PREU BOHLIG & PARTNER

Challenges in the demarcation of material medical devices.

Differences between legal and scientific assessment.

Peter v. Czettritz, Preu Bohlig & Partner
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Demarcation Medical Device – Medicinal Product

Definition Medical Device: § 3 Nr. 1 MPG

1. Medical devices are all instruments, apparatus, appliances, software, **substances or preparations made from substances** or other articles, used alone or in combination, including the software intended by the manufacturer to be used specifically for diagnostic or therapeutic purposes and necessary for the medical device's proper application, **intended by the manufacturer to be used for human beings, by virtue of their functions, for the purpose of**

   a) diagnosis, prevention, monitoring, treatment or alleviation of disease, ...

   and which **do not achieve their principal intended action** in or on the human body **by pharmacological, immunological or metabolic means,** but which might be assisted in their function by such means.

Demarcation Medical Device – Medicinal Product

Definition Medicinal Product: § 2 Abs. 1 AMG

(1) Medicinal products are substances or preparations made from substances which:

1. are intended for use on or in the human or animal body and are intended for use as remedies with properties for the curing, alleviating or preventing of human or animal diseases or disease symptoms **(medicinal product by presentation)** or

2. can be used in or on the human or animal body or can be administered to a human being or an animal, either:

   a) to restore, correct or to influence the physiological functions through a pharmacological, immunological or metabolic effect **(medicinal product by function)**, or

   b) to make a medical diagnosis.

Demarcation Medical Device – Medicinal Product

§ 2 Abs. 3 AMG

The term ‚Medicinal Product' shall not apply to:
1. foodstuffs
2. cosmetic products

…

7. medical devices and assessories for medical devices within the meaning of §3 of the Medical Devices Act unless they are medicinal products within the meaning of section 2 sub-section 1 number 2 letter b…

The In-Case-of-Doubt Regulation: § 2 Abs. 3 a AMG

(3a) Medicinal products are also products which are or contain substances or preparations made from substances which, taking into account all the properties of the product, fall under the definition contained in sub-section 1 and, at the same time, can fall under the definition of a 'product' pursuant to sub-section 3.

Demarcation Medical Device – Medicinal Product

MEDDEV 2.1/3 rev. 3 – Definition of a pharmacological means:

"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.

Demarcation Medical Device – Medicinal Product

VG Köln, Decision of 14.10.2009 – Case No. 24 K 4394/08 (Cistus incantus)

- The products in dispute were medicinal products by presentation according to § 2 Abs. 1 Nr. 1 AMG, because the products were marketed with a package leaflet and the intended purpose of prevention and supplementary treatment of colds and viral diseases
- The medicinal characteristic would not be excluded according to § 2 Abs. 3 Nr. 7 AMG, because it remained uncertain, whether the products had a physical or pharmacological effect
- This was not to be pursued further according to § 2 Abs. 3a AMG
- The In-case-of-Doubt Regulation served for legal security of borderline products. Its application required, that the medicinal properties of a product could be assessed positively, which was the case here.
- Remaining doubts shall be to the detriment of the plaintiff

Demarcation Medical Device – Medicinal Product

OVG NRW Decision of 15.03.2010 Case No. 13 A 2612/09:

- The products in dispute would fulfill the requirements of a medicinal product by presentation according to § 2 par. 1 No. 1 AMG, which also had not been questioned by the plaintiff.
- From the In-case-of-Doubt Regulation it followed, that substance based medical devices in general fall under the definition of a medicinal product by presentation according to § 2 par. 1 No. 1 AMG due to their intended medical purpose.
- § 2 par. 3 a AMG would therefore be applicable, if the preparation falls under the definition of a medicinal product by presentation and could also fall under the definition of a product according to § 2 par. 3 AMG, if the intended purpose assumed by the manufacturer is not sufficiently supported by scientific evidence, primary medicinal effects however can also not be excluded.

Demarcation Medical Device – Medicinal Product

BGH Decision of 10.12.2009 Case No. I ZR 189/07 Golly Telly

Guiding principle:

> „A bowel rinse solution (prep), which achieves its effect by an osmotic and physical effect, is no medicinal product, but a medical device.“

In this procedure on a Macrogol rinse solution (Golly Telly) produced by a pharmacist the senat set aside the judgement of the OLG Hamburg (Decision of 11.10.2007, 3 U 127/06, PharmaRecht 2008, 448) based on AMG and sentenced the defendant only with respect to a violation of MPG (Marketing without CE mark) in the light of his alternative claim.

Demarcation Medical Device – Medicinal Product

BGH, Decision „Golly Telly“ – follow-up

On the basis of the findings the intended purpose of the product is the cleaning, i.e. emptying of the intestines, which is achieved by Macrogol raising the water content in the intestines due to the osmotic pressure and by hydrogen bonds, by which the existing feces are hydrated and its volume is increased, which causes a pressure on the intestine wall on which it reacts with the defaecation reflex.

Therefore the intended purpose of the preparation is neither achieved pharmacologically nor metabolically, but primarily by an osmotic and then physical way.

Without the BGH having mentioned it explicitely, he in this respect orientated himself on the MEDDEV and the definition of a pharmacological effect included there.

Demarcation Medical Device – Medicinal Product

OLG Köln, 11.12.2009 – Case No. I-6 U 90/09 „Macrogol“

- Macrogol primarily triggers a reflex by the fact that due to the softening of the feces and the enlargement of its volume, pressure is applied to the intestine wall. Thereby the intestinal muscles are stimulated to an intensified activity, which does not correspond anymore to its natural bodyfunctions and body´s natural processes and which therefore is no natural physiological process anymore.
- The demarcation according to the standards of the MEDDEV-Guidelines would only be theoretical, however not suitable in practice for demarcation.
- Relevant and necessary with respect to the goal to find an appropriate balance between health protection and free movements of goods, remains the overall balance on a case-by-case basis. Remaining doubts concerning the classification as medicinal product or medical device result in a classification as medicinal product.

Demarcation Medical Device – Medicinal Product

BGH – Decision of 24.11.2010, File No. I ZR 204/09 „Darmreinigungspräparat“

The BGH confirmed the decision of the OLG Köln and came to the conclusion that the products were medcinal products by function.
Relevant for the demarcation of borderline products is the intended primary effect which had to be determined in each individual case and all characteristics of the product were to be evaluated.
The regulation in Art 2 par. 2 Dir 2001/83/EC however stipulates that not only the primary effect of a product needed to be assessed but also side- and follow-up effects are to be considered.
Therefore a product has to be classified as medicinal product by function even if its primary effect is purely physical but triggeres further effects which are pharmacological and which represent the intended primary effect.
Since Magrogol had significant effects on the body functions and provoked physiological effects which could not be triggered in that way by food this has to be considered a pharmacological effect.

Demarcation Medical Device – Medicinal Product

BGH, 05.10.2010, Case No. I ZR 90/08 „Mundspüllösung“

Guiding principle:

„The interaction necessary to affirm a pharmacological effect of asubstance between its molecules and body cells also exists, if the molecules prevent an effect of other substances on the body cells which would otherwhise exist.“

The mouth rinse in dispute containing Chlorhexidine was marketed as cosmetic product and advertised as follows: „Mouth rinse for oral hygiene, reduces bacterial plaque and prevents its reformation, protects the gums and contributes to preserving oral health.“

The district court as well as the higher district court have dismissed the claim, because the mouth rinse was neither a medicinal product by function nor a medicinal product by presentation.

Demarcation Medical Device – Medicinal Product

BGH - „Mundspüllösung“ – follow up

The BGH comes to the conclusion, that the preparation has rightly not been considered a medicinal product by presentation. Because the consumer was given the impression that it was a product which was to be applied in the oral cavity of humans for cleaning and preserving a good condition, it would fulfill the requirements of a cosmetic product. The previous instances however had wrongly denied the pharmacological effect of the preparation.

In assessing whether a preparation has a pharmacological effect, one could orientate oneself on the definition of the term „pharmacologic“ in the guideline on the demarcation of medicinal products and medical devices (MEDDEV).

Demarcation Medical Device – Medicinal Product

BGH - „Mundspüllösung“ – follow up

Accordingly a pharmacological effect existed not only if the interactions of the molecules of the substance in question and a cellular constituent (receptor) resulted in a direct reaction (answer), but also, if the reaction of another agent is blocked.

Therefore, for the assumption of a pharmacological effect, any interaction between the molecules of the substance in question and the cellular constituent was sufficient. Since Chlorhexidine reacted with constituents of bacterial cells, a pharmacological effect could not be excluded from the start.

Because the MEDDEV in one chapter explicitely classifies Chlorhexidine as medicinal substance and Chlorhexidine was inter alia suitable to heal Gingivitis, the appeal court therefore would have to assess this further.

Demarcation Medical Device – Medicinal Product

BGH Decision of 24.06.2010, Case No. : I ZR 166/08 „Photodynamische Therapie“

Guiding principle:

„On the decisions to be taken on a case-by-case basis, whether a product is a medicinal product (by function) or a medical device, besides its direct effects also its side- and consequential effects have to be considered, and if they lie in the immunological, metabolic or pharmacological field lead to its classification as medicinal product.“

The product in dispute was marketed as medical device for the defense against certain tumors in the course of a photodynamic Therapie.

Demarcation Medical Device – Medicinal Product

BGH „Photodynamische Therapie“ – follow up

The agent is applied intravenously after dissolution in a saline solution and reaches by spreading through the body also the tumor tissue. There the agent is enriched and transmits energy to the oxygen dissolved in the cells when returning from an exciting state, caused by laser light to its ground state. This so called singulett oxygen, which is generated from the oxygen molecules altered by laser light, then leads to death of the tumor cells. The agent itself is not changed in the course of the treatment and is eliminated from the body unmodified.

Demarcation Medical Device – Medicinal Product

BGH „Photodynamische Therapie“ – follow up

The OLG Hamm assumed a pharmacological effect because the agent was in the course of its cascade of effects intended to be applied in the human body for influencing human physiological functions.

According to the BGH the intended main effect was not the primary effect of the agent which was physical, but the further effects triggered thereby, which were pharmacological.

Again the BGH then consults the MEDDEV-Borderline-Guideline. Accordingly a pharmacological effect would be an interaction between the molecules of the substance in question and a cellular constituent (receptor), which resulted either in a direct reaction (answer) or which blocked the reaction (answer) of another agent.

Demarcation Medical Device – Medicinal Product

BGH - „Photodynamische Therapie“ – follow up

The guideline would therefore not require a direct interaction with „cellular constituents of the user“, but consider sufficient any interaction between the molecules of the substance in question and „a cellular constituent“.

From the In-case-of-doubt Regulation in Art. 2 par. 2 of Directive 2001/83/EC it would result, that the decision to be taken on a case-by-case basis, whether a product is a medicnal product by function, all its properties need to be considered. Therefore in borderline-cases, especially also the side- and consequential effects of an agent are to be brought in account, and if they would lie in the pharmacological area as it was here, this results in a classification as medicinal product by function.

Demarcation Medical Device – Medicinal Product

ECJ – Case C- 109/12, 03.10.2013, „Laboratoires Lyocentre“

In this case the ECJ took a fundamental decision on the demarcation of medical devices and medicinal products.
Matter of the procedure was the question of classification of Gynocaps, vaginal capsules containing live lactobacilli intended to restore balance to the vagina's normal protective bacterial flora.
Until 2008, Gynocaps was marketed in Finland as a 'medical device or accessory', bearing a CE marking. The capsule was also marketed as a 'medical device or accessory' bearing a CE marking in a number of other Member States, including the Kingdom of Spain, the French Republic, the Italian Republic and the Republic of Austria.
The Finnish Authority was informed of the marketing as a medicinal product, of a vaginal preparation similar to Gynocaps, containing live lactobacilli. In the light of that information, the Authority took the view that, taking into account its composition and its mode of action, Gynocaps was not a medical device, but a preparation that may be used as a medicinal product.

Demarcation Medical Device – Medicinal Product

ECJ - Case C- 109/12, 03.10.2013, „Laboratoires Lyocentre“

Guiding principles:

1. The classification of a product in one Member State as a medical device bearing a CE marking, in accordance with Medical Devices Directive 93/42/EEC concerning, does not preclude the competent authorities of another Member State from classifying the same product, on the basis of its pharmacological, immunological or metabolic action, as a medicinal product within the meaning of Article 1(2)(b) of Directive 2001/83/EC relating to medicinal products for human use.

Demarcation Medical Device – Medicinal Product

ECJ - Case C- 109/12, 03.10.2013, „Laboratoires Lyocentre“

2. In order to classify as a medicinal product in accordance with Directive 2001/83, a product already classified in another Member State as a medical device bearing a CE marking, in accordance with Directive 93/42, the competent authorities of a Member State must, before applying the classification procedure under Directive 2001/83, apply the procedure under Article 18 of Directive 93/42 and, where appropriate, the procedure under Article 8 of Directive 93/42.

Demarcation Medical Device – Medicinal Product

ECJ - Case C- 109/12, 03.10.2013, „Laboratoires Lyocentre“

3. Within the same Member State, a product which, while not identical to another product classified as a medicinal product, none the less has in common with it an identical substance and the same mode of action, cannot, in principle, be marketed as a medical device in accordance with Directive 93/42 unless, as a result of another characteristic that is specific to that product and relevant for the purposes of Article 1(2)(a) of Directive 93/42, it must be classified and marketed as a medical device, which is a matter for the referring court to verify.

Demarcation Medical Device – Medicinal Product

ECJ - Case C- 109/12, 03.10.2013, „Laboratoires Lyocentre“

The ECJ reasoned its decision as follows:

“44 As regards more particularly the distinction between medicinal products and medical devices, Article 1(5)(c) of Directive 93/42 specifically requires the competent authorities to take particular account of the principal mode of action of the product. It thus follows from Article 1(2)(a) of that directive that only a product which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means may be classified as a medical device.

45 None the less, as Union law currently stands, until harmonisation of the measures necessary to ensure the protection of health is more complete, it will be difficult to avoid the existence of differences in the classification of products as between Member States in the context of Directive 2001/83

Demarcation Medical Device – Medicinal Product

ECJ - Case C- 109/12, 03.10.2013, „Laboratoires Lyocentre“

“46 As the Advocate General has stated in point 63 of her Opinion, asymmetries in scientific information, new scientific developments and differing assessments of risks to human health and the desired level of protection can explain why different decisions are taken by the competent authorities of two Member States as regards the classification of a product.

47 In addition, the fact that a product is classified as a medical device in accordance with Directive 93/42 in one Member State does not prevent it being classified, in another Member State, as a medicinal product in accordance with Directive 2001/83 if it displays the characteristics of such a product.”

Demarcation Medical Device – Medicinal Product

ECJ – Case C- 308/11, Decision of 06.09.2012

Here the ECJ took a principle decision on the term „pharmacological action“concerning the interpretation of Article 1(2)(b) of Directive 2001/83/EC. The product in question was a mouthwash solution containing chlorhexidine. It was marketed as a cosmetic product in which chlorhexidine, an antiseptic, accounted for 0.12% of the product contents. It was stated on the packaging ‘Mouthrinse for oral care – Helps reduce dental plaque accumulation – Protects gums and maintains oral health’.
The other party was of the view that this mouthwash was a medicinal product inasmuch as it has a pharmacological action. It would be 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% reduced salivary bacteria and, in this way, had a therapeutic or clinical effect in cases of gingivitis.

Demarcation Medical Device – Medicinal Product

ECJ - Case C- 308/11, Decision of 06.09.2012 – follow up

Guiding principles:

1. Article 1(2)(b) of Directive 2001/83/EC relating to medicinal products for human use, 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.

Demarcation Medical Device – Medicinal Product

ECJ - Case C- 308/11, Decision of 06.09.2012 – follow up

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.

Demarcation Medical Device – Medicinal Product

Summary Assessment

The actual problem in the demarcation between substance-based medical devices and medicinal products has been created by the BGH.

It is a mere result of the discrepancy between the point of view of scientists and the point of view of legal specialists without scientific knowledge.

Thank you for your attention

Preu Bohlig & Partner
Peter von Czettritz
Leopoldstraße 11a
D- 80802 München

Tel: +49 89 383870-0
Fax: +49 89 383870-22
E-Mail: pcz@preubohlig.de
www.preubohlig.de

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