EPTRI
European Paediatric Translational Research Infrastructure

Challenges and opportunities for paediatric research from the new proposed EU rules

Viviana Giannuzzi

Fondazione per la Ricerca Farmacologica Gianni Benzi onlus

EPTRI Scientific Meeting and General Assembly– BOLOGNA – 13/03/2025

Disclaimer

The views expressed in this presentation are the personal views of the author and may not be understood or quoted as being made on behalf of, or reflecting the position of, the EMA and its committees and working parties with which the author is affiliated. The Union is not liable for any use that may be made with the information contained therein.

No financial disclosure to declare

ePTRI®
European Paediatric Translational Research Infrastructure

Pharma legislation revision - aims

- Maintain and reinforce the position of the EU pharma industry both within EU and globally
- Attract pharmaceutical R&D providing a future-proof, stable legal framework and a favourable environment
- Boost regulatory support for the development of promising medicines
- Provide a more targeted incentives framework for innovation with a focus on patient access and addressing unmet medical needs
- Boost innovation and EU competitiveness through an efficient and simplified regulatory framework to reduce regulatory burden

ePTRI®
European Paediatric Translational Research Infrastructure

Modified by: Humphreys presentation, RSNN 2023

Upcoming EU rules?

Reg (EC) 726/2004

Reg (EC) 141/2000

Reg (EC) 1901/2006

Dir. 2001/83/EC

Regulation

Directive

+ annexes

EUROPEAN COMMISSION

Brussels, 26.4.2023
COM(2023) 193 final

2023/0131 (COD)

Proposal for a

REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency, amending Regulation (EC) No 1394/2007 and Regulation (EU) No 536/2014 and repealing Regulation (EC) No 726/2004, Regulation (EC) No 141/2000 and Regulation (EC) No 1901/2006

(Text with EEA relevance)

{SEC(2023) 390 final} - {SWD(2023) 192 final} - {SWD(2023) 193 final} - {SWD(2023) 194 final}

Brussels, 26.4.2023
COM(2023) 192 final

2023/0132 (COD)

Proposal for a

DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

on the Union code relating to medicinal products for human use, and repealing Directive 2001/83/EC and Directive 2009/35/EC

(Text with EEA relevance)

{SEC(2023) 390 final} - {SWD(2023) 191 final} - {SWD(2023) 192 final} - {SWD(2023) 193 final}

EPTRI
European Paediatric Translational Research Infrastructure

SWD(2023) 192 Final; COM(2023) 193 final 2023/0131 (COD)

Upcoming EU rules?

Reg (EC) 1901/2006

Regulation

Directive

EUROPEAN COMMISSION

Brussels, 26.4.2023
COM(2023) 193 final

2023/0131 (COD)

Proposal for a

REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency, amending Regulation (EC) No 1394/2007 and Regulation (EU) No 536/2014 and repealing Regulation (EC) No 726/2004, Regulation (EC) No 141/2000 and Regulation (EC) No 1901/2006

(Text with EEA relevance)

{SEC(2023) 390 final} - {SWD(2023) 192 final} - {SWD(2023) 193 final} - {SWD(2023) 194 final}

Brussels, 26.4.2023
COM(2023) 192 final

2023/0132 (COD)

Proposal for a

DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

on the Union code relating to medicinal products for human use, and repealing Directive 2001/83/EC and Directive 2009/35/EC

(Text with EEA relevance)

{SWD(2023) 193 final}

+ annexes

Paediatric Regulation

ANNEX VIII

CORRELATION TABLE

Directive 2001/83 (EC)	Regulation (EC) No 1901/2006	This Directive
Art. 2(1)		Art. 1(1) and (2)
Art. 2(2)		Art. 1(4)

ePTRI
European Paediatric Translational Research Infrastructure

SWD(2023) 192 Final; COM(2023) 193 final 2023/0131 (COD)

Pharma legislation revision - promises

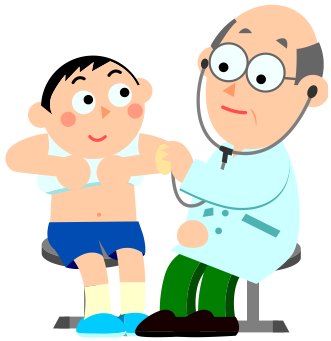
1. BETTER ACCESS TO EFFECTIVE AND AFFORDABLE MEDICINES
2. REDUCING SHORTAGES
3. MORE MEDICINES FOR CHILDREN AND RARE DISEASES
4. A STRONGER VOICE FOR PATIENTS
5. EASIER ACCESS TO INFORMATION
6. MORE ENVIROMENTALLY SUSTAINABLE MEDICINES

ePTRI®
European Paediatric Translational Research Infrastructure

European Commission
Reform of the EU Pharmaceutical legislation
A single market for medicines putting patients at the centre
APRIL 2023

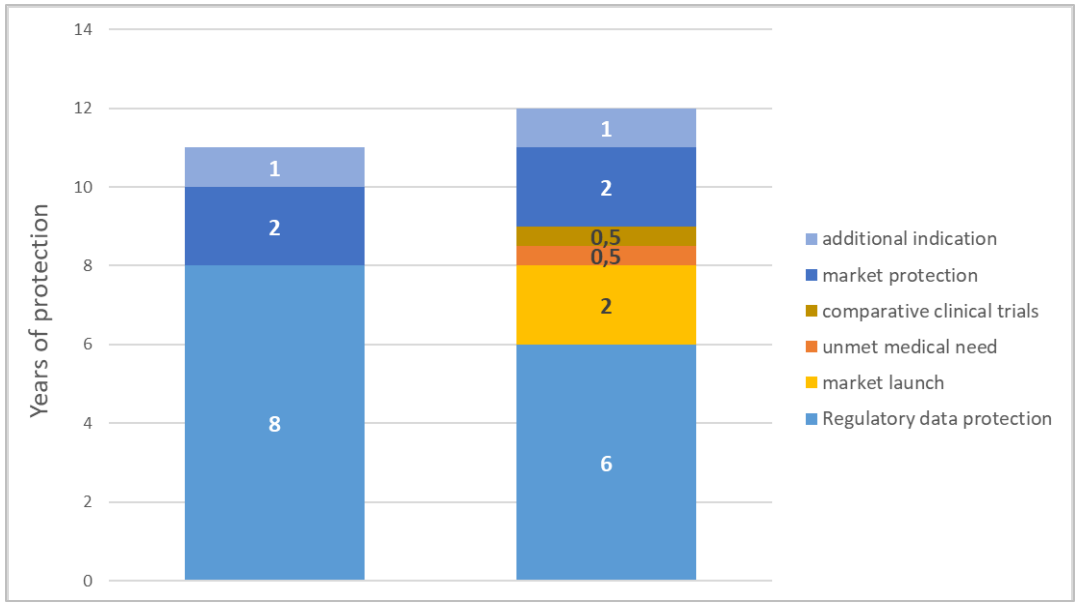
Which proposed rules impact on not-for-profit paediatric research?

1. Unmet medical needs identification
2. Repurposing
3. Mechanism of action criteria for PIPs
4. PIP procedure
5. Hospital exemptions
6. Participation in EMA activities

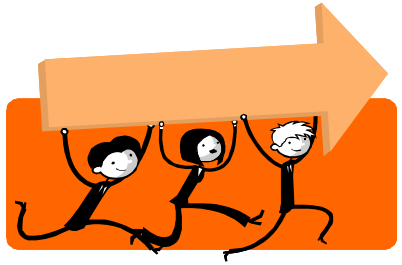


ePTRI®
European Paediatric Translational Research Infrastructure

Products addressing ‘unmet medical needs’ - incentives



- Conditional MA
- Increased scientific support by EMA ⇨ access to PRIME
- +6 months of data protection period ⇨ 12 months proposed by the EU Parliament



ePTRI®
European Paediatric Translational Research Infrastructure

Regulation EC proposal COM(2023) 193 final - 2023/0131 (COD); EU Parliament CAs 2023/0131(COD); Directive EC proposal COM(2023) 192 final - 2023/0132 (COD); EU Parliament CAs 2023/0132(COD)

1. Unmet medical needs identification

Products addressing ‘unmet medical needs’ identified

- through specific criteria defined in the directive, and
- by multi-stakeholder consultations, guidelines

Article 162

Consultation process

The Agency shall establish a consultation process with relevant national authorities or bodies for the exchange of information and pooling of knowledge on general issues of scientific or technical nature related to the tasks of the Agency, in particular guidelines on unmet medical needs and the design of clinical trials, other studies and the generation of evidence along the life cycle of medicinal products.

EU Parliament Regulation CAs

CHMP to assess if the medicine addresses an unmet need at the time of MAA

ePTRI® European Paediatric Translational Research Infrastructure

Regulation EC proposal COM(2023) 193 final - 2023/0131 (COD); EU Parliament CAs 2023/0131(COD); Directive EC proposal COM(2023) 192 final - 2023/0132 (COD); EU Parliament CAs 2023/0132(COD)

1. Unmet medical needs identification

Products addressing 'unmet medical needs' identified

- through specific criteria defined in the directive

> *Amendment*
>
> ***(50a) The concept of morbidity in the definition of 'unmet medical need' should encompass a multiplicity of factors. Morbidity should be understood to include aspects of quality of life of patients, a high burden of disease and treatment and the inability to perform daily life activities. Therefore, the assessment of 'unmet medical need' should take into account relevant patient experience data.***

Therapeutic indication relating to a life threatening/severely debilitating disease and:

a) there is no medicinal product authorised in EU for such disease, or the disease is associated with a remaining high morbidity/mortality

b) the use of the medicine results in a meaningful reduction in disease morbidity or mortality **for the relevant patient population**

ePTRI®
European Paediatric Translational Research Infrastructure

Article 83 Directive EC proposal COM(2023) 192 final - 2023/0132 (COD); EU Parliament CAs 2023/0132(COD)

1. Unmet medical needs identification

- Will require implementing acts by the EC
- Criteria in a directive ⇨ any difference by country?
- All orphans considered ‘addressing unmet needs’…incidence threshold not set ⇨ no harmonisation
- **Nothing paediatric-specific….**

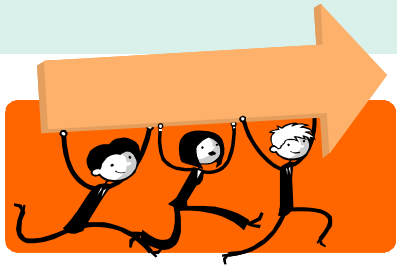
~~*Lists of paediatric unmet needs*~~

ePTRI®
European Paediatric Translational Research Infrastructure

2. Repurposing

- Not-for-profit entities may submit non-clinical or clinical evidence for a new therapeutic indication + any(possible) additional evidence submitted by the MA holders
- Opinion favourable ⇨ MAH shall submit a variation to update the product information with the new therapeutic indication
- 4 years of data protection for repurposed products

- more infos on off-label uses ⇨ paediatrics, pregnancy and unmet needs
- paediatric drug R&D faster and easier



ePTRI®
European Paediatric Translational Research Infrastructure

Article 48 *Regulation EC proposal COM(2023) 193 final - 2023/0131 (COD); EU Parliament CAs 2023/0131(COD); Article 84 Directive EC proposal COM(2023) 192 final 2023/0132 (COD)*

2. Repurposing

frontiers | Frontiers in Medicine

TYPE Perspective
PUBLISHED 16 September 2024
DOI 10.3389/fmed.2024.1456247

Check for updates

OPEN ACCESS

EDITED BY
Sandor Kerpel-Fronius,
Semmelweis University, Hungary

REVIEWED BY
Anando Sen,
Newcastle University, United Kingdom

Paediatric formulations—part of the repurposing concept?

Siri Wang[1]* and Viviana Giannuzzi[2]

[1]Norwegian Medical Products Agency, Oslo, Norway, [2]Fondazione per la Ricerca Farmacologica Gianni Benzi onlus, Research Department, Valenzano, Italy

- Paediatric- appropriate formulations are still lacking
- ***No definition/term currently stated by EU law…and still lacking in the proposed revision of legislation!***

In our opinion, an age-appropriate formulation, targeting a relevant off-label use in children, even for a disease or condition already authorised in adults or older children, would qualify as 'reformulation' within the repurposing term

ePTRI®
European Paediatric Translational Research Infrastructure

REPURPOSING

3. Mechanism of action criteria for PIPs

EMA may impose a PIP based on the Mechanism of Action of the drug for potentially effective against a different disease in children - within the same therapeutic area

EPTRI Paediatric Medicines Discovery TRP

academia

ePTRI®
European Paediatric Translational Research Infrastructure

Regulation EC proposal COM(2023) 193 final - 2023/0131 (COD); EU Parliament CAs 2023/0131(COD)

4. PIP procedure

'STEP-WISE' PIP	a dynamic plan on the basis of the clinical results obtained
ADAPTED	possibly simplified in selected situations: paediatric-only and PUMA products
DECISION	in ~~120~~ 90 day
LENGTH OF DEFERRAL	capped to 5 years (prolonged in 'justified cases')

ePTRI®
European Paediatric Translational Research Infrastructure

Regulation EC proposal COM(2023) 193 final - 2023/0131 (COD); Directive EC proposal COM(2023) 192 final 2023/0132 (COD); EU Parliament CAs 2023/0132(COD)

5. Hospital exemptions

ATMPs prepared under hospital exemption

*prepared on a **non-routine** basis*

*in a **hospital** (within the same Member State)*

*under the exclusive professional **responsibility of a medical practitioner***

*with an individual medical prescription for a **custom-made product** for an **individual patient***

Manufacturing approval

by the national competent authority where the hospital is located

Requirements

GMP and traceability for ATMPs, pharmacovigilance

Data collection

of data on use, safety and efficacy from the hospital to the national competent authority

Revocation

Approval revoked due to safety or efficacy concerns

ePTRI®
European Paediatric Translational Research Infrastructure

Directive EC proposal COM(2023) 192 final 2023/0132 (COD); EU Parliament CAs 2023/0132(COD)

New EMA structure

SCIENTIFIC COMMITTEES

WORKING GROUPS, WORKING PARTIES, POOL OF EXPERTS

will retain the expertise from other current committees:

Committee for Medicinal Products for Human Use (CHMP)

- 4 HCPs + 1 alternate + 1-5 experts
- 4 patients + 4 alternates

Pharmacovigilance Risk Assessment Committee (PRAC)

- 2 HCPs + 2 alternates
- 2 patients + 2 alternates

Committee for Advanced Therapies (CAT)

Committee for Orphan Medicinal Products (COMP)

Paediatri...

an ad-hoc working group on paediatric medicines

Committee on Herbal Medicinal Products (HMPC)

ePTRI®
European Paediatric Translational Research Infrastructure

Regulation EC proposal COM(2023) 193 final - 2023/0131 (COD); EU Parliament CAs 2023/0131(COD)

6. Participation in EMA activities

EMA shall develop a EU network of patient representatives, academics, medicines developers, investigators and centres with expertise in paediatric studies

- to discuss priorities in clinical development of medicines for children, in particular in areas of UMN
- to coordinate studies relating to paediatric medicines
- to build up the necessary scientific and administrative competences at EU level
- to avoid unnecessary duplication of paediatric studies

EnprEMA NETWORK

network of research networks, investigators and centres with expertise in paediatric studies

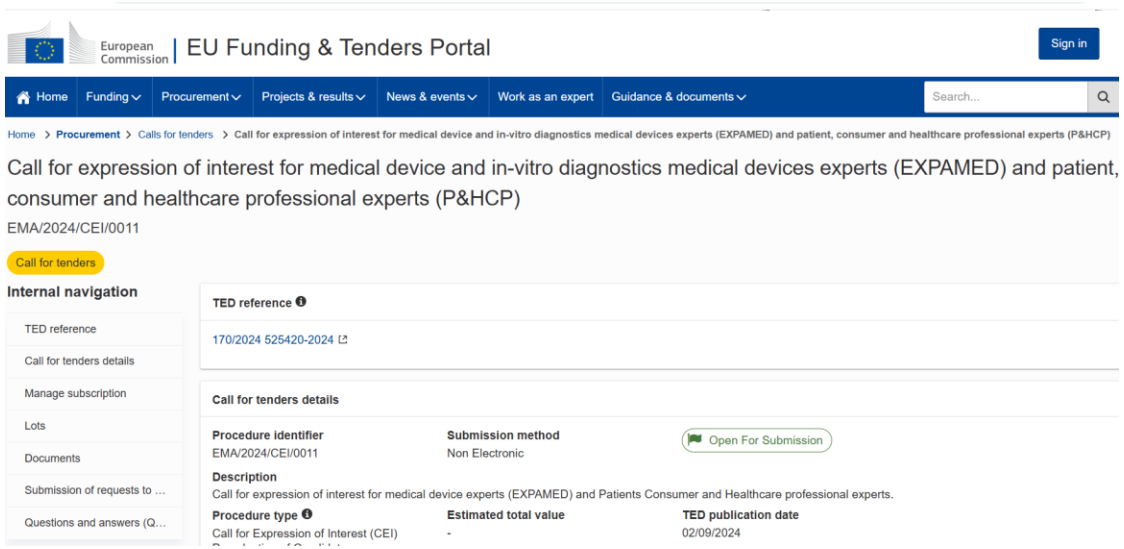
- sharing good practices
- promoting research into medicines for children
- building necessary competences at EU level
- dialoguing with ethics committees
- avoiding unnecessary duplication of studies

ePTRI®
European Paediatric Translational Research Infrastructure

Article 95 Regulation EC proposal COM(2023) 193 final - 2023/0131 (COD)

6. Participation in EMA activities

- EU call to establish a pool of patient, consumer, and healthcare professional experts for the period 2024-29
- assisting EMA with clinical, scientific expertise or experience in a particular condition and/or patient/consumer perspectives in the identified areas



ePTRI®
European Paediatric Translational Research Infrastructure

P&HCP call for expression of interest

Take home messages

- The ongoing revolution in the regulatory pharmaceutical landscape will affect paediatric research
- Academia and not-for-profit entities will be demanded to strengthen their regulatory expertise to participate in the R&D of paediatric medicines, and in particular in:
    - identifying unmet medical needs
    - providing regulatory agencies with evidence on repurposing and also turning and off-label uses into fully approved uses
    - providing ATMPs within own hospitals
    - possibly accessing to simplified PIP applications
    - participating in EMA activities

Viviana Giannuzzi

PharmD, PhD

vg@benzifoundation.org

FONDAZIONE
PER LA RICERCA FARMACOLOGICA
GIANNI BENZI
ONLUS

ePTRI
European Paediatric Translational Research Infrastructure