# Paediatric and Regulatory Considerations:

# The Proposed Changes to European Legislation

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# Topics

1. Data/Marketing Protection - Current Regime
2. European Commission Proposal
3. European Parliament Proposal
4. Orphan Drugs
5. Paediatric Rewards

# The Current Regime

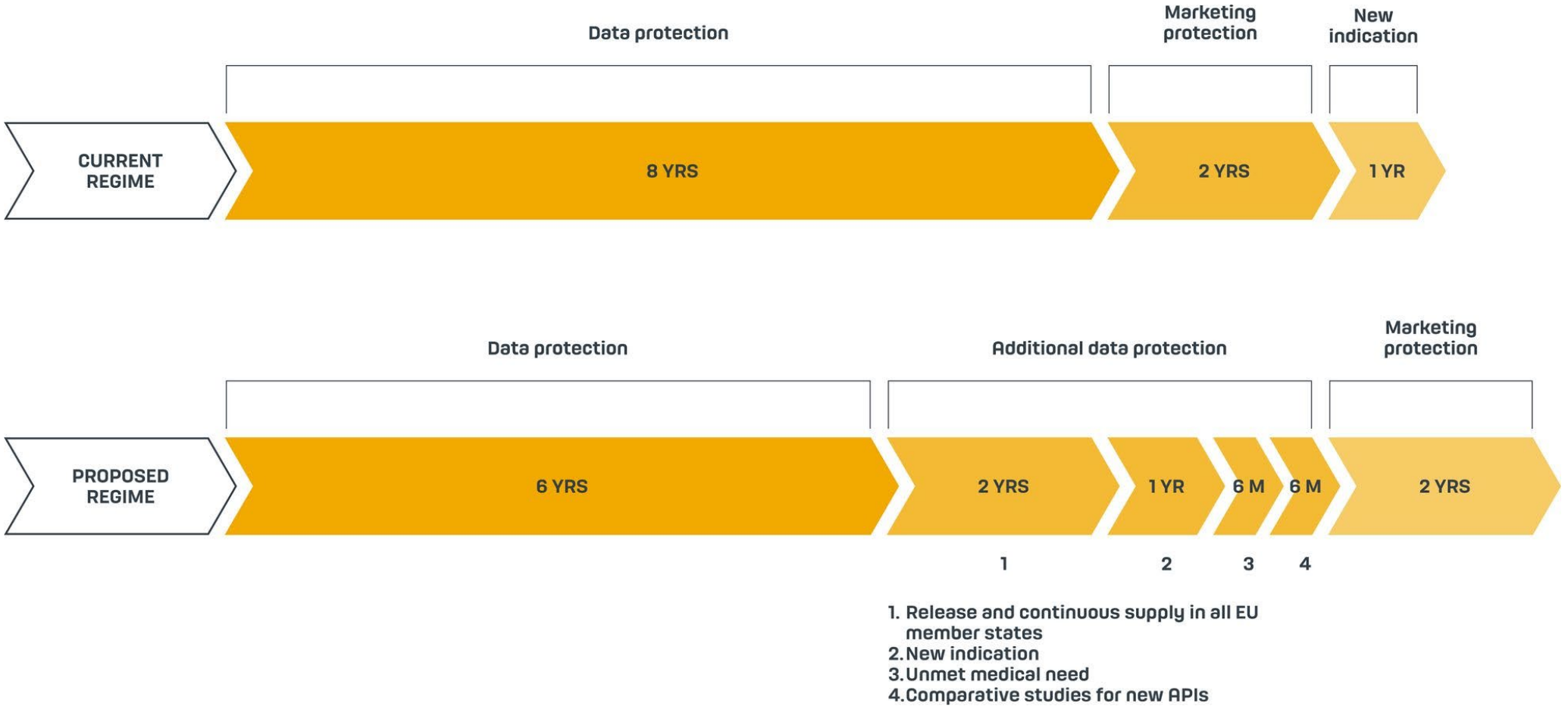

8 Years – Data Protection

2 Years – Marketing Protection

1 Year – New Indication

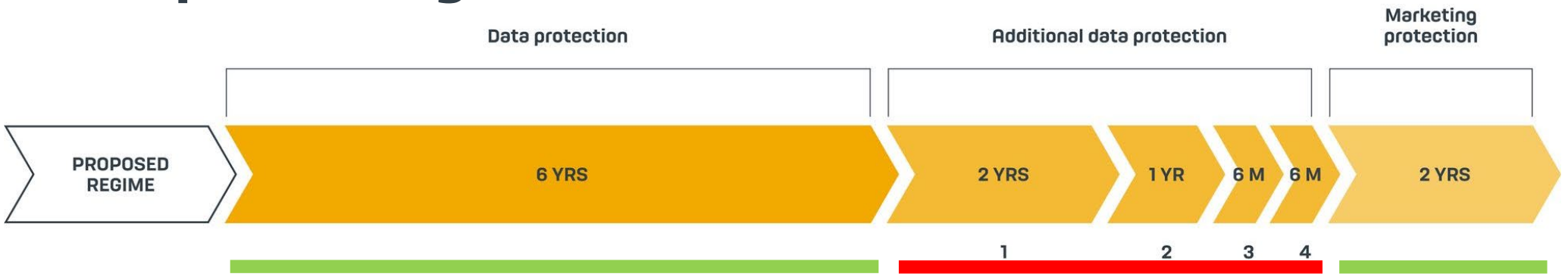
Directive 2001/83/EC and Regulation (EC) No 726/2004

# The Proposed Regime (European Commission)




Repeal of Directives 2001/83/EC and 2009/35/EC, and incorporation of parts of Regulation (EC) No 1901/2006 (the Paediatric Regulation)

# The Proposed Regime – Overview

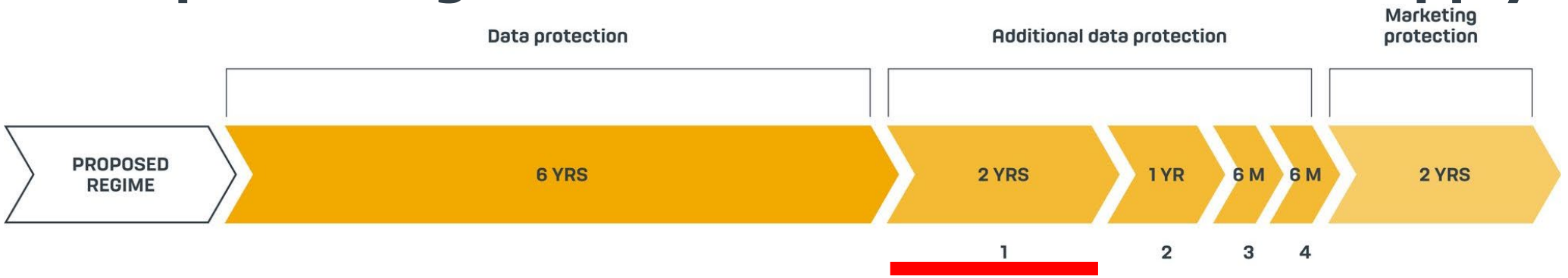



Default minimum protection is shortened to 8 years (6 DP + 2 MP)

Data protection period can be extended:

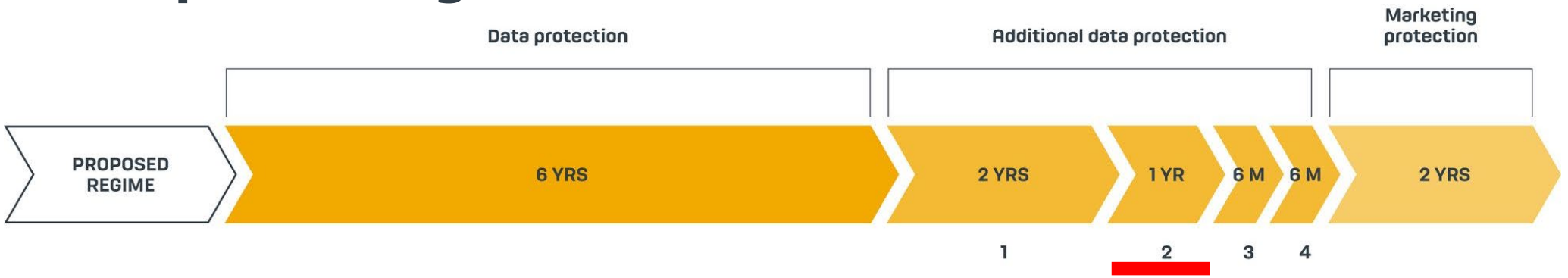
1. Release and continuous supply in EU (2 years)
2. New indication (1 year)
3. Unmet medical need (½ year)
4. Clinical trial used evidence-based comparator (½ year)

# The Proposed Regime – Release and Continuous Supply



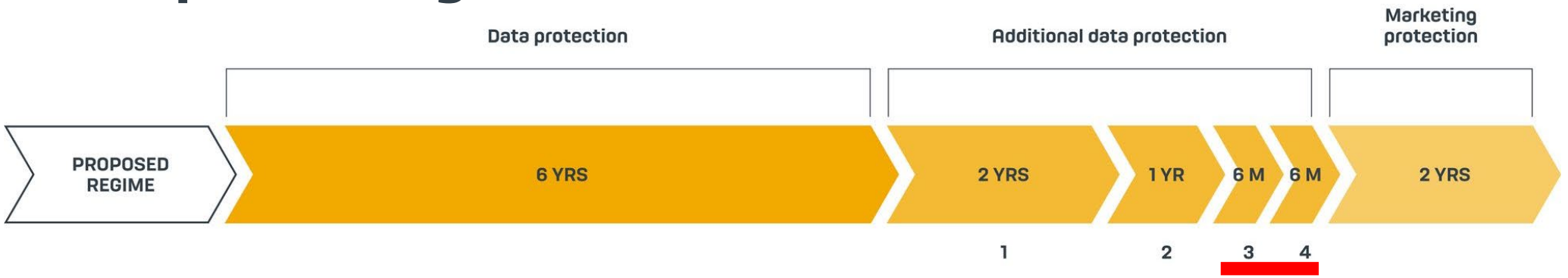

- New product must be released and continuously supplied "in a sufficient quantity and in the presentations necessary to cover the needs of the patients"
- Supply required in all EU states in which MA is valid
- Launch must occur within 2 years of approval (3 years for SMEs)
- Application for extra 2 years submitted in 34-36 month window

# The Proposed Regime – New Indication




- MA holder must receive authorisation for additional therapeutic indication "during the data protection period"
- Replaces existing "+1"
- Treatment must give significant clinical benefit in comparison with existing therapies
- incompatible with 6-month paediatric SPC extension

# The Proposed Regime – Other Data Protection Extensions




1. Unmet Medical Need

    - Life threatening or severely debilitating disease for which there is either no medicinal product authorised in EU or the indication is associated with high morbidity or mortality.

    - Product must achieve "meaningful reduction" in morbidity or mortality.

2. Clinical trial (for new API) uses evidence-based comparator

# The Proposed Regime – European Parliament's Comments

| | EC Proposal | EP Draft |
|---|---|---|
| Standard period of data + market protection [Arts. 80(2) + 81(1)] | **6 + 2 years** | **9 + 2 years** |
| Release and supply in sufficient quantities [Arts. 81(2)(a) + 82] | **+ 2 years** data protection | Deleted |
| Product addresses an unmet medical need [Arts. 81(2)(b) + 83] | **+ 6 months** data protection | **+ 1 year** data protection; broader definition of UMN |
| Comparative clinical trials conducted in accordance with EMA scientific advice [Art. 81(2)(c)] | **+ 6 months** data protection (only for initial applications containing a NAS) | **+ 6 months** data protection (for all applications) |
| New therapeutic indication [Art. 81(2)(d)] | **+ 1 year** data protection (available once) | **+ 1 year** data protection (available once) |

# The Proposed Regime – Orphan Drugs


Repeal and replacement of Regulation (EC) No 141/2000 (the Orphan Regulation)
Repeal and incorporation of Regulation (EC) No 1901/2006 (the Paediatric Regulation)

# The Proposed Regime – Orphan Drugs – Overview


- Market exclusivity – base period of **9 years**
- **+1 year** if product addresses "high unmet medical need":
  - either no medicinal product is authorised in EU, or the approved product will bring "exceptional therapeutic advancement";
  - product must achieve "meaningful" reduction in morbidity or mortality.
- **+1 year** for new indications of orphan medicinal products **(max 2)**
- **+1 year** if product is launched in all EU member states

# Orphan Drugs – European Parliament's Comments

| | EC Proposal | EP Draft |
|---|---|---|
| Standard orphan market exclusivity [Art. 71(2)(a)] | **9 years** | **8 years** |
| Products addressing a high unmet medical need (HUMN) [Art. 71(2)(b)] | **10 years** | **10 years** (HUMN defined more narrowly) |
| New orphan therapeutic indication [Art. 71(2)(ba)] | Not specified | **5 years** |
| Orphan products with MA based on bibliographic data [Art. 71(2)(c)] | **5 years** | **3 years** |
| Release and supply in sufficient quantities in relevant MS [Art. 72(1)] | **+ 1 year** | Deleted |
| New indication for a different orphan condition [Art. 72(2)] | **+ 1 year** (if indication obtained >2 years before the end of exclusivity period) | **+1 year** (if indication obtained >3 years before the end of exclusivity period) |

# The Proposed Regime – Repurposed Drugs

- New category for data protection
- 4 years of data protection [Art. 84]
- Available once and in narrow circumstances:
- Approved drug must provide a significant clinical benefit, and
  - there has been no prior data protection in the EU, or
  - first marketing approval in EU occurred >25 years ago

# Bolar Exemption - Proposed Changes

## European Commission's Proposal [Art. 85]

The Commission's proposal **extends** the Bolar exemption scope and clarify some uncertainties

The following acts would not be considered as infringing acts:

*a) studies, trials and other activities conducted to generate data for an application for:*

*i. a marketing authorisation of generic, biosimilar, hybrid or bio-hybrid medicinal products and for subsequent variations;*
*ii. health technology assessment as defined in Regulation (EU) 2021/2282;*
*iii. pricing and reimbursement.*

*b) the activities conducted exclusively for the purposes set out in point (a), may cover the submission of the application for a marketing authorisation and the offer, manufacture, sale, supply, storage, import, use and purchase of patented medicinal products or processes, including by third party suppliers and service providers.*

*This exception shall not cover the placing on the market of the medicinal products resulting from such activities*

# Bolar Exemption - Proposed Changes

## European Parliament's Draft Report

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a) *studies, trials and other activities conducted to generate data for an application for:*

   i. *a marketing authorisation ~~of generic, biosimilar, hybrid or bio-hybrid medicinal products and for subsequent variations~~;*
   ii. *health technology assessment as defined in Regulation (EU) 2021/2282;*
   ~~iii. pricing and reimbursement.~~

b) *the activities conducted exclusively for the purposes set out in point (a), may cover the ~~submission of the application for a marketing authorisation and the offer,~~ manufacture, sale, supply, storage, import, use and purchase of patented medicinal products or processes, including by third party suppliers and service providers.*

   *This exception shall not cover the placing on the market of the medicinal products resulting from such activities*

# Paediatric Rewards

# Paediatric Rewards – The Current Regime

- In the EU, paediatric rewards are governed by Regulation (EC) No. 1901/2006 ('the Paediatric Regulation')
  - Six-month extension to SPC term available if application for MA/subsequent request for variation includes results from agreed PIP (Art 36(1)), and drug is authorised in all EU member states (Art 36(2))
  - Not available if:
    - Drug has orphan status (Art. 36(4))
    - +1 year of marketing protection obtained for the paediatric indication (Art. 36(5))
  - Possibility to obtain 2-year extension to 10-year orphan designation market exclusivity (Art. 37)
  - Off-patent products approved by paediatric use marketing authorisation entitled to 8+2 years exclusivity (Art. 38)

# Paediatric Rewards and orphan designation

- Orphan drug status precludes the possibility of obtaining a paediatric extension (Art. 36(4) Paediatric Regulation).

- However, if orphan status is revoked before paediatric studies are complete, a paediatric extension is likely to be available
  - *Novartis v Mylan,* District Court of The Hague, 2020[1]
    - Novartis obtained paediatric extension of deferasirox (Exjade®), which was previously designated as an orphan drug.
    - Court held that as orphan market exclusivity had expired when paediatric studies were completed, there was no double incentive for paediatric studies
    - Paediatric extension therefore valid

- Expected that this approach will be followed by Courts in other countries


[1]Decision no. C/09/595262 KG ZA 20-605

# Paediatric extensions in Switzerland

- Available since 2019
- Requirements mirror those in EU - Application for Swiss MA must include the results of studies performed in accordance with agreed PIP (which must be certified by Swissmedic)
- Application for Swiss MA (or the relevant extension to the MA) must be made not more than six months from the relevant MA application in Europe
  - Swiss attorneys have advised that this deadline is triggered by the first MA application ***containing a PIP***, rather than the results of the PIP.
  - Best practice to mirror EU regulatory steps in Switzerland within 6 months
- During transition period (1 January 2019-31 December 2023) deadline is 6 months before expiry of the SPC. From 1 January 2024, deadline will match EU deadline (2 years before SPC expiry).
- Paediatric SPC (6-month extension to patent term) also available

# Paediatric extensions in the UK

- From 1 January 2021, UK Human Medicines Regulations (2012) replaced EU legislation
- Deadlines are the same as in the EU (applications must be filed 2 years before SPC expiry).
- MHRA statement of compliance required (for GB)
- No requirement that medicinal product is authorised in all member states

# Proposed changes to Paediatric Rewards in Europe

The European Commission's Proposals

- The EC's proposed regulation would repeal the Paediatric Regulation, with relevant parts incorporated into the new Regulation and Directive.
- Rewards for paediatric medicinal products described in Art. 86 of the Proposed Directive.
  - 6-month paediatric extension (Art. 86(1))
  - Prohibition on paediatric extension and '+1' year data exclusivity being granted for the same paediatric indication (Art. 86(4))
  - +2 years orphan exclusivity for completion of PIP removed
  - Prohibition on paediatric extension for orphan products also removed
- Products approved under PUMA entitled to (new) data and marketing protection periods (Art. 93, Proposed Regulation)

# Proposed changes to Paediatric Rewards in Europe

The Draft European Parliament Reports

- The draft European Parliament Reports do not suggest many changes to the European Commission's Proposals

- The Report on the Directive proposes an amendment to Art 86(1) to provide for a one-year paediatric extension if the PIP is conducted for a different disease from the intended use in the adult population

# Thank you

# Any questions?

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