

# Enpr-EMA off-label working group

Final update Oct 2023

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# Update

- Paper on use of existing data
- Level of evidence of off-label drug use
- Next steps

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# Working group members

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# Paper on use of existing data

## Off-label is not always off-evidence: authorising paediatric indications for old medicines



Approximately half of all paediatric medicine prescriptions in the EU are off-label, yet evidence to support the efficacy and safety of these prescriptions is not adequate.<sup>1</sup> Legislation now mandates, where relevant, paediatric clinical trials for new medicines and for medicines still under patent protection.<sup>2</sup> By contrast, for financial and practical reasons, older medicines are unlikely to be investigated to the same extent.<sup>3</sup> Nevertheless, many sick children need to be treated

hormone replacement therapy for menopausal women, 17 $\beta$  estradiol matrix patches are cut into smaller pieces before application.<sup>5</sup> Investigator-initiated studies have shown that estradiol is evenly distributed across these matrix patches, such that cutting the patch does not impair its stability.<sup>6</sup> Finally, medicines authorised for one indication in children can be prescribed off-label for another indication. For example, tocilizumab is an important alternative for the 20% of children with



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# Include more existing data in the label

- Off-label evidence working group
  - *Academics and regulators*
- **Proposal to include more paediatric data in the medicine label:**
  - Consistent guideline and benefit-risk assessment procedure by the regulators
  - Financial incentives for academic groups to prepare data packages
  - Support by all stakeholders



European Network of  
Paediatric Research at  
the European Medicines  
Agency (Enpr-EMA)

# Include more existing data in the label

- Off-label evidence working group
  - *Academics and regulators*
- **Proposal to include more paediatric data in the medicine label**
  - Consist

*Article 48*  
*Scientific opinion on data submitted from not-for-profit entities for repurposing of authorised medicinal products*

European Network of  
Paediatric Research at  
the European Medicines  
Agency (Enpr-EMA)

for academic  
prepare data packages

Support by all stakeholders

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# Project Dutch Pediatric Formulary

> Clin Pharmacol Ther. 2022 Sep 7. doi: 10.1002/cpt.2736. Online ahead of print.

## Off-Label, but on-Evidence? A Review of the Level of Evidence for Pediatric Pharmacotherapy

Tjitske M van der Zanden <sup>1 2 3</sup>, Nori J L Smeets <sup>1 2</sup>, Marika de Hoop-Sommen <sup>1 3 4</sup>,  
Michiel F T Schwerzel <sup>1</sup>, Hui Jun Huang <sup>1</sup>, Lieke J C Barten <sup>1</sup>, Joyce E M van der Heijden <sup>1</sup>,  
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Matthijs de Hoog <sup>5</sup>, Saskia N de Wildt <sup>1 2 3</sup>

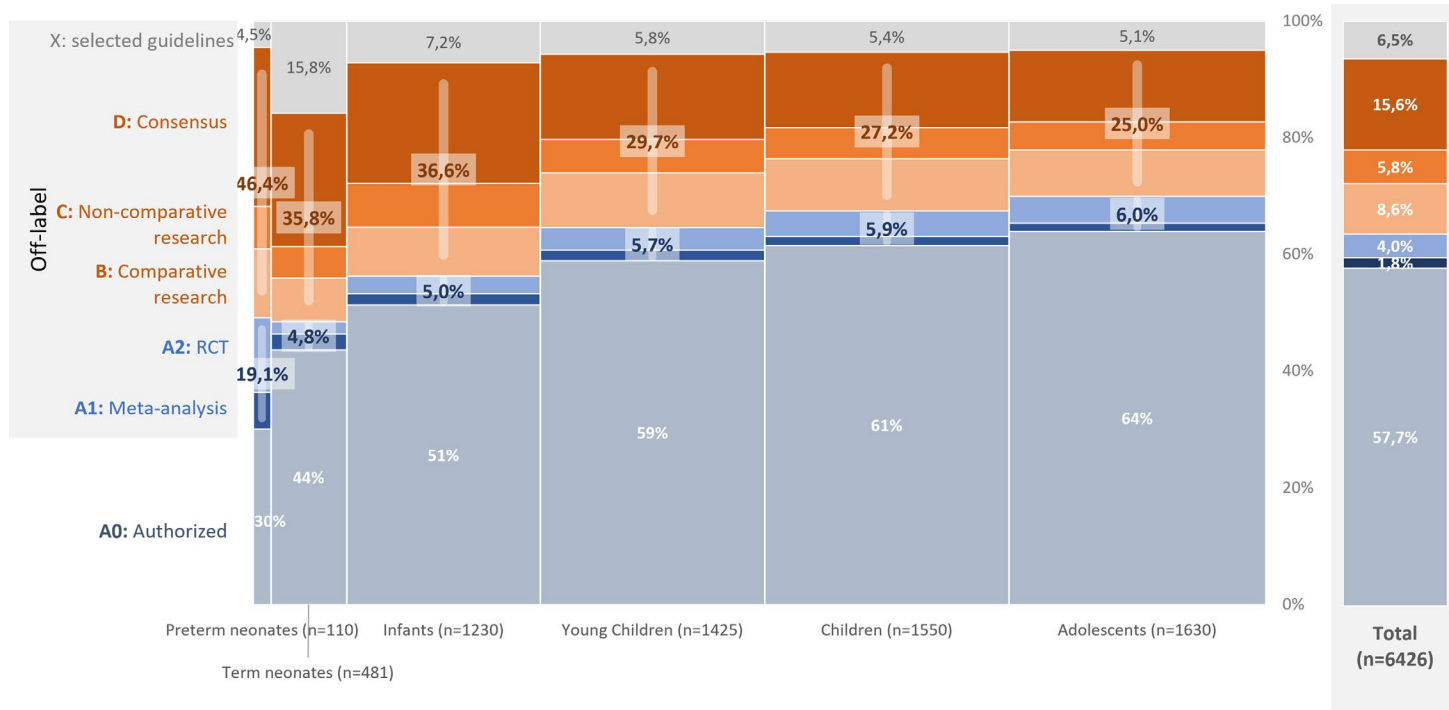
Affiliations + expand

PMID: 36069288 DOI: 10.1002/cpt.2736

For every drug-indication-age group in the formulary (800 drugs),  
highest level of evidence assessed



# Off-label: Low quality evidence



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# From off-label to effective and safe therapies



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**Uitgelicht traject: Van off-label naar  
effectieve en veilige  
geneesmiddeltherapie voor kinderen**

Dutch government sponsored project  
Develop solutions for future affordable sustainable therapies

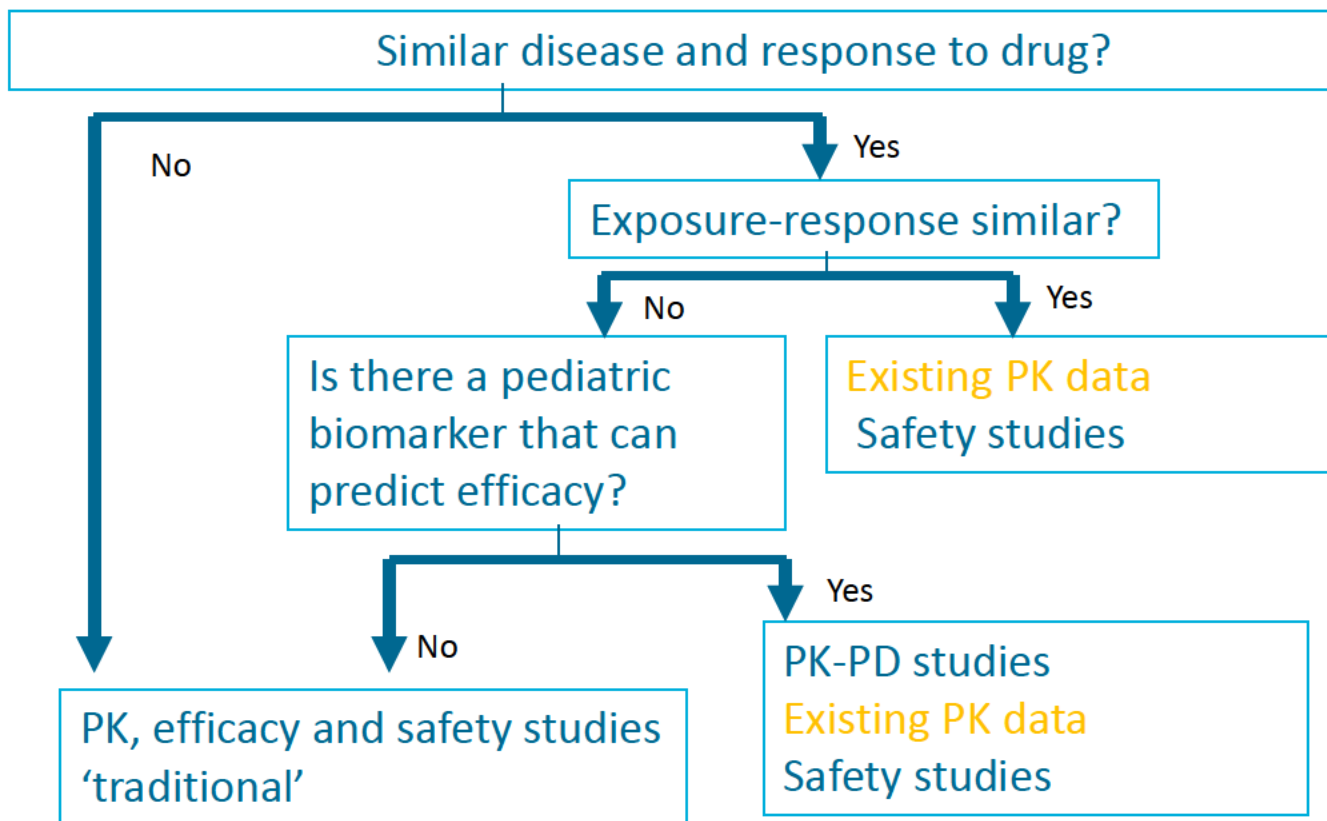
# Off-label: from problem to solution

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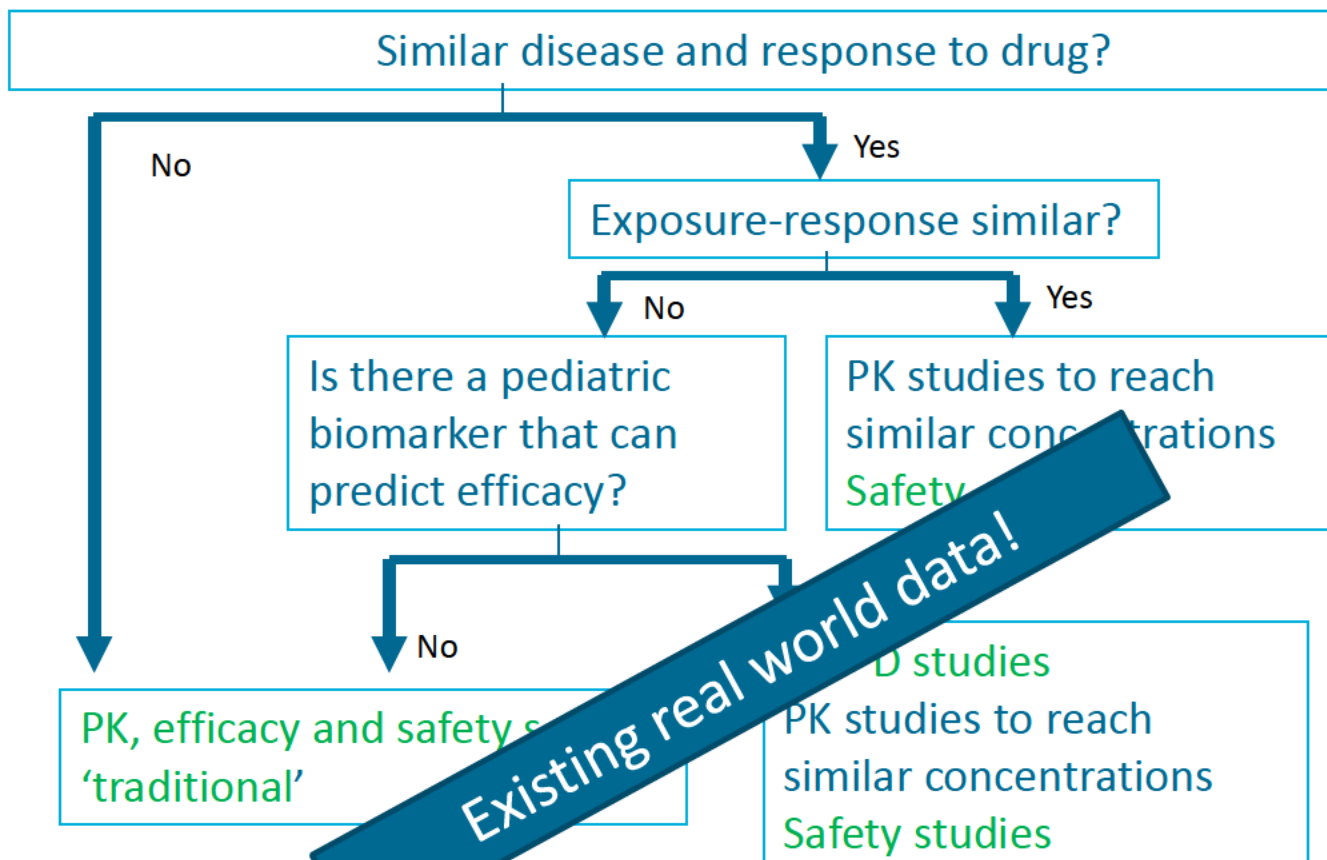
- **Step 1: A decision model for evidence generation**
- **Step 2: How to prioritize - international consensus**
- Step 3: Research agenda by subspecialty
- Step 4: Generate the evidence
- Step 5: Implement in practice
- Step 6: Market authorization?



# Extrapolation from adults to kids- decision tree



# Extrapolation from adults to kids- decision tree



## Questions?



**Kiddy Goodpills**

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# NO CHILD DESERVES BAD MEDICINE

[DONEER NU](#)

**The 2035 goal:**  
**every child effective and safe medicine!**

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