The current revision of the orphan medicines regulation in the EU: what is at stake for gene and cell therapy?

Aurélie Mahalatchimy[1] and Éloïse Gennet[2]

[1] Permanent Researcher in law at the French National Centre for Scientific Research (CNRS, CR), Law Faculty, UMR 7318 DICE CERIC, CNRS, Aix Marseille University, Toulon University, Aix-en-Provence, France; [2] Post-doctoral Researcher in Law, Law Faculty, UMR 7318 International, Comparative and European laws (DICE) CERIC, CNRS, Aix- Marseille University, Toulon University, Aix-en-Provence, France.

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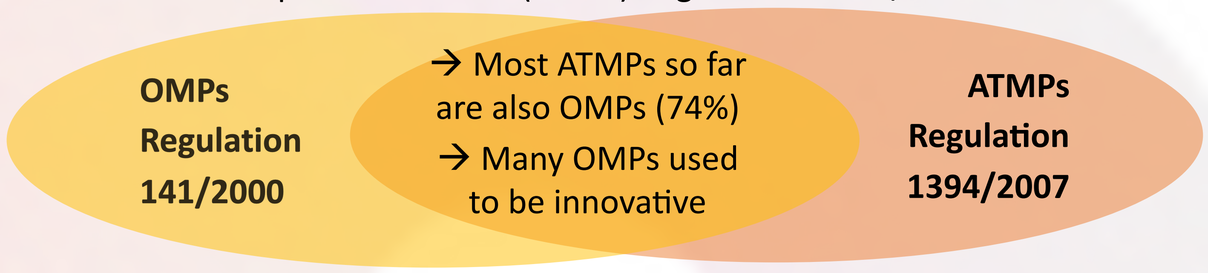
REGULATORY CONTEXT

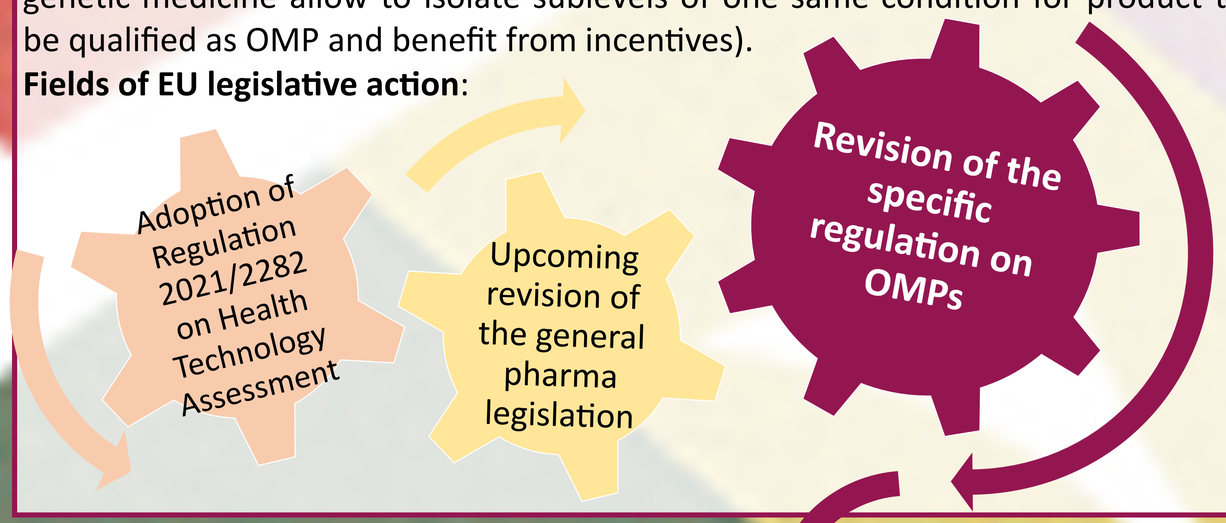
In the European Union, gene and cell therapy medicinal products are mainly regulated by the specific legal framework applicable to Advanced Therapy Medicinal Products (ATMPs) Regulation n°1394/2007; but also possibly by the Orphan Medicines (OMPs) Regulation n°141/2000.



CHALLENGES AND ACTION PLAN

After 20 years of OMPs Regulation's implementation, results remain unsatisfactory. **OMPs & ATMPs still fail in being equally accessible to patients in all Member States**: *e.g.* their price and reimbursement level may vary between countries, or they are not even commercialized in others. Plus, OMPs look increasingly similar to standard medicines rather than innovative medicines like ATMPs (personalised and genetic medicine allow to isolate sublevels of one same condition for product to be qualified as OMP and benefit from incentives).

Fields of EU legislative action:



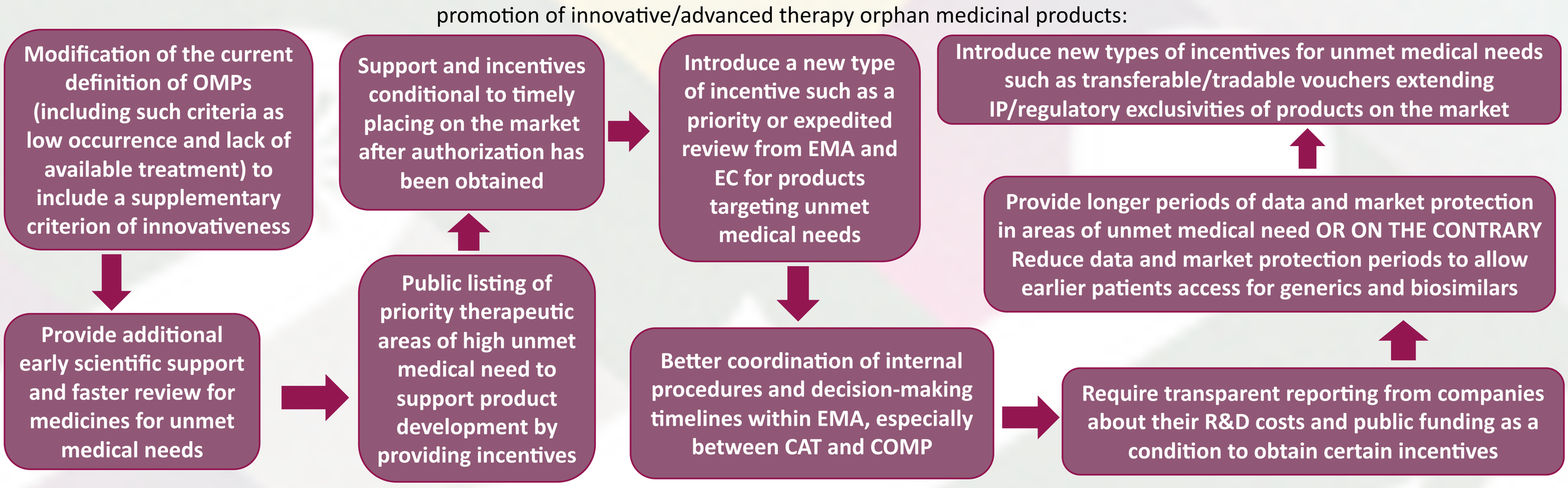
CURRENT INCENTIVES

EU Law, especially Regulation 141/2000 and Regulation 1394/2007, aims to incentivize the development and marketing of OMPs and ATMPs to palliate acute scientific and financial difficulties that these medicines represent.

Incentives for OMPs		Incentives for ATMPs (except hospital exemption)
Research funding for instance the E-RARE project, the European Joint Programme on Rare Diseases		Research funding for instance with the Joint undertaking on Innovative Medicines Initiative
Free scientific assistance from the European Medicines Agency and its Committee on Orphan Medicinal Products (COMP)		Fee reduction on scientific assistance from the European Medicines Agency and its Committee on Advanced Therapies (CAT)
Partially or totally reduced administrative fees for the marketing authorisation application process		Partially reduced administrative fees for the marketing authorisation application process
Mandatory centralized procedure for marketing authorization, valid in all EU Member States		Mandatory centralized procedure for marketing authorization, valid in all EU Member States
Ten-year commercial exclusivity		

POTENTIAL REGULATORY EVOLUTIONS

The European Commission has issued reports and conducted several public consultations from which potential solutions have emerged in order to enhance the promotion of innovative/advanced therapy orphan medicinal products:



CONCLUSION

Some proposed new incentives are challenging:

- Priority review: already tight timelines pressuring regulators
- Tradable exclusivity vouchers: hindered timely access to market for generics and biosimilars for the most expensive products; unfair for patients by delaying lower prices of more used medicines; increased healthcare systems expenditures; increased uncertainty and litigation regarding IP/regulatory exclusivities

Nevertheless, **the revision of OMP regulation has the potential to provide solutions to address unmet medical needs of rare disease patients and greatly enhance innovation, and as such to be beneficial for ATMPs development**:

- Focus on unmet medical needs that should be defined dynamically, ie taking into account the evolving scientific and medical context, in a multi-stakeholder setting;
- Dedicated public funding and financial incentives to promote research on unmet medical needs and neglected illnesses, health conditions, and populations;
- To introduce a corrective mechanism to prevent unaffordable prices or excessive return on investment: e. g. developer to justify the proposed price would be particularly relevant for high manufacturing costs of ATMPs.

The proposal for a new pharmaceutical legislation, including the revision of the OMP regulation, should be published by the European Commission **by the end of 2022**. The Council of the EU and the European Parliament will then try to reach an agreement and adopt a (usually amended) legislative act.

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