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From: Secretary-General of the European Commission,  
signed by Mr Jordi AYET PUIGARNAU, Director

date of receipt: 11 August 2020

To: Mr Jeppe TRANHOLM-MIKKELSEN, Secretary-General of the Council  
of the European Union

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Subject: COMMISSION STAFF WORKING DOCUMENT EXECUTIVE  
SUMMARY OF THE EVALUATION Joint evaluation of Regulation (EC)  
No 1901/2006 of the European Parliament and of the Council of 12  
December 2006 on medicinal products for paediatric use and  
Regulation (EC) No 141/2000 of the European Parliament and of the  
Council of 16 December 1999 on orphan medicinal products

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Delegations will find attached document SWD(2020) 164 final.

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Brussels, 11.8.2020  
SWD(2020) 164 final

**COMMISSION STAFF WORKING DOCUMENT**  
**EXECUTIVE SUMMARY OF THE EVALUATION**

**Joint evaluation of Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products**

{SEC(2020) 291 final} - {SWD(2020) 163 final}

## 1. CONTEXT

In the 1980s and 1990s, the level of awareness concerning the lack of satisfactory treatments for patients with rare diseases and for children in the EU started to increase.

The pharmaceutical industry showed insufficient interest in investing in the development of medicines for rare diseases and for children. Doctors treating patients with rare diseases often had no medicines available, and a similar situation occurred for children. In 2000 and 2007 the EU therefore introduced two regulations to foster the development of medicines for rare diseases<sup>1</sup> and for children<sup>2</sup>.

The results of the evaluation will guide reflections on any future changes to the legislative framework. It will also inform the EU's pharmaceutical strategy, which seeks to improve and accelerate patients' access to safe, effective and affordable medicines and to support innovation in the EU pharmaceutical sector.

## 2. EVALUATION

The evaluation assesses the strengths and weaknesses of the two regulations over 2000-2017 (medicines for rare diseases) and 2007-2017 (medicines for children). It follows an evidence-based analysis of the functioning of the two instruments from a public health and socio-economic perspective. The two regulations are evaluated together as the majority of rare diseases may appear already in children and many children's diseases are also rare.

Three independent studies<sup>3</sup> were used, as well as reports by the European Commission<sup>4</sup> and the European Medicines Agency.<sup>5</sup> The evaluation also gathered information from all relevant interested parties through workshops, public and targeted consultations. Triangulation of information has been sought through the use of different sources of information and inclusion of a large number of stakeholders. However, some areas are supported by less robust evidence than others. That was in particular the case for the baseline scenario and the cost-benefit assessment.

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<sup>1</sup> Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products.

<sup>2</sup> Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/200.

<sup>3</sup> Study on the economic impact of the Paediatric Regulation, including its rewards and incentives; Orphan study report (2019); Study on the economic impact of supplementary protection certificates, pharmaceutical incentives and rewards in Europe (2018).

<sup>4</sup> Commission Report on the Paediatric Regulation, COM(2017) 626

<sup>5</sup> General report on the experience acquired as a result of the application of the Paediatric Regulation (10-year Report from EMA to the European Commission, 2017); General report on the experience acquired as a result of the application of the Paediatric Regulation (5-year Report from EMA to the European Commission, 2012) and annual reports from the Agency.

### 3. KEY FINDINGS

The evaluation found that both regulations have fostered the **development and availability** of medicines for patients with rare diseases and for children. They have redirected private and public investment towards previously neglected areas through incentives, obligations and rewards. Member States alone could not have achieved this result due to the small number of patients concerned and the fragmentation of the market.

A number of both EU and national research programmes in the field of rare diseases have complemented the legislation. However, the information available does not allow a direct link to be drawn between the public funding and the medicines effectively developed.

The number of medicines for patients with rare diseases and for children has increased. Medicines for patients with rare diseases have also become available faster and have reached a higher number of patients in the Member States. Similarly, the Regulation on medicines for children increased the number of clinical trials in children and, consequently, the development of new medicines for them. It reduced the ‘off-label’ use of medicines for adults in children, which were not specifically tested or adapted for use in children (‘off-label’ use) and favoured the creation of a ‘paediatric research environment’ in Europe.

Nevertheless, both regulations have not adequately managed to support **development in areas where the need for medicines is greatest**. Products tend to be developed in certain more profitable therapeutic areas for which the number of available treatments is increasing.

The evaluation questions focus on whether the threshold of fewer than 5 in 10 000 patients is the right tool for identifying rare diseases which need specific support in medicines development. Advances in science, such as personalised medicine and the use of biomarkers could add another layer of complexity to the current regulatory framework. While such developments may hold great potential for optimal tailoring of treatments to diseases, they should not lead to unnecessary multiplications of rare diseases out of common diseases, neither proliferation of exclusivity periods.

The Regulation for medicines for rare diseases can also support products (such as antibiotics) for which companies cannot expect sufficient return on investment. However, this possibility was difficult to implement and has never been used.

The Regulation for medicines for children obliges companies to test new medicines in children but has no dedicated instrument to direct development in areas relevant for children. The development of new medicines for children therefore remains mainly driven by adults’ needs. As a result, it does not necessarily address the greatest therapeutic needs of children (such as treatments for children’s cancers and for newborns).

The evaluation found that **incentives** remain relevant to encourage the development of medicines for rare diseases. However, for some rare diseases the market has started to look more similar to ‘standard’ medicines. Hence, in such cases it could be questionable whether a 10-year market exclusivity is justified. The Orphan Regulation allows for a shortening of the market exclusivity period once a medicine becomes commercially successful. In practice, Member States did not trigger the procedure because it is too difficult to provide the necessary evidence.

For medicines for children, the cost of conducting clinical studies in children can be compensated by extending the patent (Supplementary Protection Certificate, ‘SPC’). While this reward is partly fulfilling its role, it has not shown to be effective in stimulating the development of medicines whose development for adults is not attractive. Obtaining this reward may be complex, as companies have to request it individually at the various national patent offices.

The incentives and rewards provided by both regulations come with a cost. The evaluation found that both regulations have increased costs for **healthcare systems**. However, thanks to the treatment with medicines for rare diseases, patients benefited from an improvement in their quality of life. The benefits the legislation brought for children appear to outweigh the costs imposed on both industry and society.

The evaluation has also shown that the medicines developed thanks to the two regulations are not accessible by patients equally in all Member States. This is mainly due to factors outside the scope of the regulations, such as strategic launch decisions by pharmaceutical companies and national pricing policies and reimbursement systems.

For both regulations, some inefficiencies and undesirable consequences were observed. Any future solution to the shortcomings identified should strike a balance between the needs of fostering innovation and ensuring the availability of and access to medicines for patients with rare diseases and for children. These aspects are closely linked to the key objectives of the Pharmaceutical strategy for Europe, which includes these regulations. The strategy aims to create a future-proof regulatory framework through a holistic reflection on the pharmaceutical sector.