include protecting the commercial interests of its members. Many of its members distribute medicinal products and medical devices.

2 The first defendant distributed the product ‘Femannose®’ as a medical device ‘for the treatment and prevention of cystitis (bladder infection) and other urinary tract infections’. The product contained D-mannose and cranberry extract as essential ingredients. The second defendant operates a website on which the product was advertised until mid-October 2017. Since October 2017, the first defendant has marketed the product without the cranberry extract as an ingredient under the name ‘Femannose® N’. The packaging now states ‘for the prevention and to support the treatment of cystitis (bladder infection) and other urinary tract infections’. The applicant considers that the products cannot be marketed as medical devices; rather, they are medicinal products – and are indisputably not authorised as such. Following an unsuccessful letter of formal notice, the applicant requested that the first defendant be ordered, on pain of punitive administrative measures to compel specific conduct, to refrain from marketing and/or placing on the market, in the course of trade, the product ‘Femannose’ as a medical device, and to refrain from marketing and/or placing on the market and/or advertising as shown in the submitted advertisement, in the course of trade, the product ‘Femannose N’ as a medical device, and that the second defendant be ordered, on pain of administrative measures to compel specific conduct, to refrain

from advertising, in the course of trade, the product ‘Femannose’, in so far as is evident from the internet advertising submitted. It also requested the payment of a lump sum by way of reimbursement of the costs associated with the letter of formal notice plus interest.

3 The Landgericht (Regional Court) upheld the action (LG Cologne, judgment of 15 January 2020 – 84 0 224/17, juris). The appeal court dismissed the defendants’ appeal (Oberlandesgericht (Higher Regional Court; ‘OLG’) Cologne, PharmR 2021, 144). By their appeal on a point of law, for which this Chamber has granted leave and which the applicant claims should be dismissed, the defendants are pursuing their application to have the action dismissed.

4 The Chamber stayed the proceedings following two requests for a preliminary ruling from the Federal Administrative Court to the Court of Justice of the European Union (Federal Administrative Court (‘BVerwG’), ZMGR 2021, 380 and PharmR 2021, 593). Since then, the Court of Justice of the European Union has ruled on the requests for a preliminary ruling (judgment of the Court of Justice of 19 January 2023, C-495/21 and C-496/21, PharmR 2023, 160 – *Bundesrepublik Deutschland (Nasal drops)*).

5 B. The success of the appeal on a point of law depends on the interpretation of the first case in Article 1(2)(b) of Directive 2001/83/EC of 6 November 2001 on the Community code relating to medicinal products for human use. Before a ruling can be given on the appeal on a point of law, the proceedings must therefore be stayed and a preliminary ruling obtained from the Court of Justice of the European Union pursuant to point (b) of the first paragraph and the third paragraph of Article 267 TFEU.

6 I. The appeal court held in essence that the applicant is entitled to claim injunctive relief under competition law because the first defendant has infringed Paragraph 3a of the Heilmittelwerbegesetz (Law on the advertising of medicinal products, ‘the HWG’) and the second defendant has infringed Paragraph 21 of the Arzneimittelgesetz (Law on medicinal products, ‘the AMG’). According to that court, the products at issue are medicinal products by function which cannot be placed on the market without authorisation. The products have a pharmacological action as there is an interaction between their main active ingredient (D-mannose) and a cellular constituent. The products also appreciably restore, correct or modify physiological functions in human beings. The required overall assessment, taking into account the other characteristics of the product, also leads to the conclusion that the products must be regarded as medicinal products by function.

7 II. The appeal court rightly recognised the applicant’s standing to bring proceedings under Paragraph 8(3)(3) of the Gesetz gegen den unlauteren Wettbewerb (Law against unfair competition, ‘the UWG’) in the version applicable until 30 November 2021 (see Paragraph 15a(1) of the UWG). The prohibition of the advertising of medicinal products which require authorisation and which are not authorised or deemed to be authorised under the law on

medicinal products laid down in the first sentence of Paragraph 3a of the HWG and the prohibition of the placing on the market of finished medicinal products which have not been approved by the competent Federal authorities or for which the European Community or the European Union has not granted a marketing authorisation, laid down in the first sentence of Paragraph 21(1) of the AMG are – as the appeal court rightly determined – rules designed to regulate market behaviour within the meaning of Paragraph 3a of the UWG, the infringement of which has a noticeable adverse effect on the interests of the market participants concerned (see Federal Court of Justice ('BGH'), judgment of 25 June 2015 – I ZR 11/14, PharmR 2016, 82 (paragraph 9) – Chlorhexidine, with further references). In so far as the appeal court correctly held that there was an infringement of the first sentence of Paragraph 3a of the HWG and the first sentence of Paragraph 21(1) of the AMG, there is a commercial practice which is unfair under Paragraph 3a of the UWG and inadmissible under Paragraph 3(1) of the UWG, which justifies an order to cease and desist being obtained (first sentence of Paragraph 8(1) of the UWG) due to the risk of recurrence in the present case.

8 III. The success of the appeal on a point of law depends on whether the appeal court was right to find an infringement of the first sentence of Paragraph 3a of the HWG and the first sentence of Paragraph 21(1) of the AMG, since the first defendant's products have a pharmacological action which is capable of modifying physiological functions in human beings significantly and are therefore medicinal products by function in accordance with Paragraph 2(1)(2)(a) of the AMG and Article 1(2)(b) of Directive 2001/83/EC.

9 1. According to Paragraph 2(1)(2)(a) of the AMG, medicinal products are, inter alia, substances or preparations made from substances which may be used in or on the human body or can be administered to human beings with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action. That provision is intended to transpose the first case in Article 1(2)(b) of Directive 2001/83/EC and must therefore be interpreted in accordance with EU law (BGH, judgment of 8 January 2015 – I ZR 141/13, GRUR 2015, 811 paragraph 9) = WRP 2015, 969 – Mouthwash solution II). According to the first case in Article 1(2)(b) of Directive 2001/83/EC, medicinal products are 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. Under Article 2(2) of Directive 2001/83/EC (transposed by Paragraph 2(3a) of the AMG), that directive is to apply in cases of doubt, where, taking into account all its characteristics, a product may fall within the definition of a 'medicinal product' and within the definition of a product covered by other Community legislation.

10 2. In accordance with the principles set out in the case-law of the Court of Justice of the European Union and the Chamber, the concept of medicinal product is to be broadly construed. This also applies to medicinal products by function in

accordance with Article 1(2)(b) of Directive 2001/83/EC (see judgment of the Court of Justice of 20 September 2007, C-84/06, [2007] ECR I-7609 (paragraph 31) – *Antroposana*; BGH, order of 18 October 2012 – I ZR 38/12, GRUR-RR2013, 272 (paragraph 7) with further references). The existence of a medicinal product by function must be set out and, in the event of a challenge, proved by the person who invokes it (see BGH, judgment of 25 June 2015 – I ZR 205/13, GRUR 2016, 302 (paragraph 13) = WRP 2016, 191 – Mouthwash solution III, with further references). It is for the courts of the Member States to determine whether the product in question constitutes a medicinal product by function (see judgment of the Court of Justice of 6 September 2012, C-308/11, GRUR 2012, 1167 (paragraph 35) = WRP 2013, 175 – *Chemische Fabrik Kreussler*; BGH, GRUR-RR 2013, 272 (paragraph 7)). In the absence of scientific evidence of a pharmacological, immunological or metabolic action, it cannot be assumed that the product is a medicinal product by function (see Court of Justice, GRUR 2012, 1167 (paragraph 30) – *Chemische Fabrik Kreussler*, with further references; PharmR 2023, 160 paragraph 44 – *Bundesrepublik Deutschland (Nasal drops)*).

11 Useful information in order to clarify what is meant by 'pharmacological … action' within the meaning of Article 1(2)(b) of Directive 2001/83/EC may be taken from the guidelines on the delimitation of medicinal products and medical devices, compiled by an expert group of representatives of authorities and industry under the auspices of the European Commission under Council Directive 93/42/EEC of 14 June 1993 concerning medical devices ('Medical Devices: Guidance document – Borderline products, drug-delivery products and medical devices incorporating, as integral part, an ancillary medicinal substance or an ancillary human blood derivative', MEDDEV 2.1/3 rev. 3, 'the MEDDEV Guidelines') (see BGH, judgment of 24 June 2010-1 ZR 166/08, GRUR 2010, 1026 (paragraph 17) = WRP 2010, 1393 – Photodynamic therapy; judgment of 24 November 2010 -IZR 204/09, PharmR 2011, 299 (paragraph 14) with further references; with regard to the Guidance Document on the demarcation between the Cosmetic Products Directive 76/768/EEC and the Medicinal Products Directive 2001/83/EC, see Court of Justice, GRUR 2012, 1167 (paragraphs 21 to 27) – *Chemische Fabrik Kreussler*; BGH, PharmR 2016, 82 (paragraph 11) – Chlorhexidine, with further references), which, however, are not legally binding as such (see Court of Justice, GRUR 2012, 1167 (paragraph 23) – *Chemische Fabrik Kreussler*). Those guidelines, which have since been replaced by the 'Guidance on borderline between medical devices and medicinal products under Regulation (EU) 2017/745 on medical devices' (MDCG 2022-5), state:

> 'Pharmacological means' is understood as 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 which blocks the response to another agent. Although not a completely reliable criterion, the presence of a dose-response correlation is indicative of a pharmacological effect.

12 3. The appeal court proceeded from the principles set out and held that the products at issue have a pharmacological action.

13 In its reasoning, the appeal court referred to the findings of the expert appointed by the court and stated that the main active ingredient of the products is D-mannose, a monosaccharide of high importance for human metabolism, especially in the glycosylation of molecules. These use bacteria to attach to human mucous membranes or other surfaces. The bacteria use adhesins for this purpose. In the case of *Escherichia coli* bacteria, the adhesin FimH is located at the tip of the fimbriae. The fimbriae use FimH to attach themselves to the bladder wall and prevent the bacteria from being flushed out by the flow of urine. In addition, after the bacteria have attached to the surface of the bladder mucosa, FimH also triggers the biochemical process. The transcription of various genes and various biochemical processes takes place in the host cell, ultimately leading to a kind of rupture of the cell membrane and the inclusion of the bacterium in the human cell.

14 The main effect of D-mannose is to bind to FimH in urine and thus to block the FimH and structures containing mannose from adhering to the bladder wall. By blocking further interaction between the bacterial FimH and the body's own cells, the physiological processes of the bacterium and the pathophysiological processes of the urinary tract infection are undermined. A change in the transcription of various genes is observed in the bacterium in response to the binding of the FimH to structures containing mannose. This can best be interpreted in accordance with the definition in the MEDDEV Guidelines as meaning that the D-mannose on FimH adhesins has the effect of blocking the response to another agent. D-mannose causes the physiological processes of the bacteria, which accompany adhesion to human cells, to be blocked by binding specifically to the cell structures of those bacteria. By blocking the adhesion of the FimH on the bacterium to mannosylated structures on the bladder wall, there is no biochemical reaction between the bacterium and the host cell. There is an interaction between D-mannose molecules and a cellular constituent. The bacteria cell clearly reacts by biochemical processes to the binding of FimH and the surface structures containing D-mannose. Whether the binding of D-mannose to the bacterium is reversible is irrelevant.

15 4. By taking the position that the effect of the D-mannose on FimH adhesins is to block the response to another agent, in accordance with the MEDDEV Guidelines, the appeal court considered that the second alternative of the definition of 'pharmacological action' given therein was satisfied, which requires an interaction between the molecules of the substance in question and a cellular constituent, usually referred to as a receptor, which blocks the response to another agent. It must be established whether, in so doing, the appeal court based its decision on a correct understanding of the concept of pharmacological action.

16 a) The view taken in the appeal on a point of law is that, contrary to the opinion of the appeal court, the active substance D-mannose does not interact with a cellular constituent. Interaction would require a substance-induced irreversible interaction

between the substance and a cellular constituent due to prior binding. By contrast, binding which is physically reversible establishes only an interdependence, which does not constitute a sufficient characteristic of the required chemical-pharmacological interaction. It has not been established whether and which processes are triggered between D-mannose and the bacterium. The substance does not interact with a harmful messenger or with a human target cell in a relevant way, but merely causes the harmful messenger to be flushed out of the body unchanged. The (reversible) binding to a bacterium alone cannot be equated to an adhesion to a human target cell.

17 aa) As a preliminary point, the appeal on a point of law wrongly claims that it has not been established whether – and if so, which – processes are triggered between D-mannose and the bacterium.

18 (1) The appeal court stated that the bacterial cell reacts by biochemical processes to the binding of FimH to the surface structures containing D-mannose; the physiological processes of the bacterium and the pathophysiological processes of the urinary tract infection are undermined, and a change in the transcription of various genes is observed in the bacterium in response to the binding of the FimH to structures containing mannose. In so doing, the appeal court explained in detail, in the exercise of its duty to assess the facts of the case, whether and the extent to which the bacterium reacts to D-mannose.

19 (2) The expert, whose findings were considered by the appeal court, also stated that it must be assumed that the binding of FimH to dissolved D-mannose molecules also initiates at least part of the biochemical processes for tissue invasion, which are ineffective, however, and cannot be identical to the response to the adhesion to surface structures of human cells containing D-mannose. On that basis, it has not been established that the interaction described by the appeal court, namely the triggering of biochemical processes as a reaction of the bacterial cell to the binding to D-mannose, causes the intended main effect of the substance at issue, namely to block the adhesion of bacterial cells to the bladder wall. Whether such causation is a prerequisite for the substance to have a pharmacological action is not apparent from the definition of pharmacological action in the MEDDEV Guidelines and requires clarification by the Court of Justice of the European Union.

20 (3) In addition, the expert stated that (even) the reversible binding of D-mannose to bacteria is accompanied by the creation of hydrogen bonds, which must not be regarded as a purely mechanical or physical mechanism. Rather, the specific adhesion of FimH to the glycosylated structures on the cell surface of the urinary tract initiates biochemical changes in the bacterial cell. The Chamber is of the opinion that the creation of hydrogen bonds described by the expert could also constitute an interaction within the meaning of the definition of pharmacological action in the MEDDEV Guidelines, which would also cause the intended main effect of the substance at issue. Whether that is the case also needs to be clarified.

21 bb) The appeal on a point of law unsuccessfully challenges the finding of the appeal court that the binding to a bacterium cannot be equated to an adhesion to a human target cell. It has been clarified by the case-law of the Court of Justice of the European Union and of the Chamber 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. A substance the molecules of which do not interact with a human cellular constituent may also constitute a medicinal product within the meaning of Article 1(1)(b) of Directive 2001/83/EC (see Court of Justice, GRUR 2012, 1167 (paragraph 31 et seq.) – *Chemische Fabrik Kreussler*; BGH, GRUR 2010, 1026 (paragraph 17) – Photodynamic therapy; GRUR 2015, 811 (paragraphs 4 and 9) – Mouthwash solution II).

22 cc) The appeal on a point of law should also not be upheld in so far as it challenges the appeal court's view that the existence of the required interaction does not depend on whether the binding of D-mannose to the bacterium (thus of the substance at issue to a cellular constituent) is reversible.

23 (1) It has not yet been clarified in the case-law of the highest courts under which criteria pharmacological and non-pharmacological means can be distinguished in cases in which, as in the present case, the substance at issue is not absorbed by the target cell, but is bound only temporarily (see, in this regard, BVerwG, ZMGR 2021, 380, paragraph 11 et seq.); PharmR 2021, 593 (paragraph 10 et seq.)). The definition contained in the MEDDEV Guidelines does not provide any indications that could lead to the conclusion that such binding must be permanent. That would suggest that the view taken by the appeal court, according to which, if such an interaction exists, the question of the reversibility of the adhesion to a cellular constituent is irrelevant, is correct. This also requires clarification by the Court of Justice of the European Union.

24 (2) Contrary to the view taken in the appeal on a point of law, the dispute does not raise the question whether a pharmacological action can also be assumed in the case of a mere attachment of the active substance to the exterior of the cell if this does not lead to a change in the state or a function of the cell. The appeal court did not find the latter, rather it stated that a change in the transcription of various genes was observed in the bacterium in response to the binding of the FimH to structures containing mannose and that the bacterial cell reacts by biochemical processes to the binding of FimH to the surface structures containing D-mannose. In so doing, it affirmed a change in the function of the bacterial cell and the substance-induced triggering of a biochemical reaction inside the cell.

25 b) The appeal on a point of law also contests the appeal court's view that there is also no pharmacological action because the consequence of the – assumed – interaction is not, in accordance with the definition of the MEDDEV Guidelines, the blocking of another agent.

26 aa) The view taken in the appeal on a point of law is that the second alternative of the definition of 'pharmacological action' given in the MEDDEV Guidelines should cover cases in which, although there is no direct reaction in the sense of the first alternative, indirectly, as a result of the binding to a target cell, a (harmful) reaction to another messenger is blocked. However, the definition does not contain a 'general clause' according to which it is sufficient for the reaction of a human target cell to be prevented even indirectly, regardless of how that objective is achieved. The blocked substance must be an agent, thus a substance intended to exert a specific (harmful) effect on a target cell. In addition, the blocked agent must be different from the cellular constituent involved in the interaction, since the blocking of 'another' agent is required. Neither is the case here. It is not the bladder mucosa which is blocked, but the bacterium itself. In so far as inflammation of the bladder mucosa is prevented as a result, this is not the response of another agent but that of another receptor. The products therefore have no pharmacological action.

27 bb) It is necessary to clarify whether the mode of action of D-mannose established by the appeal court may be regarded as blocking the response to an agent in accordance with the definition in the MEDDEV Guidelines or whether it rather – in accordance with the view taken in the appeal on a point of law – constitutes the blocking of the response to a receptor and therefore the conditions for the existence of a pharmacological action are not satisfied.

28 (1) The appeal court proceeded on the basis that D-mannose causes the physiological processes of the bacteria, which accompany adhesion to human cells, to be blocked through the specific binding to the cell structures of those bacteria. The active substance blocks the adhesion of the FimH on the bacterium to mannosylated structures on the bladder wall. This could be interpreted broadly as blocking the response to another agent. The appeal court thus regarded human cell constituents, namely glycoproteins on cell membranes of the urinary tract, as another agent to which the response of the FimH is blocked. In order to be able to answer whether this is permissible, it is necessary to clarify the concept of 'agent' used in the MEDDEV Guidelines.

29 (2) On the basis of the understanding of the term advocated in the appeal on a point of law, according to which an agent is a substance intended to exert a specific effect on a target cell, it is justified in objecting that glycoproteins on the cell membranes of the urinary tract cannot be regarded as agents because they do not exert any effect (for example on other cells).

30 (3) In the Chamber's view, the broad understanding of the term advocated by the appeal court appears convincing nevertheless. There is much to be said for a broad concept of 'agent' which generally describes a binding partner without specifying the material or structural nature of that binding partner. It seems logical that the binding partner may also be sourced from the human body.

31 Many medicinal products work in such a way as to block the response of a cellular constituent to parts of the human body. By way of example, the expert cited beta blockers, which block the adhesion of the body's own adrenalin to the adrenoceptors (receptors in innervated tissue). Here too, there is no blocking of the response to another agent in the sense of the narrower understanding of the concept advocated in the appeal on a point of law. In addition, the expert referred to agents which were examined in the context of human immunodeficiency virus (HIV) infection therapy. So-called attachment inhibitors block the binding of glycosylated proteins of HIV to surface structures of human cells, which is necessary for an infection. The main mechanism of action is blocking the binding of pathogens and human cells. In this case too, the human cell or the receptor serving as a molecular binding partner on the cell would have to be regarded as an agent.

32 cc) In so far as the appeal on a point of law emphasises that the blocked agent must be different from the cellular constituent involved in the interaction, since the definition of 'pharmacological action' given in the MEDDEV Guidelines refers to 'another' agent, it is not able to invalidate the line of argument of the appeal court. It found in addition to the relevant definition that D-mannose (the substance at issue) blocks the binding of FimH on the bacterium (receptor) and the mannosylated structures on the bladder wall (another agent). Moreover, according to the appeal court's understanding, the blocked agent is therefore different from the cellular constituent involved in the interaction.

33 5. The answer to the question referred for a preliminary ruling is material to the decision.

34 a) The defendants' appeal on a point of law cannot succeed merely because the appeal court carried out an incorrect overall assessment.

35 aa) According to the case-law of the Court of Justice of the European Union and the Chamber, in order to assess whether products containing a substance which has a physiological effect are medicinal products by function in accordance with Article 1(2)(b) of Directive 2001/83/EC, a careful examination must be carried out of each individual case, taking into account not only the pharmacological, immunological or metabolic properties of the product but also all its other characteristics, such as 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 judgment of the Court of Justice of 30 April 2009 – C-27/08 [2009], ECR I-3785 = GRUR 2009, 790 (paragraph 18) – *BIOS Naturprodukte*; Court of Justice, GRUR 2012, 1167 (paragraph 33 et seq.) – *Chemische Fabrik Kreussler*, with further references; BGH, PharmR 2016, 82 (paragraph 12) – Chlorhexidine).

36 bb) The appeal court based its decision on that point, stating that, in the context of the required overall assessment, the manner in which the products are used militates in particular in favour of classifying the products as medicinal products

by function. In the case of medicinal products, it is customary for the products to be distributed with a leaflet in the packaging indicating the dosage and administration. They are marketed in a form which is also commonly used for medicines. They should also be used to support the treatment of an illness. Reference is made to side effects such as intolerance, nausea, bloating and loose stools. The extent of distribution is considerable. Although numerous criteria apply in the same way to medical devices, with the result that delimitation has to be primarily on the basis the determination of pharmacological properties, the overall assessment reveals that the products are medicinal products.

37 cc) The challenges raised in the appeal on a point of law against that assessment of the facts of the case are ineffective. The appeal court carried out the overall assessment required by the case-law of the Court of Justice of the European Union and the Chamber, taking into account the relevant criteria in that regard, in a manner that is not objectionable from the perspective of an appeal on a point of law. In that regard, contrary to the view taken in the appeal on a point of law, it did not rely on the incorrect legal principle that a product is always a medicinal product by function when it has a pharmacological action. Furthermore, in so far as it is claimed in the appeal on a point of law that the appeal court failed to take account of the fact that the absence of risks associated with use militates against classification as a medicinal product by function, this is not consistent with the finding of the appeal court which is accepted in the appeal on a point of law, according to which the products have various side effects which are listed in detail.

38 b) The answer to the question referred for a preliminary ruling is also a precursor of the other complaint in the appeal on a point of law, by which it challenges the appeal court's assertion that, under normal conditions of use, the products appreciably restore, correct or modify physiological functions in human beings.

39 aa) According to the case-law of the Court of Justice of the European Union and the Chamber, to be capable of being regarded as being a medicinal product by function, the product in question must, having regard to its composition and if used as intended, be capable of appreciably restoring, correcting or modifying physiological functions in human beings by exerting a pharmacological, immunological or metabolic action (see Court of Justice, GRUR 2012, 1167 (paragraphs 30 and 35) – *Chemische Fabrik Kreussler*; BGH, GRUR-RR 2013, 272 (paragraph 7); PharmR 2016, 82 (paragraph 12) – Chlorhexidine, both with further references).

40 bb) The appeal court affirmed this on the ground that the blocking of FimH on the bacterial surface has the effect of preventing bacteria from binding to the cell membrane, which thwarts the biochemical reaction between the bacterium and the host cell, with the result that the physiological function of the human body is influenced as the onset or progression of the inflammation of the urinary tract is repressed. The fact that the clinical significance of the therapy and prevention

remains unclear due to a lack of sufficient data does not preclude that outcome. According to the expert's findings, it has been proven beyond doubt that D-mannose binds to FimH and thus undermines the physiological processes of the bacterium and the pathophysiological processes of the urinary tract infection.

41 cc) That view is countered in the appeal on a point of law, which argues that the influence inherent in a therapeutic or preventive effect on physiological functions is not, in itself, sufficient for the assumption of a medicinal product by function; rather, the intended therapeutic purpose must be achieved by significant interference with the physiological functions of human beings, which in turn must be classified as pharmacological. That is not the case with D-mannose, which binds to bacteria solely by reversible, physical means without destroying them and also does not interact with the human bladder mucosa.

42 dd) According to the aforementioned case-law of the Court of Justice of the European Union, the appreciable influence on physiological functions required for the assumption of a medicinal product by function presupposes a pharmacological action (or an immunological or metabolic action, which, however, is not at issue in the present case) (see Court of Justice, GRUR 2012, 1167 (paragraph 30) – *Chemische Fabrik Kreussler*, with further references). The pharmacological (or immunological or metabolic) properties of a product are 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/EC, be administered to human beings with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in human beings (judgment of the Court of Justice of 15 November 2007, C-319/05 [2007], ECR I-9811 (paragraph 59) = EuZW 2008, 56 – *Commission* v *Germany*; Court of Justice, EuZW 2009, 545 (paragraph 20) – *BIOS Naturprodukte*, both with further references). Assuming that the appeal court was right to find that there was a pharmacological action, its assessment that the products appreciably restore, correct or modify physiological functions in human beings is not open to objection from the perspective of an appeal on a point of law.

43 c) An answer to the question referred for a preliminary ruling is also necessary for that reason, since, in addition to the classification of the products at issue as medicinal products by function, their classification as medicinal products by presentation could also be considered (see, in this regard, Court of Justice, PharmR 2023, 160 paragraphs 49 to 51 – *Bundesrepublik Deutschland (Nasal drops)*). In the appeal on a point of law, it is necessary to examine only whether a medicinal product by function is present, since the appeal court based the judgment on that factor alone. Moreover, the judgment cannot be upheld from the point of view of the existence of a medicinal product by presentation, since the appeal court did not make sufficient findings in that respect.

44 d) Lastly, the fact that the legal opinion of the appeal court is in line with the assessment of the European Commission, as expressed in its manual on borderline products (version 1.2 (05-2019), point 4.20), does not render an answer to the

question referred for a preliminary ruling obsolete either. In that manual, the use of D-mannose to prevent urinary tract infections was mentioned as an example of a pharmacological (and not a physical) action of a medicinal product. However, the views of the Commission expressed in the manual are not binding […]. On the contrary, it expressly states that only the Court of Justice of the European Union can give an authoritative interpretation of Community law […].

[…]