The notion of 'pharmacological action' in the legal concept of medicinal product

A look at the judgment of the Court of Justice in Case C-589/23, *Cassella-med and MCM Klosterfrau*, ECLI:EU:C:2025:173.

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1. 'Pharmacological action' in the definition of medicinal product and its role in the delimitation between medicinal products and medical devices

In European Union law, a double criterion is used to determine what is legally understood as a medicinal product, so that medicinal products can exist according either to their presentation or to their function. Thus, in the current wording 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, a medicinal product is defined as "(a) [a]ny 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" (Article 1(2) of Directive 2001/83/EC).

With regard to the second of these criteria, the EU Court of Justice has held that the concept of medicinal product by function covers "all products which are intended to

restore, correct or modify physiological functions and which may thus have an effect on health in general" [Judgment of 16 April 1991, *Upjohn,* C-112/89], whether they are products with curative or preventive properties, or products which alter physiological functions in the absence of disease (e.g. contraceptive substances) (Judgment of 30 November 1983, *Leeendertwan van Bennekom,* C-227/82).

The concept of 'medicinal product' is to be interpreted broadly

If a substance meets these parameters, it will be legally considered a medicinal product, even if it is not presented as such, and it is also irrelevant whether the substance or product also falls within the regulatory definition of other types of products, such as cosmetics or foodstuffs, since Article 2(2) of Directive 2001/83/EC [introduced by Directive 2004/27/EC expressly taking over what had already been the doctrine of the Court of Justice, in judgments such as that of 21 March 1991, C-60/89, *Jean Monteil, Daniel Samanni*] expressly provides that, "[i]n 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 the provisions of this Directive shall apply".

For its part, the legal concept of medical device is currently set out in Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, which defines it (art. 2.1) as "any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes: diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease; diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability; investigation, replacement or modification of the anatomy or of a physiological or pathological process or state; providing information by means of *in vitro* examination of specimens derived from the human body, including organ, blood and tissue donations; and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means".

Therefore, and as expressly established in Article 1(6) of Regulation (EU) 2017/745, "[i]n deciding whether a product falls under Directive 2001/83/EC or under this Regulation, particular account shall be taken of the principal mode of action of the product". In other words, if the substance has a pharmacological, immunological or metabolic action within or on the surface of the human body, it is a medicinal product, and if not, a medical device

And these same delimitation guidelines were established in the previous Council Directive 93/42/EEC of 14 June 1993 concerning medical devices, repealed by the current Regulation (EU) 2017/745.

2. The Judgment of the Court of Justice of 13 March 2025, C-589/23

2.1. The application of the abovementioned criterion of conceptual delimitation between medicinal products and medical devices causes some difficulties in practice, giving rise to a recent judgment of the Court of Justice which sets out some useful elements in this respect. This is the judgment of the Court of Justice of 13 March 2025, C-589/23, ECLI:EU:C:2025:173.

The case at the heart of this judgment concerns a company which markets as medical device a product "for the treatment and prevention of cystitis (bladder infection) and other urinary tract infections", the main constituents of which are D-mannose and cranberry extract; and another product which does not contain cranberry extract and which is presented "for the prevention and to support the treatment of cystitis (bladder infection) and other urinary tract infections". This company (and another company that advertised the first of the products on its website) are being sued by an association on the grounds that the products in question are not medical devices, but medicinal products, the marketing of which as such has not been subject to the required administrative authorisation.

The German court of first instance upheld the claim, a decision that was affirmed on appeal, on the ground that the products were medicinal products by function, in which a pharmacological action is produced by means of D-mannose, an active substance which, by attaching in urine to the adhesin FimH that is present on *Escherichia coli* bacteria, prevents the latter from adhering to certain structures in the bladder wall.

On appeal on a point of law to the *Bundesgerichtshof* (Federal Supreme Court for Civil and Criminal Matters), the latter referred a question to the Court of Justice for a preliminary ruling, essentially asking whether there is a pharmacological action where a substance (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). Doubts arise in particular because the binding of the substance to the bacteria is reversible.

2.2. The Court of Justice has ruled that the concepts of pharmacological action in the Medicinal Products Directive and the Medical Devices Directive (and now the Regulation) "must therefore be interpreted uniformly". A very useful hermeneutical tool for this purpose is the guidance document adopted by the European Commission's Directorate-General for Enterprise and Industry 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 – MEDDEV 2.1/3 rev. 3", and "MDCG 2022 – 5 Rev. 1 – Guidance on borderline between medical devices and medicinal products under Regulation (EU) 2017/745 on medical devices".

Furthermore, the Court insists that the concept of 'medicinal product', within the meaning of Directive 2001/83/EC, is to be broadly construed (as already emphasised in its judgment of 20 September 2007, *Antroposana and Others*, C-84/06), which means that a narrow interpretation of the concept of 'pharmacological action' is not possible.

2.3. Against this background, the Court of Justice addresses the interpretation of the concept of 'pharmacological action' and states that:

a) the term "designates the effects of a substance on a living organism, notably for therapeutic or preventive purposes";

b) as already held in its judgment of 6 September 2012 in Case C-308/11 *Chemische Fabrik Kreussler*, "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";

c) the type of interaction required is defined relatively broadly in the Meddev Guidance and MDCG Guidance, that is to say, 'between the molecules' or 'typically at a molecular level', so that it cannot, a priori, be required, as MCM Klosterfrau maintains in its written observations, that such an interaction should give rise to a modification of the molecular structure of the cellular constituent in question;

d) the binding of a substance to the cellular constituent in question by means of a hydrogen bond constitutes an interaction that falls within the definition of 'pharmacological means';

e) it does not follow either from Directives 2001/83 and 93/42 or from the guidance documents that the molecules of the substance concerned should necessarily have to interact with a cellular constituent by means of a binding that is permanent, and therefore it cannot be ruled out that a substance whose binding to a cellular constituent is reversible may be regarded as exerting a pharmacological action;

f) the interaction between the substance concerned and the cellular constituent present within the user's organism must result in 'initiation, enhancement, reduction or blockade of physiological functions or pathological processes'; and the process by which a substance attaches to a bacterium and thereby prevents that bacterium from adhering to a human cellular constituent must be regarded as a 'blockade of pathological processes'; and

g) a narrow interpretation of the concept of 'pharmacological action' - excluding interactions consisting, as in the present case, in a reversible binding of a substance to bacteria by means of a hydrogen bond - would jeopardise the objective pursued by that directive of ensuring a high level of protection of human health.