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The concept of unmet medical needs as negative space in EU Pharmaceutical Law: Legal definitions and regulatory reforms

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Abstract: The concept of "unmet medical needs" plays a crucial role in the regulation, development, and reimbursement of medicinal products within the European Union. This paper explores the current legal definition of unmet medical needs in EU law, highlighting its fragmented nature and the implications for pharmaceutical innovation, particularly in areas with few or no satisfactory treatment options. The paper also examines proposed revisions to the EU's general pharmaceutical legislation, which aim to streamline and refine the legal definition of unmet medical needs, thereby enhancing its clarity and importance in EU biolaw. The proposed changes to the definition of unmet medical needs in EU law seek to better incentivize the development of therapeutic innovations for areas of indications that remain inadequately addressed. This paper concludes by assessing the potential impact of these revisions on the future regulatory landscape of pharmaceuticals in the EU.

Keywords: EU pharmaceutical law, market authorization, regulatory incentives, orphan medicinal products, market failures.

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The concept of unmet medical needs as negative space in EU Pharmaceutical Law*

Legal definitions and regulatory reforms

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Introduction

There exists no uniform common concept of "unmet medical needs" that is recognised across stakeholder groups in relation to the development, regulation, and reimbursement of medicinal products.[1] In general, stakeholders in pharmaceutical policymaking agreed that the dearth of available alternative treatments is a key characteristic of an unmet medical need that can be addressed by pharmacotherapies.[2] By this broad understanding, unmet medical needs exist for a range of conditions affecting large and small patient populations.[3] These needs are the result of a lack of pharmaceutical innovation for certain diseases, conditions, or functions. Prominent examples include the weak track record of biomedical innovation for some neurodegenerative diseases (e.g. Alzheimer's and Huntington's diseases) and genetic conditions, conditions affecting children, and reproductive health.[4] These unmet needs persist because of the challenges of a market-driven model of research and development (R&D) that generally incentivises innovation for "profitable" conditions, such as conditions affecting many people and/or wealthy populations.[5]

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1 Stakeholders include regulatory and health technology assessment bodies, industry associations, payer networks, healthcare professionals, patient organisations, and the World Health Organization as described by R. A., Vreman, I., Heikkinen, A., Schuurman, C., Sapede, J. L., Garcia, N., Hedberg, . . . & W. G., Goettsch, "Unmet medical need: an introduction to definitions and stakeholder perceptions," *Value in health*, volume 22, issue 11, 2009, p. 1276.

2 R. A., Vreman, et al., *op. cit.*, p. 1276.

3 Z., Kusynová, G. M., Pauletti, H. A., van den Ham, H. G. M., Leufkens, & A. K., Mantel-Teeuwisse, "Unmet medical need as a driver for pharmaceutical sciences–a survey among scientists," *Journal of Pharmaceutical Sciences*, volume 111, issue 5, 2022, p. 1323.

4 Z., Kusynová, et al., *op. cit.*, p. 1323.

5 M., Mazzucato, & Li, H. L., "A market shaping approach for the biopharmaceutical industry: governing innovation towards the public interest," *Journal of law, medicine & ethics*, volume 49, issue 1, 2021, p. 39-49.

This model also produces so-called "market failures," which are medicinal products that are clinically needed but that the drug development pipeline has failed to deliver because the market incentive is too weak (i.e. not profitable enough) to motivate a pharmaceutical company to take the risk of R&D in this area. Examples of market failure innovations are often diagnostic, preventative and/or therapeutic alternatives for diseases of poverty, neglected (tropical) diseases, pandemic pathogens, and antibiotics, among others.

There is a societal imperative for defining the legal concept of unmet medical needs and for designing regulatory interventions to incentivise pharmaceutical innovation to address those needs. Patients experience a host of unmet medical needs for medicinal products that have not been developed or marketed yet, and if they have, then the existing alternatives offer limited therapeutic value for patients (for example, possibly because they also cause severe side effects, have formulations that are difficult to administer in the target population, etc.). There are a range of policy interventions that could incentivise the development and marketing of new diagnostic, preventative or therapeutic alternatives to meet these unmet needs.[6] These policy interventions may be applied at different points in the lifecycle of a medicinal product (e.g. at the point of research and development, market approval, price determination, or reimbursement/insurance coverage).[7]

In response to these challenges, the EU has adopted regulatory incentives and pathways to attempt to address unmet medical needs for diagnostic, preventative or therapeutic methods.[8] However, the current package of regulatory incentives has been insufficient to fully address gaps in biomedical innovation. For instance, the European Commission's evaluation of the Paediatric and Orphan Regulations reported that these regulations have fostered the development and marketing of some medicines for children and for patients with rare diseases, these particularly for more profitable therapeutic indications, sometimes where multiple treatments are already available. Yet, these Regulations have not stimulated innovation in areas where the medical needs are the greatest.[9]

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6 E., Torreele, et al., "From private incentives to public health need: rethinking research and development for pandemic preparedness," *The Lancet Global Health*, volume 11, issue 10, 2023, e1658-e1666.

7 Chan, A. Y., et al., "Access and unmet needs of orphan drugs in 194 countries and 6 areas: a global policy review with content analysis," *Value in Health*, volume 23, issue 12, 2020, p. 1580-1591.

8 Note that these regulatory incentives and pathways are just one approach to "pull" biomedical innovations to the market. The EU also offers "push" incentives such as biomedical R&D funding (sometimes specifically for unmet medical needs), which is not addressed in this paper.

9 European Commission, "Joint Evaluation of Regulation (EC) 1901/2006 and Regulation (EC) 141/2000" COM(2020) 2 final. E. Gennet and A. Mahalatchimy, "Orphan Medicines," in S. Garben and L. Gormley (eds), *The Oxford Encyclopedia of* EU *Law* (OUP 2023)

A legal concept of unmet medical needs is required to apply these policy interventions with precision to deliver meaningful benefits for patients, particularly those whose medical needs have long gone under or unaddressed by pharmaceutical innovation. A logical first step towards addressing these gaps requires defining (however broadly or loosely) those conditions or diseases that have few or no diagnostic, preventative, or therapeutic options. For this reason, the legal concept of "unmet medical needs" has been adopted.[10] A core characteristic in the EU's legal definition is that such needs arise due to the dearth of available alternative treatments in the Union.[11] In this paper, we assert that the EU's current legal definition of unmet medical needs represents a "negative space," which are the gaps in methods for diagnosis, prevention and treatment that left among the existing medical innovations. Moreover, we argue that EU lawmakers have instrumentalised the concept of unmet medical needs as a "means" for determining which medicinal products are eligible for conditional marketing approval pathways, rather than delivering new innovations for unmet medical needs as an "end," in itself. The forthcoming revision of the EU's general pharmaceutical legislation proposes to introduce changes to the EU's legal approach to the concept of unmet medical needs, which is an opportunity to address the critiques we raise.[12]

Therefore, this paper interrogates the contours and content of the legal definition of "unmet medical needs," and its position vis-à-vis other regulatory concepts, in EU law. This paper also examines how the legal definition of unmet medical needs would evolve should the European Commission's proposed revisions to the EU general pharmaceutical legislation be adopted in the future. Such an evolution will determine how effectively the EU can address significant gaps in the availability of treatments for conditions that currently lack sufficient medical options.

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[10] See article 4, Regulation 507/2006. This approach is consistent with stakeholders" perceptions of the defining features of the term "unmet medical need," in R. A., Vreman, I., Heikkinen, A., Schuurman, C., Sapede, J. L., Garcia, N., Hedberg, . . . & W. G., Goettsch, "Unmet medical need: an introduction to definitions and stakeholder perceptions," *Value in health*, volume 22, issue 11, 2009, p. 1277.

[11] See article 4, Regulation 507/2006. This approach is consistent with stakeholders" perceptions of the defining features of the term "unmet medical need," in R. A., Vreman, I., Heikkinen, A., Schuurman, C., Sapede, J. L., Garcia, N., Hedberg, . . . & W. G., Goettsch, "Unmet medical need: an introduction to definitions and stakeholder perceptions," *Value in health*, volume 22, issue 11, 2009, p. 1277.

[12] Article 80 of Commission, Proposal for a directive on the Union code relating to medicinal products for human use, and repealing Directive 2001/83/EC and Directive 2009/35/EC COM (2023) 192 final. Commission, Proposal for a Regulation laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency, amending Regulation (EC) No 1394/2007 and Regulation (EU) No 536/2014 and repealing Regulation (EC) No 726/2004, Regulation (EC) No 141/2000 and Regulation (EC) No 1901/2006 COM (2023) 193 final.

This paper is organised in the following parts. The second part describes and analyses the EU's legal concept of an unmet medical need including the meaning of sub-concepts in the legal definition (i.e. "condition," "satisfactory," "method," "major therapeutic advance"). The third part briefly describes the proposed revisions to the legal definition of unmet medical needs foreseen in the review of the EU's general pharmaceutical legislation, initiated by the European Commission in 2023. The revision bundles five EU laws into a proposed Regulation and a Directive, which sketches the EU's direction of travel in relation to incentives for pharmaceutical innovations.[13] Finally, the fourth part synthesises the scope and content of the EU's legal definition of unmet medical needs and looks forward towards the potential changes to the legal concept that the EU's revision of the pharmaceutical legislation may bring.

I. Limited scope of the legal concept of an unmet medical need in current EU law

This part interrogates the contours of the legal concept of unmet medical needs in EU law. Before delving into this discussion, it is important to take note of the position and purpose of this concept within EU pharmaceutical law. First, the concept of "unmet medical needs" is defined in Commission Regulation (EC) 507/2006 in relation to the criteria for granting a conditional market approval to a medicinal product.[14] The EU's functional definition[15] considers unmet medical needs as those health needs satisfying one of two criteria found in Commission Regulation (EC) 507/2006:

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[13] These 6 EU laws constituting "EU pharmaceutical law" are: Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products [2000], *OJ L* 18/1. 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 [2001], *OJ L* 311/67. Regulation (EC) No 726/2004 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 [2004], *OJ L* 136/1. Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use [2006], *OJ L* 378/1. Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products [2007], *OJ L* 324/121. Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use [2014], *OJ L* 158/1.

[14] Commission Regulation (EC) 507/2006 of 29 March 2006 on the Conditional Marketing Authorisation for Medicinal Products for Human Use Falling within the Scope of Regulation (EC) No 726/2004 of the European Parliament and of the Council [2006], *OJ L* 92/6.

[15] By "functional definition," we aim to highlight that, within the context, the way the legislator decided to define the concept shows a concern with the the role it plays and the purposes it serves for providing market access.

1. a condition for which there exists no satisfactory method of diagnosis, prevention or treatment authorised in the Community, or
2. even if such a method exists, in relation to which the medicinal product concerned will be of major therapeutic advantage to those affected.[16]

Establishing the legal concept of an unmet medical need appears not to be the "end" intention of the lawmaker, but rather the lawmakers." Intention is to develop criteria for determining what is an unmet medical need as a "means" to grant access to the conditional marketing approval pathway. New medicinal products for certain conditions that otherwise lack any or satisfactory alternatives may seek a conditional market authorization. A conditional approval attempts to serve the public health and industrial interests of making a promising product available on the EU market sooner and based on less comprehensive data than is required by the standard centralised EU market approval procedure.[17] In this way, the EU has attached certain market rewards (i.e. faster market access) to medicinal products deemed to respond to an unmet need for a diagnostic, preventative or therapeutic product on the single market. Other EU incentives (e.g. market exclusivity) also exist for medicinal products that satisfy the unmet medical need criterion alongside other criteria (e.g. orphan drug designation).

Second, the EU's current concept of "unmet medical needs" does not appear in a unified article in the main EU legal texts governing the single pharmaceutical market. Instead, the concept is currently established by reading articles 2 and 4 together in Commission Regulation (EC) 507/2006. While Article 4(2) provides specific criteria for identifying unmet medical needs, the broader regulatory framework remains flexible and open-ended, allowing it to evolve with medical innovation.

The following sections will explore how the concept of unmet medical needs functions within the EU legal framework, focusing first on its role in defining areas where innovation is needed (A), and then examining the specific areas of indications identified as having unmet medical needs under EU law (B).

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[16] Commission Regulation (EC) 507/2006 of 29 March 2006 on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC) 726/2004 of the European Parliament and of the Council [2006], *OJ L* 92/8, Article 4.

[17] In the centralised procedure, applications are submitted by pharmaceutical manufacturers to the European Medicines Agency (EMA), which evaluates the quality, safety, and efficacy of the medicines through scientific assessments by committees and experts, notably the Committee for Medicinal Products for Human Use (CHMP). Based on the CHMP recommendation of the benefit-risk balance, the European Commission decides whether or not to authorize the product for sale on the single market.

A) A flexible definition of negative spaces

The EU's legal concept of unmet medical needs is focused on the intended use of the end product, not on the process of developing or manufacturing it, nor on the nature of the product itself. These general characteristics give regulators a degree of flexibility to apply the contours of the concept to the dynamic reality of continuously evolving innovation. Consequently, such general characteristics do not allow for specific unmet medical needs to be pre-determined by lawmakers. Therefore, the concept of unmet medical needs in EU law can be seen as the hole in a donut: they are the gaps left among the existing diagnostic, preventative and/or therapeutic options that are left unaddressed by past innovations. Unmet medical needs exist in the negative space (i.e. the hole) among innovative medicinal products (i.e. the donut). The holes within the centre of the three donuts represent the lack of new methods for diagnosis, prevention and treatment methods that are of major therapeutic advantage to those who need them.

Image credits: Alexas_Fotos

Recalling the EU's functional definition of unmet medical needs in Commission Regulation (EC) 507/2006, it hinges on the scope of four key sub-concepts within the main concept of unmet medical need, "condition," "satisfactory," "method of diagnosis, prevention or treatment," "major therapeutic advantage," which will each be discussed in turn.

First, the term "condition" is not explicitly defined in Commission Regulation (EC) 507/2006. Nevertheless, the term allows for a much wider scope of application to the range of human states that would benefit from pharmacotherapies, than the term "disease" typically would allow for. Although there is no common agreement on the scope of the term "disease'[18][19], it is commonly associated with a dysfunction

[18] M. J., Walker, & W. A., Rogers, "A new approach to defining disease," *Journal of Medicine and Philosophy: A Forum for Bioethics and Philosophy of Medicine,* volume 43, 2018 p. 408-412.

[19] The US National Cancer Institutes defines a disease as "an abnormal condition that affects the structure or function of part or all of the body and is usually associated with specific signs and symptoms." in National Cancer Institute, *NCI Dictionary of Cancer Terms* (*National Institutes of Health*, 2 October 2011) (accessed 16 June 2024).

of the human body, that is "harmful, causing suffering or incapacitation, in principle explainable in terms of facts about human biology and psychology; and is beyond the direct conscious control of the individual."[20] This definition of disease does not catch different states or "conditions" of the human body that may be part of normal functioning unrelated to disease, such as the aging body, reproductive health and control over one's reproduction, and antimicrobial resistance, which is not necessarily a disease. Indeed, pharmaceuticals can be beneficial for addressing, alleviating, or controlling some of these "conditions" that stretch beyond the common understanding of a "disease."

Second, the EU's definition of unmet medical needs incorporates the concept of a "satisfactory" method of diagnosis, prevention, or treatment authorised for marketing within the Community.[21] In the absence of a definition in EU hard law, we turn to the soft law guidance from the EMA, which does not explicitly define how to determine what is "satisfactory," beyond indicating that an unmet medical need must be adjudicated on a case-by-case basis.[22] Additionally, according to the EMA, justifications "should quantify the unmet medical need based on medical or epidemiologic data".[23]

Third, the EU's definition of unmet medical needs includes the term any "method of diagnosis, prevention or treatment'. Although this language suggests unmet medical needs may apply to a wide scope of methods of diagnosis, prevention, or treatment, the actual scope is narrowly focused on medicinal products.[24] Unmet medical needs—as a concept—serves the purpose of Commission Regulation (EC) 507/2006, which is to establish rules for granting conditional market authorization to medicinal products for human use.[25]

Fourth, the EU's definition includes cases in which the medicinal product in question would confer a "major therapeutic advantage" beyond these existing methods.[26] A major therapeutic advantage is demonstrated through enhanced efficacy and/or improved safety compared to existing alternatives.[27] Exceptionally, a "major

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20 Walker & Rogers, *op. cit.*, p. 412.

21 Commission Regulation (EC) 507/2006, Article 4.

22 Committee for Medicinal Products for Human Use, Guideline on the scientific application and the practical arrangements necessary to implement Commission Regulation (EC) No 507/2006 on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC) No 726/2004, EMA/CHMP/509951/2006, Rev.1, 2016, p. 8.

23 Committee for Medicinal Products for Human Use, *op. cit.,* p. 8.

24 Commission Regulation (EC) 507/2006, Article 2.

25 Commission Regulation (EC) 507/2006, Article 2.

26 Commission Regulation (EC) 507/2006, Article 4.

27 For example a product that has "an impact on the onset and duration of the condition, or improving the morbidity or mortality of the disease" see p. 9 of EMA/CHMP/509951/2006, Rev.1 and EMA Regulatory Affairs Office, "'Significant Benefit' across provisions" (*STAMP*, 3 December 2018) (accessed 15 February 2024).

improvement" to patient care[28] will also be considered by the drug evaluators.[29] "Robust evidence. . . normally from well conducted randomised controlled trials" is required by the EMA from the applicant to demonstrate the above advantages over available products.[30] These guidelines offer a general scope of what may constitute a "major therapeutic advantage"; however, the precise determination is to be made on a case-by-case basis using the available evidence.

Regarding the geographical scope of unmet medical needs considered under EU law, the first criterion uses the term "in the Community," which indicates that the European lawmaker has limited this aspect of unmet medical needs to those in the Union and intentionally excluded needs that remain important but unsatisfied outside the EU's borders (e.g. neglected tropical diseases). Although the law is unclear about the express territorial scope of this second criterion, it would be reasonable to assume that it is also limited to products marketed on the EU territory as it refers to part of the first criterion. Understanding the flexible definition of unmet medical needs provides the context for evaluating the specific areas of indications that qualify medicinal products for conditional market authorization within the EU regulatory framework.

B) Towards a definition based on a list of areas of indications

Building on this definition, EU law specifies three indications of medicinal products that may seek a conditional market authorization. These indications, defined in article 2 of Commission Regulation (EC) No 507/2006, may, by extension, be considered to illustrate the scope of the concept of unmet medical needs. The following medicinal products may seek a conditional market authorisation: Medicinal products. . .

1. for the diagnosis, prevention, or treatment of "seriously debilitating diseases or life-threatening diseases";
2. for medicinal products "to be used in emergency situations, in response to public health threats duly recognised either by the World Health Organisation or by the Community;"[31]
3. for medicinal products "designated as orphan medicinal products."[32]

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[28] For example, a product that permits ambulatory or community care rather than requiring hospital admission. See p. 9 of EMA/CHMP/509951/2006, Rev.1 and EMA Regulatory Affairs Office, "'Significant Benefit' across provisions" (*STAMP*, 3 December 2018) (accessed 15 February 2024).

[29] Office, "'Significant Benefit' across provisions" (*STAMP*, 3 December 2018) (accessed 15 February 2024).

[30] Committee for Medicinal Products for Human Use, Guideline on the scientific application and the practical arrangements necessary to implement Commission Regulation (EC) No 507/2006 on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC) No 726/2004, EMA/CHMP/509951/2006, Rev.1, 2016, p. 9.

[31] Decision (EC) 2119/98/EC of the European Parliament and of the Council of 24 September 1998 setting up a network for the epidemiological surveillance and control of communicable diseases in the Community [1998], *OJ L* 268/1.

[32] Commission Regulation (EC) 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products [2000], *OJ L* 18/2, Article 3.

By adopting a finite list of areas of indications, EU lawmakers signal that there is a limited scope of conditions that may have unmet medical needs and are entitled to receive priority treatment (namely a conditional market authorization) under EU pharmaceutical law.

II. A guiding legal concept of unmet medical needs in the proposed revision to the EU's pharmaceutical legislation

This section explains the revised definition of an unmet medical need in the proposed Directive.[33]

First, it is noteworthy that in the proposed legal text, the EU's definition of an unmet medical need is no longer spread over multiple articles (articles 2 and 4 of Commission Regulation (EC) 507/2006) that serve to govern which products may access the conditional market approval pathway. Instead, article 83 of the European Commission's proposal for a Directive collects and streamlines the definition of and criteria to assess medicinal products addressing an unmet medical need. It also explains the relationship between this definition and related concepts (e.g. orphan medicinal products). Article 83 is referenced throughout the European Commission's legislative proposals to support different regulatory incentives. By streamlining the definition of unmet medical needs in a single article, the European Commission's proposal gives the concept more visibility and prominence as a guiding concept in the EU's governance of its pharmaceutical market.

Second, the revised definition builds on the existing definition in EU law and adds additional specificity to focus on persistent needs determined by the European Commission to be diseases without or only with suboptimal or highly burdensome treatments, or with treatments targeting only sub-populations of a disease.[34] According to the revised definition, an unmet medical need must satisfy two requirements:

> (a) there is no medicinal product authorized in the Union for such disease, or, where despite medicinal products being authorized for such disease in the Union, the disease is associated with a remaining high morbidity or mortality;
>
> (b) the use of the medicinal product results in a meaningful reduction in disease morbidity or mortality for the relevant patient population.

[33] Commission, Proposal for a directive on the Union code relating to medicinal products for human use, and repealing Directive 2001/83/EC and Directive 2009/35/EC COM (2023) 192 final.

[34] Commission, Proposal for a directive, article 83.

The introduction of qualifying sub-concepts such as a "meaningful reduction in disease morbidity or mortality" into the definition is an attempt to catch only those products whose use has "meaningful" impacts on disease severity.[35] This evolved definition in part (a) moves away from focusing purely on the presence or absence of alternative methods of diagnosis, prevention, or treatment (as is done in the current definition) towards instead recognizing the clinical importance of the new product for the patient. One could consider this revised definition to be a step towards placing the patient's needs at the centre of EU regulatory incentives. Additionally, the revised definition introduces an added layer of objectivity to the determination of an unmet medical need. The revised definition employs more specific terms such as "no authorized product" (instead of the current phrase: no "satisfactory method" authorized), and a "meaningful reduction in morbidity or mortality" (instead of the current term: "major therapeutic advantage"). Although both terms in the revised definition deserve further specification at an operational level, the EU lawmaker has made additional efforts to narrow the scope of application compared to the language in existing legislation. This specification is likely proposed by the European Commission in response to the finding that the current regulatory incentives (and by extension, the definition of unmet medical need) has delivered new products to the market for the more profitable indications while neglecting areas of greatest medical need.[36]

Moreover, the proposed definition of unmet medical needs unifies the concept in a single article that includes more specific sub-concepts than current legal definition. First, products for unmet medical needs must, according to the European Commission's proposal, explicitly address therapeutic indications for "a life threatening or severely debilitating disease."[37] In the current legislation, the link between disease severity and unmet medical needs is established by reading articles 2 (on scope) and 4 (on requirements) together to determine when a product may be eligible for a conditional market authorisation.[38] Second, designated orphan medicinal products are explicitly classified as addressing unmet medical needs in the European Commission's proposal.[39] By contrast, the current legislation implies that designated orphan medicinal products must address an "unmet medical need" to be eligible for a conditional market approval but does not clarify the relationship between the two concepts.[40]

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35 Commission, Proposal for a directive, article 83.

36 Commission, Evaluation of Regulations 1901/2006 and 141/2000; E. Gennet and A. Mahalatchimy.

37 Commission, Proposal for a directive.

38 Commission Regulation (EC) 507/2006.

39 Commission, Proposal for a directive, article 83.

40 Commission, Proposal for a directive, article 83 (2); Commission Regulation (EC) 507/2006, article 4.

The European Commission's proposal also introduces an extension of the concept of unmet medical needs targeting orphan indications without existing treatments or those offering exceptional therapeutic advancements: the high unmet medical needs.[41] The purpose of introducing this conceptual extension is to differentiate between orphan products for therapeutic areas "where research is most needed and investment is riskier"[42] and products for orphan products for "well-established use" that have required less investment than the former.[43] The European Commission's proposal offers extended market exclusivity to incentivise products targeting areas where needs are greater. According to the European Commission's proposals, orphan medicinal products for high unmet medical needs will need to satisfy the criteria for an unmet medical need (article 83 of the proposed Directive), and where other medicinal products are already authorised for the same condition, then the orphan product will need to demonstrate that it has a "significant benefit" and will bring "exceptional therapeutic advancement'.[44] The act of adopting conceptual extensions into a legal definition also further embeds and strengthens the visibility of the overarching legal concept of unmet medical needs.

Conclusions

The EU applies a "negative" concept of unmet medical needs (in relation to medicinal products), in that such needs are produced by and occupy the "negative space" (or the dearth of clinical alternatives) left by existing medical innovations. The EU's concept of unmet medical needs is functional in that it primarily exists to as a criterion to assess which medicinal products may access a conditional market approval pathway. To qualify as an "unmet medical need," EU law currently provides broad principles concerning the availability of alternative medicinal products and an indicative list of the areas of indications for which unmet medical needs will be recognised. It can be deduced from the EU's hard and soft law on the subject that unmet medical needs must be quantifiable and manifest, and the burden of proof rests on the pharmaceutical manufacturer seeking conditional market authorisation for its product. The EU's definition expresses solidarity with patients with rare or orphan conditions, even though the position of these related concepts (i.e. of unmet medical needs and orphan status) vis-à-vis the other are not well explained in current EU law.

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41 Commission, Proposal for a Regulation laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency, amending Regulation (EC) No 1394/2007 and Regulation (EU) No 536/2014 and repealing Regulation (EC) No 726/2004, Regulation (EC) No 141/2000 and Regulation (EC) No 1901/2006 COM (2023) 193 final, article 70.

42 Commission, Proposal for a Regulation COM (2023) 193 final, p. 15-16, Explanatory Memorandum.

43 Commission, Proposal for a Regulation COM (2023) 193 final, recital 102.

44 Commission, Proposal for a Regulation COM (2023) 193 final, article 70 (1)(a).

For these reasons, the revision of the general EU pharmaceutical legislation holds potential to streamline the legal definition of unmet medical needs into a single article and in relation to related concepts, such as orphan products. Moreover, EU lawmakers have introduced more specificity into the language defining an unmet medical need (compared to the terminology in the existing legal definition). This unified approach to the definition, combined with extension of the concept to "high" unmet medical needs, elevates the importance of unmet medical needs as a guiding concept in EU pharmaceutical regulation. This observation is consistent with the European Commission's own motivation for the legislative review, which focuses heavily on the unmet medical needs that patients experience despite having certain regulatory incentives for new pharmacotherapies in place over the last 20 years (e.g. market exclusivities for orphan products). At the time of writing, the review of the EU's general pharmaceutical legislation is ongoing; time will tell whether the EU lawmaker retains this proposal for a clearer, more prominent legal definition of unmet medical needs in relation to the regulation of pharmaceuticals on the single market.