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# Open Public Consultation on the revision of EU rules on medicines for children and rare diseases

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## Introduction

The EU rules on medicines for rare diseases and medicines for children were adopted in 2000 and 2006, respectively. The rules were designed to improve the treatment options available to 30 million European patients affected by one of over 6000 rare diseases, as well as for 100 million European children affected by paediatric diseases. At the time, there were limited or no medicinal products available for treatment of both groups.

A recent evaluation of the rules showed that they have stimulated research and development of medicines to treat rare diseases and other conditions affecting children. However, the evaluation also revealed shortcomings in the current system. The rules have not been effective for stimulating the development of medicines in areas of unmet needs (e.g. 95% of rare diseases still have no treatment option), and they have not ensured that the medicines are accessible to all European patients across all Member States.

The rules provide incentives and rewards, and their design can influence business decisions on research and development for new medicines, as well as whether such investment can be focused in areas of the greatest need for patients. In addition, the system of incentives can impact market competition and indirectly influence the availability of and access to those medicines by EU patients.

## About you

* I am giving my contribution as

- ○ Academic/research institution
- ○ Business association
- ○ Company/business organisation
- ○ Consumer organisation
- ○ EU citizen
- ○ Environmental organisation
- ○ Non-EU citizen
- ◉ Non-governmental organisation (NGO)

- Romanian
- Slovak
- Slovenian
- Spanish
- Swedish

## Questionnaire on the revision of EU rules for medicines for rare diseases and children

**Q1: The main problems identified in the evaluation of the legislation for medicines for rare diseases and for children were the following:**

- **Insufficient development in areas of the greatest needs for patients.**
- **Unequal availability, delayed access, and often unaffordable treatments for patients in the EU Member States.**
- **Inadequate measures to adopt scientific and technological developments in the areas of paediatric and rare diseases.**

**In your opinion, are there any other barriers to the development of treatments for rare diseases and children?**

*2000 character(s) maximum*

Varying quality of national assessment processes:Orphan/paediatric medicines often encounter challenges when being evaluated by national assessment/reimbursement processes. These processes are not designed to manage orphan/paediatric medicines which are often high cost, sometimes once-off medicines which have limitations in terms of available clinical data. Greater European cooperation is needed to tailor the national processes to ensure that these medicines receive fair consideration and equal market access (as non-rare/adult counterparts). Member States should also agree to explore joint approaches to assessment/reimbursement to grow their purchasing power and their evidence base.

Low levels of early patient involvement:The absence of early, multi-stakeholder dialogue around unmet needs may lead to lower levels of research and innovation in these areas as the health/business case for investment is not being fully made. Research priorities, especially when supported by public funding, must be transparently identified, and research into specific conditions must not be pushed aside simply because patients are too few in number or their treatment is too commercially uncompetitive. Member States need to share a list of publicly-funded research projects to identify the attention given to rare/paediatric disease and to shore up efforts. Patients must be involved in co-designing research agendas at the national and European level, and initiatives which support education so that patients can learn more about the research lifecycle, such as those organised by EURORDIS and EUPATI, must be supported by public funding.

Weak real world data usage and poor data infrastructure: Challenges associated with clinical trials for rare /paediatric disease may benefit from real-world data to support efficacy/safety claims during assessment processes. Member States need to put the infrastructure in place to collect this data, and regulators need to modernise their decision making.

**Q2: In your opinion, and based on your experience, what has been the additional impact of COVID-19 on the main problems identified through the evaluation? Is there a 'lesson to be learned' from the pandemic that the EU could apply in relation to medicines for rare diseases and children?**

*2000 character(s) maximum*

Perhaps the greatest lesson learnt is a shift in perspective – each and every European now has a tangible understanding of how it feels to have an unmet medical need and to have no means of meeting it, without the help of others. We must reimagine our society so that, in so far as it is possible, no one has to feel this way in the future. This involves adopting a new philiosophy when applying regulations to assessing and making available medicines for rare diseases and children.

COVID has shown us that solutions to some of our greatest health challenges will increasingly lie in our capacity to generate data to inform research and innovation. The EU must show leadership to encourage the integration and interoperability of Member State health information systems up to agreed minimum standards. IPPOSI convened a Citizens' Jury on Access to Health Information in April 2021 to explore public attitudes around who we should share health information with and for what purposes (service improvement, policy development, research, innovation). The findings show support for greater data sharing.

COVID has also shown us that there is an expectation of 'fair return' on publicly-funded investments made in research and innovation. There is also growing debate around certain aspects of intellectual property, risk appropriation, and market supply. The parameters of public-private partnerships may be the focus of increasing public scrutiny, and efforts should be made to lead out on this conversation at an EU level.

**Q3: In your opinion, how adequate are the approaches listed below for better addressing the needs of rare disease patients?**

*at most 4 answered row(s)*

| | Very adequate | Moderately adequate | Not at all adequate |
|---|---|---|---|
| When considering whether a particular medicine is eligible for support, the rarity of the disease – the total number of cases of a disease at a specific time, currently less than 5 in 10 000 people – forms the main element of the EU rules on medicines for patients suffering from rare diseases. | ○ | ◉ | ○ |
| Some diseases occur frequently, but last for a relatively short period of time (for example, some rare cancers). These are covered by the EU rules on medicines for rare diseases and the principle of rarity. However, because many patients acquire such diseases during a specified, limited period of time, those diseases should not be considered as rare in the EU anymore. | ○ | ◉ | ○ |
| Amongst all medicines for rare diseases which become available to the EU patients, only those bringing a clear benefit to patients should be rewarded. Clear rules should apply to decide if one medicine brings a clear benefit to patients when compared to any other available treatment in the EU for a specific rare disease. | ○ | ◉ | ○ |
| Additional incentives and rewards should exist for medicines that have the potential to address the unmet needs of patients with rare diseases, for example in areas where no treatments exist. | ○ | ◉ | ○ |

Other (please suggest any other criteria/approaches you think might be relevant).

*2000 character(s) maximum*

We believe all of the approaches detailed must be guided by a patient perspective. These approaches are nuanced, and it is likely that to be successfully developed and implemented they will need ongoing advise and revision from those most directly affected by their reach – patients.

The designation of less than 5/10000 is broadly perceived among the rare disease patient community as an arbitrary threshold. There are many more considerations in determining whether a disease is rare or not. Some 'rare' cancers may have a higher prevalence, some conditions with a lower prevalence may be 'artificially rare' (low numbers, but familiar to the health system). A designation of ultra-rare might be needed.

The assessment of 'benefit' is highly controversial – clinicians, regulators, payers and patients all have different perspectives. Outcomes identified for assessing benefit must be guided by the patients' lived experience of the disease and their goals for their health future (cures, symptom management, side effects).

The focus of additional incentives and rewards should concentrate on promoting a person-centered approach to medicines research and development. Those that engage in early dialogue with patients, those that create co-designed drug development plans, and those that take on real unmet need should be the primary recipients. A rigorous, independent assessment of existing and new incentives is needed to demonstrate whether they actually contribute to greater access to treatments for patients with unmet.

## Q4: What factors are important to take into consideration when deciding if one medicine for a rare disease brings more benefits compared with other available treatments?

*2000 character(s) maximum*

As mentioned, the assessment of 'benefit' is highly controversial – clinicians, regulators, payers and patients all have different perspectives. Outcomes identified for assessing benefit must be guided by the patients' lived experience of the disease and their goals for their health future

As outcomes preferred by patients are not always easy to measure, approaches must be identified to explore how these can be meaningfully and equally considered as part of the decision-making process. Patients must be involved in designing and evaluating this person-centered approach to outcome decision-making.

Clinical outcomes are important in assessing benefit. It is essential that all Member States have the infrastructure to collect timely and quality real world data. This data must be able to capture outcome variations across sub-sets of the patient community. Healthcare professionals must be able to monitor outcomes with accuracy and efficiency.

Finally, benefit should also go beyond outcomes, into the area of patient preferences. A medicine with comparable benefits should not be excluded if it is able to significantly reduce the burden of disease management, e.g. how a medicine is administered, how frequently it needs to be taken, how severe the side effects, and how successful it is in treating primary and secondary symptoms.

## Q5: What do you consider to be an unmet therapeutic need of rare disease patients and children?

- [x] Authorised medicines for a particular rare disease or a disease affecting children are not available, and no other medical treatments are available (e.g. surgery).
- [x] Treatments are already available, but their efficacy and/or safety is not optimal. For example, it addresses only symptoms.
- [x] Treatments are available, but impose an elevated burden for patients. For example, frequent visits to the hospital to have the medicine administered.
- [x] Treatments are available, but not adapted to all subpopulations. For example, no adapted doses and/or formulations, like syrups or drops exist for children.

Other (please specify).

*2000 character(s) maximum*

Unmet need means different things to different people. Developers of new medicines are required to demonstrate that there is no satisfactory method of diagnosing, preventing or treating a rare condition. However, there is no shared definition of what this means in practice and a legally binding definition may not necessarily be helpful. Also, early dialogue should take place between sponsors, regulators, payers and patients to discuss perspectives around unmet need and to agree where there is value for rare and paediatric patients. Product/medicine development plans should be co-designed.

**Q6: Which of the following measures, in your view, would be most effective for boosting the development of medicines addressing unmet therapeutic need of patients suffering from a rare disease and/or for children? (1 being the least effective, 10 being the most effective)**

*at most 4 answered row(s)*

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| Assistance with Research & Development (R&D), where medicines under the development can benefit from national and/or EU funding | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ◉ |
| Additional scientific support for the development of medicines from the European Medicines Agency | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ◉ |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Assistance with authorisation procedures, such as priority review of the application from the European Medicines Agency and/or expedited approval from the European Commission | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ◉ |
| Additional post-authorisation incentives that complement or replace the current incentives and rewards | ○ | ○ | ○ | ○ | ◉ | ○ | ○ | ○ | ○ | ○ |

Do you have other suggestions that would allow the EU to boost the development of specific medicinal products?

*2000 character(s) maximum*

Development of joint European assessment process
Cooperation in the area of health technology assessment for rare and paediatric disease – could range from helping to improve the evidence-base for national decision-making through joint assessments, to requiring national decision-makers to ensure comparable access to treatments. Cooperation could also include Europe-wide, multi-year purchase agreements, as initiatives like BENELUXA aim to suggest. Support for development needs to go beyond medicines regulation to issues of medicines assessment and reimbursement.

Creation of database of nationally-funding research
A database listing nationally-funded research would allow for greater transparency around prioritisation and allocation. The database could identify underfunded areas of research, as well as support more joined up research across Member States to avoid duplication of effort and to speed up medical breakthroughs.

Support for national and European data infrastructure
Standardising information systems would help to identify rare and paediatric disease patients and to facilitate the sharing of their health data to inform research and innovation.

Do you see any drawbacks with the approaches above? Please describe.

*2000 character(s) maximum*

**Q7: Which of the following options, in your view, could help all EU patients (irrespective of where they live within the EU) to provide them with better access to medicines and treatments for rare diseases or children?**

☑ Greater availability of alternative treatment options. For instance, by allowing a generic or biosimilar product to enter the market faster.

- [x] Allowing companies that lose commercial interest in a rare disease or children medicine product to transfer its product to another company, encouraging further development and market continuity.
- [x] For companies to benefit from full support and incentives, products need to be placed timely on the market within all Member States in need as soon as they received a marketing authorisation.

Other (please suggest any other solution you think might be relevant).

*2000 character(s) maximum*

Development of joint European assessment process
Cooperation in the area of health technology assessment for rare and paediatric disease – depending on the level of cooperation agreed – could range from helping to improve the evidence-base for national decision-making through joint assessments, to requiring national decision-makers to ensure comparable access to treatments. Cooperation could also include Europe-wide, multi-year purchase agreements, as initiatives like BENELUXA aim to suggest. Support for development needs to go beyond medicines regulation to issues of medicines assessment and reimbursement.

**Q8: Most of the medicines for rare diseases are innovative medicines. However, in some cases, an older, well-known medicine for a common disease can be repurposed (i.e., using existing licensed medicines for new medical uses) to treat a rare disease. In your view, what would be the appropriate way to award innovative medicines in cases where other treatments are available:**

- ○ Both new, innovative medicines and well-known medicines repurposed to treat a rare disease should receive the same reward
- ○ New, innovative medicines to treat a rare disease should receive an enhanced reward
- ◉ Do not know/cannot answer

**Q9: Despite the presence of a dedicated procedure (the Paediatric Use Marketing Authorisation, PUMA) in the Paediatric Regulation, many older medicines that are currently used to treat children have only been studied for use within adult populations, and therefore lack the appropriate dosage or formulation suitable for use in younger patients. However, the development of medicines that have been adapted for use in children could also result in a product being more expensive than its adult-focused counterpart. In your view:**

Should the development of appropriate dosage or formulation suitable for children of such older medicines be stimulated even if their price will be higher than that of the available alternatives?

- ○ Yes

- (●) No
- ( ) Do not know/cannot answer

Please explain your answer.

*2000 character(s) maximum*

Rather than stimulate incentives for companies to return older medicines only previously studied for use within adult populations back into the research and development process, we propose that the possibility of using real world data be explored to identify the appropriate dosage needed to deliver good health outcomes for paediatric patients. Patients and their families should be involved in co-designing and co-evaluating this approach.

Many of these older medicines have been used to treat children for many years, and it is worthwhile to develop a body of real-world data around their efficacy (and to a lesser extent their safety, which has presumably not come under question). This evidence can be used to support their continued/future use and specific clinical and patient outcomes can be agreed to measure their performance moving forward.

As the current use of real world data is typically confined to post-authorisation based on clinical trial data, work would need to be completed to set standards and provide supports around quality clinical research, as well as to agree a definition of real world data among regulators (with the input of other key stakeholders including patients).

Confidence in real world data is growing with both the FDA (USA) and Health Canada already starting down this route and inviting submissions from industry partners using real world data. In attempt to prove the reliability of real world data, an interesting initiative in the US, RCT DUPLICATE, successfully predicted the results of several ongoing phase 4 clinical trials, using real world evidence.

Adopting this approach to paediatric medicines would require a concerted effort by all to get the European health data agenda off the ground to ensure that Member States are able to generate the real world data needed.

How would you suggest stimulating further development of appropriate dosage or formulation suitable for children of such older medicines?

*2000 character(s) maximum*

How can it be ensured that such developed products are reasonably profitable for companies and also reach patients?

*2000 character(s) maximum*

**Contact**