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To:	Ms Thérèse BLANCHET, Secretary-General of the Council of the European Union
Subject:	**REGULATORY SCRUTINY BOARD OPINIONS** Revision of the general pharmaceutical legislation Revision of the EU legislation on medicines for children and rare diseases

Delegations will find attached document SEC (2023) 390.

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EUROPEAN COMMISSION

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REGULATORY SCRUTINY BOARD OPINIONS

Revision of the general pharmaceutical legislation
Revision of the EU legislation on medicines for children and rare diseases

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EUROPEAN COMMISSION
Regulatory Scrutiny Board

Brussels,
RSB

Opinion

Title: Impact assessment / Revision of the general pharmaceutical legislation

Overall 2nd opinion: POSITIVE WITH RESERVATIONS

(A) Policy context

The general pharmaceutical legislation consists of Directive 2001/83/EC and Regulation 726/2004 and seeks to guarantee high standards of quality and safety of medicines in the EU and includes measures to encourage innovation and competitiveness. Its revision is part of the pharmaceutical strategy for Europe, a building block of the European Health Union. The proposed revision focuses on regulatory protection periods to promote innovation and allow access to affordable medicines for EU citizens. Additionally, it aims to address unmet medical needs and antimicrobial resistance, the security of supply of medicines, reduce their environmental impact, adapt the legislation to new technological developments and reduce administrative burden. An evaluation of the general pharmaceutical legislation is annexed to the impact assessment.

(B) Summary of findings

The Board notes the clarifications about the factors influencing access to affordable medicines and the enabling framework nature of the general pharmaceutical legislation.

However, the report still contains significant shortcomings. The Board gives a positive opinion with reservations because it expects the DG to rectify the following aspects:

(1) The exact criteria and conditions of the voucher system to address antimicrobial resistance remain vague.

(2) The report is not sufficiently clear on the content, functioning and effectiveness of the envisaged safeguards which allows industry complying with the two year medicine launch requirement in all EU markets to benefit from extra-protection.

(3) The report should better assess the impacts of reduced regulatory protection periods on the sectors capacity to finance future innovations and international competitiveness.

This opinion concerns a draft impact assessment which may differ from the final version.

(C) What to improve

(1) The report should set out the strict conditions for defining 'novel' antibiotics and the exact award criteria for obtaining a voucher.

(2) The effectiveness of the market access measures (and the potential one or two year extra protection) depends critically on the safeguards to be put in place to ensure effective cooperation of Member States to allow industry to comply with the two year market product launch requirement. The report should be more explicit on the content, functioning and effectiveness of the envisaged safeguards. It should for instance identify the most critical ones and clarify whether non-reaction of a Member State will be considered as tacit confirmation of compliance, indicate whether there will be longer compliance periods on market access measures for SMEs and, if yes, specify how much longer these would be. It should clarify whether the safeguards have been market tested with and find the support of the affected stakeholders.

(3) The report should further elaborate the analysis of impacts of reduced regulatory protection periods on prices, preferably on the basis of representative empirical sector data. It should clarify to what extent such reduction may lead to higher prices for medicines within the shortened protectin period.

(4) The report should also better assess the impacts of reduced regulatory protection periods on the sectors capacity to finance future innovations. As under the preferred option (under the variant with a one year extra protection) there will be a significant reduction of the originators gross profits (in particular for those not benefitting from the potential voucher), the report should more thoroughly assess to what extent this will affect the origintors overall R&D investment potential for innovative medicines. In doing so, it should adequately reflect similar investment potential impacts for originators arising under the parallel initiative on medicines for children and rare diseases. It should better assess how the combined effect of the reduced gross profits for originators will affect the overall EU investment potential for innovation for medicines and the international competitiveness of EU pharmaceutical sector.

The Board notes the estimated costs and benefits of the preferred option in this initiative, as summarised in the attached quantification tables.

(D) Conclusion

The DG must revise the report in accordance with the Board's findings before launching the interservice consultation.

If there are any changes in the choice or design of the preferred option in the final version of the report, the DG may need to further adjust the attached quantification tables to reflect this.

Full title	Revision of Regulation (EC) No 726/2004 and Directive 2001/83/EC
Reference number	PLAN/2021/10601
Submitted to RSB on	28 October 2022
Date of RSB meeting	Written procedure

ANNEX: Quantification tables extracted from the draft impact assessment report

The following tables contain information on the costs and benefits of the initiative on which the Board has given its opinion, as presented above.

If the draft report has been revised in line with the Board's recommendations, the content of these tables may be different from those in the final version of the impact assessment report, as published by the Commission.

I. Overview of Benefits (total for all provisions) – Preferred Option		
Description	***Amount***	***Comments***
	Direct benefits	
Medicines for unmet medical needs (UMNs)	On average, additional **3 new medicines annually** relevant to UMNs (c. 45 new medicines over 15 years). This would result in **originators** securing an additional **€282m** gross profit sales annually (15 years: €4.23bn).	+12 months extension of RDP for innovation, particularly around unmet medical needs (UMNs) would result in a higher proportion of UMNs within all newly authorised medicines. While 1-2 additional UMN medicines are expected annually, the extension of the RDP is expected to apply to 3 UMN medicines annually.
Novel antimicrobials	An additional **1 novel antimicrobial annually** (c. 15 over 15 years). This would result in **originators** securing an additional **€387m** gross profit annually (15 years: €5.8bn).	The transferable voucher, if approved, would provide strong support for innovation in novel antimicrobials. The additional income may be secured by the developer of the novel antimicrobial where they use a voucher with another high value medicine in their portfolio or split between the developer of the antimicrobial and another originator that has purchased the (transferable) voucher. We have estimated the purchase value at €360m (assuming one voucher a year). With more breakthroughs a more vouchers the average sale price would fall.
Comparative trials	A small number of EMA medicines applications will be able to implement more robust trials and take advantage of the incentive (**8 a year**). This would result in **originators** securing an additional **€378m** gross profit annually (15 years: €5.7bn).	+6 months extension of RDP for medicines applications that include the findings of comparative trials.
Market access	The great majority of new medicines will be able to comply with the market access conditions. **8 medicines annually** (120 over 15 years) may fail to meet the conditions, and in these cases the RDP will lapse at 6+2 years (not 6+2+1). For this sub-set of products where the RDP is the last line of defence, there will be a **€384m** gain each year (€5.7bn over 15 years) to the **EU health system and patients**, because of lower prices from earlier competition by generics. **Generic companies** would secure an additional **€51m** annually in gross profits (€765m over 15 years).	+1 years protection conditional on launch in all EU markets in 2 years (the variant).
1 year general reduction of the RP	The reduced protection would allow earlier generic entry and price competition, and also the lower prices would increase patients' access to medicines. **Health system and patients** will gain **€1,008m** a year (€15.1bn over 15 years), and **generic companies** would secure an additional **€113m** per year (€2bn over 15 years).	

I. Overview of Benefits (total for all provisions) – Preferred Option		
Description	***Amount***	***Comments***
Indirect benefits		
Patients benefit from effective medicines (UMNs)	Thousands of EU citizens will have access to treatments that help recover them from or manage their debilitating conditions, improving their quality of life and life expectancy. There may also be indirect benefits / savings for health systems from more effective treatment and reduced hospitalisations. There would be benefits for families and carers too, in terms of both quality of life / independence and earning potential.	It is not possible to quantify / monetise (indirect) patient benefits given the diversity of UMNs (certain neurological conditions, cancers, muscular dystrophy, etc.). These conditions may affect hundreds of citizens or millions in the case of Alzheimer.
Patients have access to new classes of antimicrobials that help to contain AMR	It is estimated that each year about 670,000 infections occur, and that 33,000 Europeans die as a consequence of antibiotic-resistant bacteria with the burden being highest in the elderly and infants. It is also estimated that AMR costs the EU €1.5bn per year in healthcare costs and productivity losses. Even a 1% improvement in our management of AMR could save several hundred lives annually and save health systems hundreds of millions too.	It was not possible to quantify / monetise the (indirect) patient benefits that might result from new classes of antimicrobials.
Improved decision making for HTAs / Reimbursement bodies	More robust evidence from comparative trials should facilitate HTA decision making, leading to improved reimbursement decisions and faster decisions / access where medicines are approved for reimbursement.	It was not possible to quantify / monetise the (indirect) HTA and patient benefits that might result from the greater use of more robust trials.
All EU member states (inc smaller countries) have improved access to new medicines	On average, new medicines will be available to patients in 22-25 markets compared with the current situation (12-15), reaching 80% of the population compared with the current situation (c. 65%). The access to all new medicines in 5-10 additional markets will mean that hundreds of thousands of EU citizens will have better treatment options, with accompanying improvements in health equality and possibly public health.	It was not possible to quantify / monetise the (indirect) patient benefits that might result from the systematic extension of market access
Improved management of shortages	Most EU countries report increasing numbers of medicine shortages, with the great majority having recorded shortages for 200 or more medicines in the year. Fewer shortages may benefit tens of thousands of patients, with access to the more appropriate medicines. According to the Pharmaceutical Group of the EU, eliminating shortages might save healthcare systems 5-10% of their pharmacy-related staff costs as well as time wasted by frontline staff.	Fewer shortages would mean more patients have access to the medicines they need. Healthcare systems would see cost savings from avoiding time wasted deciding / finding appropriate alternative medicines.
Improved environmental performance of pharma industry	This may make a positive difference to 40-50 new medicines a year (600-750 in 15 years). This should result in a reduction in the intrinsic environmental risks of a proportion of medicines, a lowering of the levels of active ingredients getting into the environment through excretion and a lowering of the level and number of accidental releases to the environment by manufacturers (mostly non-EU).	New medicines would be subject to a more rigorous assessment, which should feed forward to more informed selection of APIs, encourage green pharma and select for higher standards across global supply chains.
Administrative cost savings related to the 'one in, one out' approach*		
Streamlining, acceleration of processes and coordination of network	**Businesses** should realise savings in the range **€15m-€30m annually** (€225m-€450m over 15 years). European and national **regulators** should see savings in the range **€33.5m-€67m annually** (€502.5m-€1005m over 15 years). Overall savings should represent on average **€72.75m annually** (€1.09bn over 15 years).	Businesses will benefit from various simplification and governance enhancements producing administrative cost savings. European and national regulators should see a reduction in duplication of effort across committees and among regulators, producing savings in enforcement costs
Digitalisation	Digitalisation savings for **businesses** in the range **€7.5m-€15m annually** (€112.5m-€225m over 15 years). Digitalisation savings for **regulators** in the range **€67m-€134m annually** (€1,005m-€2,010m over 15 years). Overall savings of on average **€112m annually** (€1.68bn over 15 years)	The various digital initiatives proposed will save time and administrative costs for businesses and deliver substantial efficiencies / reductions in enforcement costs for regulators.
Adaptations to new concepts and support SMEs and non-commercial	Enhancement savings for **businesses** in the range **€7.5m-€15m annually** (€112.5m-€225m over 15 years). Enhancement indirect benefits for **businesses** in the range **€5m-€10m**	Industry - and SMEs in particular - should benefit from better and more dynamic advice avoiding

I. Overview of Benefits (total for all provisions) – Preferred Option		
Description	***Amount***	***Comments***
organisation**s**	**annually** (€75m-€150m over 15 years). Enhancement savings for **regulators** in the range **€1.75m-€3.5m annually** (€26.25m-€52.5m over 15 years). Overall savings of on average **€21m annually** (€321mn over 15 years).	queries on applications (delay) and rework to the same (cost); regulators should benefit from more mature applications that can be assessed more easily and quickly. There may be some limited indirect benefits, whereby faster assessments, on average, may facilitate at least some new medicines being approved for sale earlier and some generics entering the market earlier.

(1) Estimates are gross values relative to the baseline for the preferred option as a whole (i.e. the impact of individual actions/obligations of the preferred option are aggregated together); (2) We indicate which stakeholder group is the main recipient of the benefit in the comment section;(3) For reductions in regulatory costs, we describe how the saving arises (e.g. reductions in administrative costs, regulatory charges, enforcement costs, etc.;)

II. Overview of costs – Preferred option							
		Citizens/Consumers		**Businesses**		**Administrations**	
		One-off	**Recurrent**	**One-off**	**Recurrent**	**One-off**	**Recurrent**
UMNs	Direct adjustment costs						
	Direct administrative costs						
	Direct regulatory fees and charges						
	Direct enforcement costs						
	Indirect costs		Costs for 'unserved' patients €246m a year €3.69bn over 15 years		Lost gross profits for generics €39m a year €585m over 15 years		Additional costs for payers €162m a year €2.43bn over 15 years
AMR	Direct adjustment costs				E.g. industry would incur costs for the development of AMR lifecycle monitoring plans; these cost could not be quantified.		E.g. regulators would incur costs to examine the AMR lifecycle monitoring plans; these costs could not be quantified.
	Direct administrative costs						
	Direct regulatory fees and charges						
	Direct enforcement costs						
	Indirect costs		Costs for 'unserved' patients €158m a year		Lost gross profits for generics €54m a year		Additional costs for payers €283m a year

II. Overview of costs – Preferred option							
		Citizens/Consumers		Businesses		Administrations	
		One-off	Recurrent	One-off	Recurrent	One-off	Recurrent
			€2.37bn over 15 years		€360m over 15 years		€4.2bn over 15 years
Comparative trials	Direct adjustment costs				Comparative trials conducted by originator €280m a year €4.2bn over 15 years		
	Direct administrative costs						
	Direct regulatory fees and charges						
	Direct enforcement costs						
	Indirect costs		Costs for 'unserved' patients €112m a year €1.68bn over 15 years		Lost gross profits for generics €52m a year €780m over 15 years		Additional costs for payers €218m a year €3.27bn over 15 years
Market access (variant with one year protection)	Direct adjustment costs						
	Direct administrative costs				Requesting confirmations of supply to obtain extension of RP; costs not quantified. More applications for P&R; costs not quantified.		Confirmation of supply by MS; costs not quantified.
	Direct regulatory fees and charges						
	Direct enforcement costs						
	Indirect costs				Lost gross profits originators €378m a year €5.6bn over 15 years		P&R bodies to decide on more applications; costs not quantified.
1 year general reduction of RP	Direct adjustment costs						
	Direct administrative costs						
	Direct regulatory fees and charges						
	Direct enforcement costs						
	Indirect costs				€991m gross profit reduction for originators		

II. Overview of costs – Preferred option							
		Citizens/Consumers		Businesses		Administrations	
		One-off	Recurrent	One-off	Recurrent	One-off	Recurrent
					€14.9bn over 15 years		
Shortages	Direct adjustment costs						
	Direct administrative costs				Additional costs for industry €10m-€20m a year (ave €15m) €150m-€300m over 15 years (ave €225m)		
	Direct regulatory fees and charges						
	Direct enforcement costs						Additional costs for regulators €10m-€20m a year (ave €15m) €150m-€300m over 15 years (ave €225m)
	Indirect costs						
Environment	Direct adjustment costs						
	Direct administrative costs				Additional costs for industry €20m-€25m a year (ave €22.5m) €300m-€375m over 15 years (ave €337.5m)		
	Direct regulatory fees and charges						
	Direct enforcement costs						Additional costs for regulators €20m-€25m a year (ave €22.5m) €300m-€375m over 15 years (ave €337.5m)
	Indirect costs						
Streamlining	Direct adjustment costs						
	Direct administrative costs						
	Direct regulatory fees and charges						

II. Overview of costs – Preferred option							
		Citizens/Consumers		Businesses		Administrations	
		One-off	Recurrent	One-off	Recurrent	One-off	Recurrent
	Direct enforcement costs					Additional one-off costs for regulators €16.8m-€33.6m (ave €25.2m)	Additional costs for regulators €33.5m-€67.5m a year (ave €50.5m) €502.5m-€1.01bn over 15 years (ave €757.5m)
	Indirect costs						
Digitalisation	Direct adjustment costs						
	Direct administrative costs						
	Direct regulatory fees and charges						
	Direct enforcement costs					Additional one-off costs for regulators €120m-€350m (ave €235m)	Additional costs for regulators €24m-€70m a year (ave €47m) €360m-€1.05bn over 15 years (ave €705m)
	Indirect costs						
Enhanced support	Direct adjustment costs						
	Direct administrative costs						
	Direct regulatory fees and charges						
	Direct enforcement costs						Additional costs for regulators €4.8m-€7.2m a year (ave €6m) €72m-€108m over 15 years (ave €90m)
	Indirect costs				Additional costs for industry for engaging with regulators €1.6m-€2.4m a year (ave €2m) €24m-€36m over 15 years (ave €30m)		

II. Overview of costs – Preferred option							
		Citizens/Consumers		Businesses		Administrations	
		One-off	Recurrent	One-off	Recurrent	One-off	Recurrent
Costs related to the 'one in, one out' approach							
Total	Direct adjustment costs						
	Indirect adjustment costs						
	Administrative costs (for offsetting)				Administrative costs to businesses €37.5m a year €562.5m over 15 years		

(1) Estimates (gross values) to be provided with respect to the baseline; (2) costs are provided for each identifiable action/obligation of the preferred option otherwise for all retained options when no preferred option is specified; (3) If relevant and available, please present information on costs according to the standard typology of costs (adjustment costs, administrative costs, regulatory charges, enforcement costs, indirect costs;). (4) Administrative costs for offsetting as explained in Tool #58 and #59 of the 'better regulation' toolbox. The total adjustment costs should equal the sum of the adjustment costs presented in the upper part of the table (whenever they are quantifiable and/or can be monetised). Measures taken with a view to compensate adjustment costs to the greatest extent possible are presented in the section of the impact assessment report presenting the preferred option.

EUROPEAN COMMISSION
Regulatory Scrutiny Board

Brussels,
RSB

Opinion

Title: Impact assessment / Revision of the general pharmaceutical legislation

Overall opinion: NEGATIVE

(A) Policy context

The general pharmaceutical legislation consists of Directive 2001/83/EC and Regulation 726/2004 and seeks to guarantee high standards of quality and safety of medicines in the EU and includes measures to encourage innovation and competitiveness. Its revision is part of the pharmaceutical strategy for Europe, a building block of the European Health Union. The proposed revision focuses on regulatory protection periods to promote innovation and allow access to affordable medicines for EU citizens. Additionally, it aims to address unmet medical needs and antimicrobial resistance, the security of supply of medicines, reduce their environmental impact, adapt the legislation to new technological developments and reduce administrative burden. An evaluation of the general pharmaceutical legislation is annexed to the impact assessment.

(B) Summary of findings

The Board notes the additional information provided in advance of the meeting and commitments to make changes to the report.
However, the Board gives a negative opinion because the report contains the following significant shortcomings:

(1) The report is not sufficiently precise about the key factors that cause unequal access to medicines and their affordability, and what exactly determines the observed differences between Member States. Accordingly, it is not clear if this revision will have a direct impact on access and affordability of medicines or if it is instead only providing an enabling framework to reach these objectives.

(2) The report does not clearly demonstrate the effectiveness of new incentive measures. It is not clear how the market launch conditionality and the transferable exclusivity vouchers for antimicrobial resistance (AMR) products will work exactly. Possible counter-effects affecting the access-affordability trade-off are not sufficiently assessed.

(3) The report is not sufficiently clear on the impacts of options on innovation and competitiveness for the EU pharmaceutical ecosystem, including SMEs, and how this will affect access to and affordability of medicines for patients.

(4) The report does not sufficiently demonstrate the EU added-value, nor the proportionality of the preferred option.

(C) What to improve

(1) The report should analyse and present, in greater detail, the multiplicity of factors (and relative determinants) that lead to accessible, affordable and quality medicinal products while separating more clearly the issues caused by business decisions from those resulting from the divergent public policy decisions of Member States' authorities. It should discuss the influence of decisions taken at Member State level and how these decisions emerge from different public policy approaches and procedures in Member States (e.g. assessment of the relative effectiveness of new medicines, their therapeutic added value or different political spending priorities, timing of new launches, etc). The report should clearly present and substantiate with evidence the mix of problem drivers that are causing underperformance on the ground and clearly indicate where this revision can realistically improve the situation, also taking into account related initiatives.

(2) The report should describe the available information about current negotiation dynamics between Member States and industry, e.g. to what extent industry already reflects different purchasing power levels in their pricing decisions. On that basis, it should analyse how the new incentives and obligations for placing a medicine on the market in all Member States within two years will change these dynamics in terms of negotiating power and tactics and what the projected impact would be on Member States' health care systems. The stakeholder views from both industry and Member States should be clearly presented throughout the report. The report should outline possible trade-offs (in terms of manufacturers' incentives) between expanding access to and improve affordability of new medicines.

(3) The impact of legal uncertainty for companies as regards materialising the additional regulatory protection period should be discussed in depth and should be substantiated with evidence given that the conditional extra years are dependent on factors outside of their control, in particular Member States' behaviour. The report should assess the impact of this legal uncertainty, including on the launch of new innovation and future pricing decisions. It should assess whether shortening the standard regulatory protection period from eight to six years is likely to lead to higher average prices for health systems during the protection period, including by learning from third countries' experience of such shorter regulatory protection. The report should discuss more thoroughly how legal certainty for innovative businesses can be adequately ensured. It should describe how the Transparency Directive affects and influences Member States' and companies' behaviour and explain how possible non-cooperative behaviour from Member States' authorities can be avoided. Additionally, the report should ensure consistency and clarity when describing the different regulatory protection options when using concepts such as standard and baseline protection periods.

(4) For the transferable exclusivity voucher prosed for AMR products, the report should clearly outline and analyse the key design parameters that affect its effectiveness and efficiency and the supporting evidence and benefit-cost analysis that will be necessary to trigger its practical application. Where trade-offs exist, these should be transparently presented. The report should clarify to what extent the transferable exclusivity voucher is expected to trigger the development of new medicines (not already having entered the development pipeline). It should better assess the impact on competition and prices on the relevant market of the existing product chosen to benefit from the application of the voucher.

(5) The report should be clear on who will benefit from the new measures and who will bear the costs and what the distributional impacts are for medicine developers, the pharma industry (including generics), SMEs, health care systems and patients.

(6) The report should more thoroughly assess the overall impact of the measures on promoting innovation and competitiveness of the EU pharmaceutical ecosystem, including SMEs. It should better assess how the reduced standard regulatory protection period will affect the long-term ecosystem innovation capacity. It should analyse how the measures will impact competition between companies (big pharma and SMEs), prices and affordability. It should anticipate unintended consequences on innovation and competitiveness and discuss the risk that the expected benefits will not materialise.

(7) The report should better compare the options, based on overall cost-benefit estimates for each option and each affected key group (including their presentation in consolidated comparison tables). It should be clear if a net positive benefit is expected as the preferred option shows a very low benefit-cost ratio.

Some more technical comments have been sent directly to the author DG.

(D) Conclusion

The DG must revise the report in accordance with the Board's findings and resubmit it for a final RSB opinion.

Full title	Revision of Regulation (EC) No 726/2004 and Directive 2001/83/EC
Reference number	PLAN/2021/10601
Submitted to RSB on	22 June 2022
Date of RSB meeting	19 July 2022

EUROPEAN COMMISSION
Regulatory Scrutiny Board

Brussels,
RSB

Opinion

Title: Impact assessment / Revision of the EU legislation on medicines for children and rare diseases

Overall 2nd opinion: POSITIVE WITH RESERVATIONS

(A) Policy context

Regulation (EC) No 141/2000 on medicinal products for rare diseases and Regulation (EC) No 1901/2006 on medicines for children aim to address specific medical needs for these small patient groups. These medicines also need to comply with the general pharmaceutical legislation which is currently under review. The Regulation on medicinal products for rare diseases aims to address specific medical needs by creating incentives, while the Regulation on medicines for children is centres on obligations to screen products for possible use in children. The revision of these two Regulations is based on a joint evaluation of these Regulations published in 2020.

(B) Summary of findings

The Board notes the improved explanations about coherence and interaction with the general pharmaceutical legislation and clarifications related to the description of options.

However, the report still contains significant shortcomings. The Board gives a positive opinion with reservations because it expects the DG to rectify the following aspects:

(1) The report does not sufficiently assess the impacts of reduced regulatory protection periods on the sectors' capacity to finance future medicine innovation and international competitiveness.

(2) The report lacks clarity regarding safeguards for market access measures.

(3) Some of the impact analyses are not sufficiently developed.

This opinion concerns a draft impact assessment which may differ from the final version.

(C) What to improve

(1) The report should deepen the analysis of the impacts of the one year reduction of market exclusivity for medicines for rare diseases (compared to the baseline) on the overall innovation capacity of the sector, reflecting that the substantial gross profit loss of originators may constrain their future capacity to finance medicines innovations. When assessing the impacts on innovation and competitiveness of EU originators, the report should also reflect similar reductions of future innovation investment potential resulting from the parallel revision of the general pharmaceutical legislation. It should assess the risk that fewer innovations (and improvements in other medical needs areas) may materialise than under the dynamic baseline.

(2) The report should clarify whether the same safeguards for market access measures will be envisaged as under the parallel revision of the general pharmaceutical legislation. If yes, it should be more explicit on the content, functioning and effectiveness of these safeguards. It should for instance identify the most critical ones and clarify whether non-reaction of a Member State will be considered as tacit confirmation of compliance, indicate whether there will longer compliance periods on market access measures for SMEs, and, if yes, specify how much longer these would be. It should clarify whether the safeguards have been market tested with and find the support of the affected stakeholders. If no safeguards are envisaged, the report should justify why these are not necessary for the present initiative.

(3) The report should present more clearly the available evidence on the price differences for orphan and rare disease medicines between Member States. It should clarify to what extent observed list prices reflect the real prices paid (following rebates and other side-incentives). It should als clarify the nature, size and source of the dedicated research funding, which will be made available as part of the common option elements for medicines for children. It should explain how this funding differs from HorizonEurope funding opportunities under the dynamic baseline.

(4) The report should further develop the analysis of some other impacts. Regarding the additional authorisations of medicines for high unmet medical needs (HUMN) the report should explain how these are estimated (both direct and indirect) and present a decline in HUMN authorisations consistently in the tables. It should clarify how the percentage of population served over time is estimated for the options. It should elaborate the explanation in case of many vouchers and the concept of rent associated with the voucher. It should better assess the sensitivity of the analysis, particularly for the unquantified benefits which are low in absolute numbers. Finally, it should discuss how the administrative costs are estimated.

(5) The qualitative comparison of options overview tables should be complemented with available key quantitative information, such as (i) new medicines compared to the baseline, (ii) net additions of patients with access or (iii) costs for patients / health systems / originators / generics etc.

The Board notes the estimated costs and benefits of the preferred option(s) in this initiative, as summarised in the attached quantification tables.

(D) Conclusion **The DG must revise the report in accordance with the Board's findings before launching the interservice consultation.** **If there are any changes in the choice or design of the preferred option in the final version of the report, the DG may need to further adjust the attached quantification tables to reflect this.**	
Full title	Revision of the EU legislation on medicines for children and rare diseases
Reference number	PLAN/2020/6688
Submitted to RSB on	28 October 2022
Date of RSB meeting	Written procedure

ANNEX: Quantification tables extracted from the draft impact assessment report

The following tables contain information on the costs and benefits of the initiative on which the Board has given its opinion, as presented above.

If the draft report has been revised in line with the Board's recommendations, the content of these tables may be different from those in the final version of the impact assessment report, as published by the Commission.

For the Orphan Regulation

I. Overview of yearly Benefits (compared to baseline benefits – million €) – Preferred Option		
Description	***Amount***	***Comments***
Direct benefits		
Pharmaceutical companies (originators)	+€94m gross profit due to +1 year of ME for HUMN medicines	
Pharmaceutical companies (generic industry)	+€38m gross profit gain due to non-complying medicines on launch conditionality +€50m gross profit due to predictable market entry ('day-1') +€13m gross profit due to abolishing 2-year ME for completing PIP	
Public payer/health systems and patients	+€288m cost saving from non-complying medicines access conditionality and broader and faster access to complying medicines +€360m cost saving due to predictable market entry ('day-1') +€96m cost saving legal clarity abolishing 2-year ME for completing PIP	
Indirect benefits		
Administrative cost savings related to the 'one in, one out' approach*		
Direct administrative costs savings	**4.5 m** €	Direct cost saving

*Estimates are gross values relative to the baseline for the preferred option as a whole (i.e. the impact of individual actions/obligations of the preferred option are aggregated together); (2) Please indicate which stakeholder group is the main recipient of the benefit in the comment section;(3) For reductions in regulatory costs, please describe details as to how the saving arises (e.g. reductions in adjustment costs, administrative costs, regulatory charges, enforcement costs, etc.;); (4) Cost savings related to the 'one in, one out' approach are detailed in Tool #58 and #59 of the 'better regulation' toolbox. * if relevant*

II. Overview of costs – Preferred option							
		Citizens/Consumers		**Businesses**		**Administrations**	
		One-off	**Recurrent**	**One-off**	**Recurrent**	**One-off**	**Recurrent**
Costs for +1 year of ME for HUMN products	Direct costs				13 m € loss in gross profits (generic industry)		82 m € additional costs
Costs for 1 year of ME condition for full EU launch	Direct costs				282 m € loss in gross profits (originators) 4 m € additional costs		
Costs Day-1 entry of generic/biosimilars after ME expiry	Direct costs				354 m € loss in gross profits (originators)		
Costs Abolishing 2-year ME extension for completing PIP	Direct costs				94 m € loss in gross profits (originators)		
Administrative costs due to increased number of orphan designations					1.3 m €		
Costs related to the 'one in, one out' approach							
Total	Direct adjustment costs	N.A	N.A	N.A	N.A		
	Indirect adjustment costs	N.A	N.A	N.A	N.A		
	Administrative costs (for offsetting)	N.A	N.A	N.A	**-3.3 m** €		

(1) Estimates (gross values) to be provided with respect to the baseline; (2) costs are provided for each identifiable action/obligation of the preferred option otherwise for all retained options when no preferred option is specified; (3) If relevant and available, please present information on costs according to the standard typology of costs (adjustment costs, administrative costs, regulatory charges, enforcement costs, indirect costs;). (4) Administrative costs for offsetting as explained in Tool #58 and #59 of the 'better regulation' toolbox. The total adjustment costs should equal the sum

of the adjustment costs presented in the upper part of the table (whenever they are quantifiable and/or can be monetised). Measures taken with a view to compensate adjustment costs to the greatest extent possible are presented in the section of the impact assessment report presenting the preferred option.

For the Paediatric Regulation

The figures are presented in comparison with the baseline and are average annual costs in m€

I. Overview of benefits (compared with baseline costs) – Preferred Option. Yearly costs		
Description	***Amount***	***Comments***
Direct benefits		
Industry, originators	169 m gross benefit	Benefits deriving from one estimated SPC extension per year
Patients	3 extra PIPs for products addressing UMN of children Faster completion of PIPs and consequently medicines reaching faster children	Not possible to determine the benefits as it will depend greatly from the products that will be developed
Administrative cost savings related to the 'one in, one out' approach*		
Direct Administrative costs savings	**2.8 m**	Administrative savings for companies deriving from the simplification and streamlining of the PIP procedures

II. Overview of costs (compared with baseline costs) – Preferred option							
		Citizens/Consumers		**Businesses**		**Administrations**	
		One-off	**Recurrent**	**One-off**	**Recurrent**	**One-off**	**Recurrent**
Costs for conducting extra PIPs for originators	Direct costs				66 m €		
Cost for delayed generic entry due to one extra SPC paediatric extension granted per year					33 m €		
Costs for public authorities due to the extra SPC paediatric extension granted					1.3 m €		76 m €

Costs for patients due to the extra SPC paediatric extension granted leading to delayed entry			75 m €				
Administrative costs due to increased number of PIP conducted					1.3 m €		
Costs related to the 'one in, one out' approach							
Total	Direct adjustment costs	N.A	N.A	N.A	N.A		
	Indirect adjustment costs	N.A	N.A	N.A	N.A		
	Administrative costs (for offsetting)	N.A	N.A	N.A	-1.5 m €		

EUROPEAN COMMISSION
Regulatory Scrutiny Board

Brussels,
RSB

Opinion

Title: Impact assessment / Revision of the EU legislation on medicines for children and rare diseases

Overall opinion: NEGATIVE

(A) Policy context

Regulation (EC) No 141/2000 on medicinal products for rare diseases and Regulation (EC) No 1901/2006 on medicines for children aim to address specific medical needs for these small patient groups. These medicines also need to comply with the general pharmaceutical legislation which is currently under review. The Regulation on medicinal products for rare diseases aims to address specific medical needs by creating incentives, while the Regulation on medicines for children is centres on obligations to screen products for possible use in children. The revision of these two Regulations is based on a joint evaluation of these Regulations published in 2020.

(B) Summary of findings

The Board notes the additional information provided in advance of the meeting and commitments to make changes to the report.

However, the Board gives a negative opinion because the report contains the following significant shortcomings:

(1) The coherence and interaction with the general pharmaceutical legalisation (and its revision) and other initiatives is not clear.

(2) The presented narrative and intervention logic do not clearly describe and link the problems, objectives, proposed measures and their impacts, particularly in the area of availability and accessibility of these medicines.

(3) The description and impact analysis of the options is unclear and their costs and benefits are neither well presented nor compared. Given the apparent small differences between the impacts of the different options, the report does not sufficiently discuss the sensitivity of the impact analysis and how this uncertainty affects the conclusions.

(C) What to improve

(1) The report should clarify the links and overlaps with the general pharmaceutical legislation and its upcoming revision. It should be clear how the ambition of the general pharmaceutical legislation is included in this initiative and how the objectives and measures of the two initiatives create synergies and/or trade-offs. The link with other initiatives should be integrated better in the report, e.g. regarding cooperation at global level. Specific research programmes for these medicines and their link to the general development of medicines should be outlined. Based on a clearer problem identification, the report should present a more coherent narrative with clarified specific objectives and better linked measures. It should better explain the enabling framework character of the initiative and that overall progress depends heavily on the effective interplay with other critical measures. This should help to better manage the expectations of the present initiative.

(2) The problems of availability and accessibility of these medicines should be clarified, together with their drivers, substantiated with robust evidence (e.g. EC pharmaceutical sector inquiry), and informed by the views of affected stakeholders. The report should be clear if the problems mainly lie with the Member States or the market behaviour of pharmaceutical industry or result from a economic market failure (e.g. lack of economic incentives). It should also be clear on the relative importance (and possible interaction) of the drivers and at which level these can be tackled most effectively while respecting subsidiarity and Member States competences. Finally, it should be clear what the different specific objectives are regarding availability and accessibility, how they relate to each other, and what the trade-offs are (e.g. higher absolute number of new medicines vs number of patients benefitting from new or less costly medicines).

(3) The description of the options should be clarified, both in content and how the specific measures work together to tackle the problem drivers and reach the specific objectives. The effectiveness of the different measures in tackling the problem drivers and delivering on the specific objectives should be better assessed. The report should clearly demonstrate that the proposed measures are complementary and compatible with the upcoming revision of the general pharmaceutical legislation.

(4) The analysis of the impacts should be structured better and presented clearly. The analysis should be understandable for a non-expert reader with cross references between results and calculations. The assumptions should be outlined clearly. The impacts on SMEs should be analysed further and the evidence available for assessing these impacts should be put forward. The report should be clear which measures are most cost-effective.

(5) The comparison of options should be supported by a clear overview of costs and benefits of the different options and a clear assessment in terms of effectiveness, efficiency and coherence. This should help the selection of a preferred option and in assessing its proportionality. The trade-offs for the different options regarding innovation, availability and affordability should be described, including possible unintended consequences such as earlier or later entering in the market of both innovative as well as generic medical products. Given the apparent small differences between the impacts of the different options, the report should better reflect the sensitivity of the impact analysis to the limitations of data and the modelling assumptions and how this uncertainty may affect the conclusions regarding the preferred options.

(6) The report should present more systematically the views of different stakeholder categories on the problems, options and their impacts.

Some more technical comments have been sent directly to the author DG.

(D) Conclusion **The DG must revise the report in accordance with the Board's findings and resubmit it for a final RSB opinion.**	
Full title	Revision of the EU legislation on medicines for children and rare diseases
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