Survey of civil society representatives in the context of the Impact Assessment of the revision of the EU legislation on medicines for children and rare diseases

I agree to participate in the survey:

Yes

Please select the stakeholder group that you represent:

Public health organisation

Please indicate the level at which your organisation operates:

EU level

Please provide your first and last name *(optional)*:

Ward Rommel

Please provide your organisational affiliation:

ECL Access to Medicines Task Force

Please specify your position in this organisation:

chair

Please select the regulatory area(s) of interest to you:

Orphan Regulation

Have you any experience or knowledge on an orphan medicinal product approved for a rare disease / condition providing a significant benefit for patients over the existing treatments?

• Niraparib for ovarian cancer. Significant benefit compared to traditional carboplatin treatment.
•
In general, effects on overall survival seem to be quite moderate for rare cancers: https://www.kce.fgov.be/en/do-innovative-medicines-against-cancer-always-have-a-real-added-value

In your view, which are the main problems, if any, relating to orphan medicines?

Lack of science in the definition of unmet needs
Limited public funding for research
Other (please specify): The red tape that academia and non commercial entities need to address before being entitled to assistencie/incentives etc. Unchecked use of incentives No intervening / assessing tool to redraw incentive/prizing periodes.

Have you experienced any problems relating to orphan medicines due to the impact of the COVID-19 pandemic over the last year?

Affecting research activities relating to rare diseases

Please provide a brief explanation on the "Affecting research activities relating to rare diseases" option that you selected in the previous question.

Covid-19 impacted all patients, no matter their category.
Considering the impact of covid-19 on cancer patients, instead, EFPIA published an addendum to the report "Every Day Counts - Improving Time to Patient Access to Innovative Oncology Therapies in Europe" that dives in the impact of COVID-19 on patient access to cancer care in Europe. The paper reports that (i) clinical trials have been delayed or postponed, (ii) HTA and reimbursement decisions have been put on hold and (iii) cancer diagnosis dropped by 50% in some countries in March 2020 compared to the previous year.

From your perspective, which of the following criteria do you consider to be relevant for defining unmet medical needs in the area of rare diseases? Please rank the following criteria according to the importance that you assign them (1 is the most important and 5 is the least important)

1. No authorised treatment for the disease is available (therefore, a clear need for any treatment for a disease), and no commonly used method that would not be subject to marketing authorisation is widely available (e.g., surgery)
2. Seriousness of the disease (life-threatening and/or seriously debilitating and/or chronically and progressively leading to a seriously debilitating status)
3. Treatments are already available, but the corresponding therapeutic efficacy and/or the safety would need to be significantly ameliorated
4. Available treatments are not addressing the unmet medical need in all subpopulations (e.g., adapted doses and/or formulations/routes of administrations specific for some populations)
5. Treatments impose an elevated treatment burden on patients

In your view, how should unmet needs of rare disease patients be identified at the EU level?

Criteria defining unmet medical needs in rare diseases should be established in the EU legislation and detailed in scientific guidelines, which could be updated regularly

With regard to the prevalence criterion, which of the following thresholds would best reflect the 'rarity' of disease and could be used for providing an orphan designation to a medicine?
Prevalence: total number of cases of a disease at a specific time.
Incidence: number of people that acquired the disease during a specified time-period.

An incidence threshold based on the rarity of disease (e.g., not more than 6 in 100,000 cases)

Please provide a brief explanation on why you selected "An incidence threshold based on the rarity of disease (e.g., not more than 6 in 100,000 cases)" in the previous question.

see Rare cancer agenda 2030: for rare cancers, incidence works best. The definition in rare cancer agenda is based on incidence, valuing that: a) unlike prevalence, incidence does not change depending on a factor other than frequency, i.e. expected survival; b) many steps of the diagnostic and therapeutic pathway occur "once" in cancers, so that incidence renders better than prevalence much of the burden of cancer disease (in terms of health resources, costs, etc.) p.15.
*challenge: The traditional definition of a disease has changed with personalised medicine, we often see salami-slicing of diseases based on tumor genomics. solution of rare cancer agenda: rare molecular subgroup will be appropriately incorporated, as soon as it is recognized in the ICD-O as a cancer entity, but not otherwise. Most probably, this may happen when any molecular characteristic is perceived to be relevant to the natural history of a disease, not just to the sensitivity of the disease to a class of anticancer agents, and the like.

Should the current rules for demonstrating significant benefit be modified to ensure that new products provide real benefits to patients?

Yes

Please provide a brief description of the changes that would be needed.

Clinical trials should include patient-reported outcomes. A re-assessment of the drug should be in place after a few years (to be clearly specified in the regulation) and consider whether 1) there is a demonstrated effectiveness (impact on OS and QOL) and 2) the product has been launched or is in the process to be launched in most or all EU MS 4) the product is affordable for the national health care systems based on previous case studies

*If registration trials for rare and paediatric cancers could be designed and executed by collaborative groups, ERNs, academia and non-profit foundations who take into account research questions from patients/health professionals and include relevant comparators and endpoints they will consequently be able to deliver appropriate data for HTA evaluation

Please rate your attitude towards each of the following options, designation criterion, incentive and reward elements.

	-3	-2	-1	0	+1	+2	+3
Option 1. The criterion for granting an orphan designation will remain the number of people affected (currently 5/10 000). The ME will remain the main incentive provided, but its duration will be variable and calculated as the sum of a fixed and a variable elements. Other incentives (protocol assistance, fee waivers and eligibility for EU and national research funding) will remain.				X			
Option 2.1. The criterion for granting an orphan designation will remain the number of people affected, but the **threshold will be reduced to 3/10 000**. The ME will remain the main incentive provided, but its duration will be variable and calculated as the sum of a fixed and a variable elements. Other incentives (protocol assistance, fee waivers and eligibility for EU and national research funding) will remain.			X				
Option 2.2. The criterion for granting an orphan designation will remain the number of people affected, but **different criteria based on incidence** to identify specific rare diseases (e.g., rare cancers and short-duration diseases) will be introduced. The ME will remain the main incentive provided, but its duration will be variable and calculated as the sum of a fixed and a variable elements. Other incentives (protocol assistance, fee waivers and eligibility for EU and national research funding) will remain.						X	
Option 3.1. The criterion for granting an orphan designation will remain the number of people affected, but the **threshold will be reduced to 3/10 000**. The ME will remain the main incentive provided, but its duration will be variable and calculated as the sum of a fixed and a variable elements. Other incentives (protocol assistance, fee waivers and eligibility for EU and national research funding) will remain. For medicinal products addressing an unmet need and for rare paediatric diseases, **novel incentives will complement the market exclusivity**.		X					
Option 3.2. The criterion for granting an orphan designation will remain the number of							

Option 3.1. The criterion for granting an orphan designation will remain the number of people affected, but **different criteria based on incidence** to identify specific rare diseases (e.g., rare cancers and short-duration diseases) will be introduced. The ME will remain the main incentive provided, but its duration will be variable and calculated as the sum of a fixed and a variable elements. Other incentives (protocol assistance, fee waivers and eligibility for EU and national research funding) will remain. For medicinal products addressing an unmet need and for rare paediatric diseases, **novel incentives will complement the market exclusivity**.		X					
Option 3.3. The criterion for granting an orphan designation will remain the number of people affected, but **the threshold will be reduced to 3/10 000**. The ME will remain the main incentive provided, but its duration will be variable and calculated as the sum of a fixed and a variable elements. Other incentives (protocol assistance, fee waivers and eligibility for EU and national research funding) will remain. For medicinal products addressing an unmet need and for rare paediatric diseases, **novel incentives will replace the market exclusivity**.			X				
Option 3.4. The criterion for granting an orphan designation will remain the number of people affected, but **different criteria based on incidence** to identify specific rare diseases (e.g., rare cancers and short-duration diseases) will be introduced. The ME will remain the main incentive provided, but its duration will be variable and calculated as the sum of a fixed and a variable elements. Other incentives (protocol assistance, fee waivers and eligibility for EU and national research funding) will remain. For medicinal products addressing an unmet need and for rare paediatric diseases, **novel incentives will replace the market exclusivity**.			X				
Option 4.1. The criterion for granting an orphan designation will remain the number of people affected, but **the threshold will be reduced to 3/10 000**. The ME will be the main incentive provided **only** for medicinal products addressing an unmet need and for rare paediatric diseases. Other incentives (protocol assistance, fee waivers and eligibility for EU and national research funding) will remain.				X			
Option 4.2. The criterion for granting an orphan designation will remain the number of people affected, but **different criteria based on incidence** to identify specific rare diseases (e.g., rare cancers and short-duration diseases) will be introduced. The ME will be the main incentive provided **only** for medicinal products addressing an unmet need and for rare paediatric diseases. Other incentives (protocol assistance, fee waivers and eligibility for EU and national research funding) will remain.						X	
Option 4.3. The criterion for granting an orphan designation will remain the number of people affected, but **the threshold will be reduced to 3/10 000.** Other incentives (protocol assistance, fee waivers and eligibility for EU and national research funding) will remain. For medicinal products addressing an unmet need and for rare paediatric diseases, **novel incentives will replace the market exclusivity.**				X			
Option 4.4. The criterion for granting an orphan designation will remain the number of people affected, but different criteria based on incidence to identify specific rare diseases (e.g., rare cancers and short-duration diseases) will be introduced. Other incentives (protocol assistance, fee waivers and eligibility for EU and national research funding) will remain. For medicinal products addressing an unmet need and for rare paediatric diseases, **novel incentives will replace the market exclusivity.**					X		

Please rate your attitude towards each of the following designation criterion (DC).

	-3	-2	-1	0	+1	+2	+3
Element DC.1. The criterion for granting an orphan designation will remain the number of people affected (currently 5/10 000).				X			
Element DC.2. The criterion for granting an orphan designation will remain the number of people affected, but the threshold will be reduced to 3/10 000.		X					
Element DC.3. The criterion for granting an orphan designation will remain the number of people affected, but different criteria based on incidence to identify specific rare diseases (e.g., rare cancers and short-duration diseases) will be introduced.							X

Please rate your attitude towards each of the following incentive and reward (IR) elements.

	-3	-2	-1	0	+1	+2	+3
Element IR.1. The ME will remain the main incentive provided, but its duration will be variable and calculated as the sum of a fixed element and a variable element. Other incentives (protocol assistance, fee waivers and eligibility for EU and national research funding) will remain.					X		
Element IR.2. Fixed element: Upon granting the initial marketing authorisation, a fixed duration of the market exclusivity will be given. This duration may differ, depending on the innovation potential of the medicine (e.g., more years for 'real' innovative medicinal products, fewer years for repurposed medicinal products and for second/multiple indication(s)).						X	
Element IR.3. Fixed element: A longer (non-extendable) market exclusivity may be granted to 'rare paediatric diseases' medicinal products.		X					
Element IR.4. Fixed element: ME duration based on the possible creation of a list of different medicinal product categories.					X		
Element IR.5. Variable (cumulative) elements: Return on Investment received; Availability of the medicine in a minimum/most/all Member States; Prevalence threshold revision.							X
Element IR.6. Regulatory incentive for unmet needs and rare paediatric diseases: i) extended market protection and data protection (surpassing the current 8+2 years) and ii) 10-year market exclusivity.	X						
Element IR.7. Transferrable voucher system linked to the (extended) regulatory incentive as under Element IR.6 (for unmet needs and rare paediatric diseases).	X						
Element IR.8. Transferrable voucher system, linked to an extension to a patent right ('transferable SPC') (for unmet needs and rare paediatric diseases).	X						
Element IR.9. Transferability of the voucher system between companies.				X			
Element IR.10. The possibility to obtain a voucher is subject to the obligation to place on the market in a minimum/most/all Member States both the 'orphan medicinal product' and the medicinal product for which the voucher is used.				X			
Element IR.11. The 'value' of the voucher will be capped in order to avoid excessive costs for health systems.					X		

If you would like to upload any files that might be relevant for the study, please do so below.

Joint_Recommendations_Paediatric_Orphan_Policy-dialogue_200521.pdf

Would you like to receive a copy of your responses to this survey?

Yes

Could you please provide your email address?

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