Welcome to the survey for a study supporting the evaluation of the EU Orphan Regulation!

Dear Sir/Madam,

You have been invited to participate in this survey as a key stakeholder in a study supporting the evaluation of Regulation (EC) N° 141/2000 on orphan medicinal products (henceforth the EU Orphan Regulation) for the European Commission (DG SANTE).

The European Commission has commissioned Technopolis Group and Ecorys BV to collect data to better understand the perspectives of stakeholders on the efficiency, effectiveness, relevance, and EU added value of the EU Orphan Regulation as well as its coherence with other regulations. The study is expected to be completed in first half of 2019. The final report will be made publicly available.

The current survey is intended for (academic) researchers and experts with an interest in:

- **genetics and pathophysiology of rare diseases**
- **development of medicinal products for the treatment of rare diseases**
- **pharmaco-economics and value assessment of medicines**
- **pharmaceutical policy**

If you are, or represent, a sponsor of a product that has received an orphan designation under the EU Orphan Regulation, you may instead complete this version of the survey.

We anticipate that completing this survey will not take more than 45-60 minutes of your time. In case you need to quit the survey before completion, it is possible to save answers and complete the survey later. Please complete the survey before the 14th of November 2018.

Should you experience any problems with this survey, please contact Technopolis Group at orphan-regulation@technopolis-group.com. If you would like to share a document or position paper that could be relevant for the study please send it to the email indicated above.

Thank you for your participation! Please click Next to start the survey.

Best regards,
Technopolis Group and Ecorys project team.

Privacy Note
The European Commission is the data controller and Technopolis Group the data processor in administering this survey. Both organisations are committed to user privacy and confidentiality, guided by the Regulation (EC) No 45/2001 regarding processing personal data by the Community institutions.

The specific privacy statement on targeted stakeholder consultation about the legislation on medicines for rare diseases and children can be accessed here.

Respondent characteristics

1. Which of the following **best describes you**?

- ◯ Researcher in the field of rare diseases
- ◯ Researcher in the field of orphan medicine development
- ◯ Researcher in the field of paediatric medicine and paediatric medicine development
- ◯ Researcher in the field of health economics or pharmaco-economics
- ◯ Researcher in the field of pharmaceutical policy
- ◯ Prefer not to say

Other (please specify)

2. What **country** are you based in?

Research on rare diseases and orphan medicines

* 3. Which of the following do you consider to have had the most significant **impact on stimulating R&D for orphan medicines in the last 20 years**? (Max. 3 answers)

- [ ] National initiatives to support R&D
- [ ] European support for research (e.g. Framework Programmes, Innovative Medicines Initiative)
- [ ] Research networks such as OrphaNet
- [ ] EU Orphan Regulation (introduced in 2000)
- [ ] US Orphan Drug Act (introduced in 1983)
- [ ] Other national orphan medicine regulations
- [ ] Changed market forces (e.g. increased emphasis on low volume - high cost models)
- [ ] Increased societal or political attention for (medicines for) rare diseases
- [ ] Other (please specify below)

4. Please provide a **brief explanation** of your answer to Question 3.

5. What impact has the EU Orphan Regulation had on the **intensity and direction of research** for rare diseases and development of medicines for rare diseases in the European academic community? **Indicate which of the following you consider most accurate.**

- ◯ It has increased the **overall intensity of research** in these fields, but the **focus of the research has not significantly shifted**
- ◯ It has increased the **overall intensity of research** in these fields, and **refocused research into other therapeutical areas or methods**
- ◯ It has **not significantly influenced the intensity or direction** of research in these fields
- ◯ It has **had a negative overall impact** on the intensity of research in these fields
- ◯ **Do not know**
- ◯ Other (please specify below)

6. Please provide a **brief explanation** of your answer to Question 5.

7. How has the EU Orphan Regulation affected **collaborations** of your institution with any of the following parties? Please indicate which of the following apply (multiple answers possible).

- ☐ **No influence** on any of my collaborations
- ☐ Increased collaboration with **large pharmaceutical or biotechnology companies**
- ☐ Increased collaboration **with small and medium-sized pharmaceutical or biotechnology companies** (including academic spin-out organisations)
- ☐ Increased collaboration with **patients, patient organisations and/or consumer organisations**
- ☐ Increased collaboration with **researchers in other disciplines**
- ☐ Increased collaboration with **other researchers in the same discipline**
- ☐ Do not know / not applicable
- ☐ **Reduced collaboration** (please specify below)

8. Please provide a **brief explanation** of you answers to Question 7.

* 9. Which of the following do you expect to have the **greatest impact on the future of research** for rare diseases and development of medicines for rare diseases in the **next 15 years**? (Max. 3 answers).

- [ ] 'omics technologies (e.g. genomics, proteomics, metabolomics)
- [ ] Molecular diagnostics (e.g. genetic tests, biomarker tests, companion diagnostics)
- [ ] Gene therapy, genome editing and stem cell therapy
- [ ] Bioinformatics, big data, real world data and patient registries
- [ ] Increased involvement of patients and patient organisations in research
- [ ] Other (please specify)

* 10. Are there currently sufficient **opportunities to support research** for rare diseases and the development of medicines for rare diseases in the EU?

- ( ) Yes
- ( ) No
- ( ) Do not know

11. What **other type of opportunities** do you consider necessary to support research for rare diseases and orphan medicine development? Please, provide a brief explanation.

Perspectives on the relevance and effectiveness of the EU Orphan Regulation

12. For each of the following statements, please indicate the level of your agreement.

	Strongly disagree	Disagree	Agree	Strongly agree	Do not know
At the time the EU Orphan Regulation was introduced in 2000, there was a **clear need** for concerted EU action beyond the efforts of individual member states.	○	○	○	○	○
The EU Orphan Regulation, which offers various incentives to developers of orphan medicines, was a relevant instrument to **promote the development** of new orphan medicines.	○	○	○	○	○
The EU Orphan Regulation has contributed to an **increase in the overall R&D** efforts to support the development of orphan medicines.	○	○	○	○	○
The EU Orphan Regulation has contributed to an **increase in the number of new orphan medicines** on the market in my country.	○	○	○	○	○
The EU Orphan Regulation has contributed to an increase in the number of orphan medicines developed for **treatment of paediatric conditions.**	○	○	○	○	○
The EU Orphan Regulation has stimulated R&D for orphan medicines in areas of **greatest unmet medical need.**	○	○	○	○	○

13. Please, provide a **brief explanation** of your answers above on the following statements.

At the time the EU Orphan Regulation was introduced in 2000, there was a **clear need** for concerted EU action beyond the efforts of individual member states.

The EU Orphan Regulation, which offers various incentives to developers of orphan medicines, was a relevant instrument to **promote the development** of new orphan medicines.

The EU Orphan Regulation has contributed to an **increase in the overall R&D efforts** to support the development of orphan medicines.

The EU Orphan Regulation has contributed to an **increase in the number of new orphan medicines** on the market in my country.

The EU Orphan Regulation has contributed to an increase in the number of orphan medicines developed for **treatment of paediatric conditions.**

The EU Orphan Regulation has stimulated R&D for orphan medicines in areas of **greatest unmet medical need**.

14. In what area(s), if any, do you see the**greatest mismatch** between orphan medicines that have been brought to market and areas of unmet need?

EU added value and coherence of the EU Orphan Regulation

15. How, if at all, has the EU Orphan Regulation created **added value beyond national efforts by member states** to support R&D of medicines for rare diseases in your country? (Tick all that applies).

- [ ] By standardising the **definition** of orphan conditions in the EU
- [ ] By developing a standard **interpretation of 'significant benefit'** for orphan medicines
- [ ] By offering an additional **set of incentives to support R&D** of orphan medicines
- [ ] By increasing **access to orphan medicines** via mandatory registration through the centralised procedure
- [ ] By promoting the **development of orphan medicines**
- [ ] **No added value**
- [ ] **Do not know**
- [ ] Other (please specify)

16. What are the main **national initiatives** in your country to stimulate R&D of orphan medicines? (e.g. tax instruments, networking and research programmes)?

17. What initiatives have been taken at national or regional level in your country that are **complementary to the EU Orphan Regulation**?

18. To what extent is the EU Orphan Regulation **coherent with other EU policy priorities and actions** related to pharmaceutical product development?

- ( ) To a large extent
- ( ) To a moderate extent
- ( ) To a small extent
- ( ) Not at all
- ( ) Do not know

Please, provide a brief explanation.

19. To what extent is the EU Orphan Regulation **coherent with other EU regulations and initiatives** that aim to support pharmaceutical product development?

- ◯ To a large extent
- ◯ To a moderate extent
- ◯ To a small extent
- ◯ Not at all
- ◯ Do not know

Please, provide a brief explanation.

National access to orphan medicines

The following questions are intended to get a better understanding offactors that influence availability of medicines for rare diseases nationally. Therefore, some of the questions are specific to (sub)national contexts. If you represent a European or international/global organisation, rather than a national one, you may select ‘does not apply’.

Note: The term ‘products’ in each of the following questions refers to medicinal products with a European orphan designation and a European marketing authorisation. A full list of these products can be found here (Part 1: List of orphan medicinal products in Europe with European orphan designation and European marketing authorization).

20. In your estimation, to what extent are these products**placed on the market by the authorisation holders** in your country?

Note: ‘Placed on the market’ here means that the company that has obtained a marketing authorisation, has set a price on the product in a particular market, where necessary has negotiated access, and has made that product available for procurement. This does not include availability through parallel import or compassionate use programmes.

- ◯ **Over 75%** are placed on the market
- ◯ **Between 50 and 75%** are placed on the market
- ◯ **Between 25 and 50%** are placed on the market
- ◯ **Do not know / does not apply**

Please provide a brief explanation

21. Which of the following best describes the**average time** when a product with a European orphan designation and a European marketing authorisation becomes **accessible** in your country?

- ◯ Most products become accessible **before the marketing authorisation** through compassionate use programmes
- ◯ Most products become accessible **at or within 2 months** of the marketing authorisation (i.e. there are no major delays)
- ◯ Most products become accessible **within 6 months** of the marketing authorisation (i.e. there are some delays)
- ◯ Most products become accessible **more than 6 months** after the marketing authorisation (i.e. there are significant delays)
- ◯ Do not know / does not apply

Please provide a brief explanation

* 22. What do you see as the **main reasons** that (some) orphan medicines are **not available** in your country? (Max. 3 answers).

- [ ] Small **market size**
- [ ] **National pricing policies** and/or **reimbursement** system characteristics
- [ ] Clinical **practices or guidelines**
- [ ] Level of existing or anticipated **competition**
- [ ] Do not know
- [ ] Other (please specify)

23. Please, provide a **brief explanation** of your answer above.

* 24. Which of the following have the greatest impact on **access** to orphan medicines in the EU (either positive or negative)? (Max. 3 answers).

- [ ] Overall pressures on **national health care budgets**
- [ ] **National pricing** and **reimbursement policies**
- [ ] Increased focus on **health technology assessment and value assessment**
- [ ] **New regulatory processes**, e.g. accelerated approval, conditional approval and adaptive pathways
- [ ] **Compassionate use** or **named-patient programmes**
- [ ] **Intellectual property rights** and **regulatory protections**
- [ ] Do not know
- [ ] Other (please specify)

25. Please, provide a **brief explanation** of your answer above.

* 26. Which of the following do you consider the main threats to **affordability** of orphan medicines in the EU? (Max. 3 answers).

- [ ] Increase in **number of known patients** with orphan diseases (e.g. due to population growth, changing epidemiology, improved diagnostics)
- [ ] Increase in **number of new treatments** for rare diseases
- [ ] Increasing **emphasis** on complex or costly treatments
- [ ] **Market inefficiencies and lack of competition**
- [ ] **Expanded interpretation** of 'orphan disease' in the context of precision medicine
- [ ] **Rediscovery of existing (off-patent) medicines** that are granted orphan market exclusivity
- [ ] **Do not know**
- [ ] Other (please specify)

27. Please, provide a **brief explanation** of your answer above.

End of the survey!

28. If you have **any further comments/views** about the EU Orphan Regulation, please leave them in the box below.

29. We may like to follow up on some of the survey responses to elaborate further.**Please provide your contact details below** if we may contact you regarding this study.

Name

Email Address

Thank you for completing the survey!