TEDDY Network General Assembly
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Ministry of Health, Madrid - Spain

Working Group on Off Label Use in Paediatrics

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Why this Working Group?

Born in mid-2016 to address the specificities of off-label medicines use in paediatrics

"Paediatric off-label use" specifically includes: 'all paediatric uses of a marketed drug not detailed in the SPC with particular reference to:

- therapeutic indication
- therapeutic indication for use in subsets
- appropriate strength (dosage by age)
- pharmaceutical form
- route of administration'

"Unlicensed use" means 'all uses of a drug which has never received a European Marketing Authorisation as medicinal for human use in either adults or children'.

(Neubert et al, 2008)

The entity of the paediatric off-label use in the EU and worldwide is still high

Despite the Paediatric Regulation has achieved significant results, the lack of medicines labeled for the use in paediatrics is still relevant

In several therapeutic subsets, there is no alternative in paediatrics than off-label treatments

The topic is of particular interest for a network dealing with paediatric clinical research

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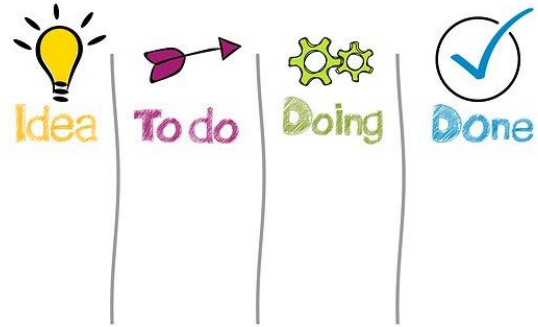

What is ongoing?

Draft of a policy statement on paediatric off-label use

- *Topics to be primarily addressed in the TEDDY have been identified through WG members consultation*
- *A non-systematic literature search has been performed to describe the topics*

To develop suggestions for further actions to be undertaken to correctly address the issue of off-label medicines use in paediatrics

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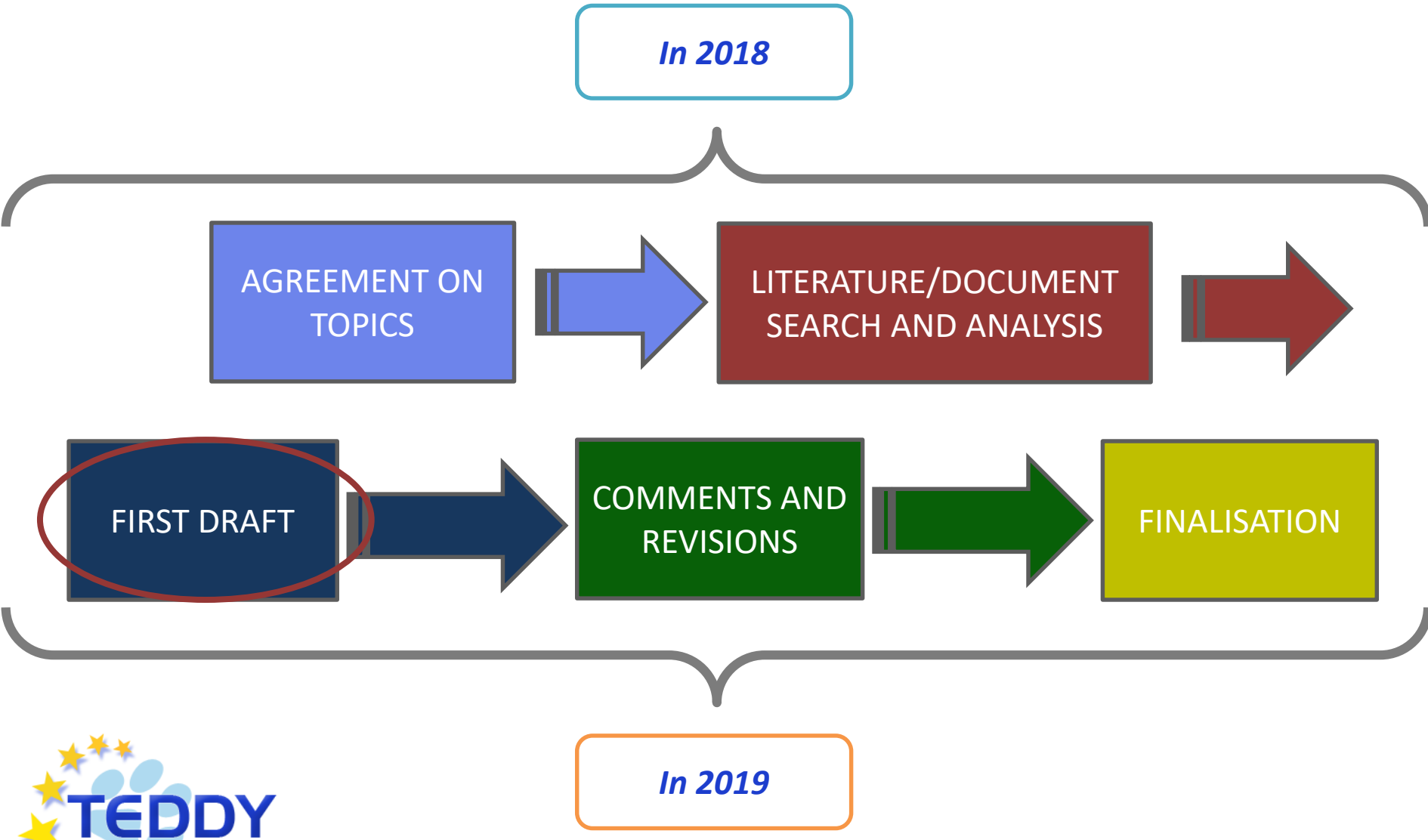
Draft process



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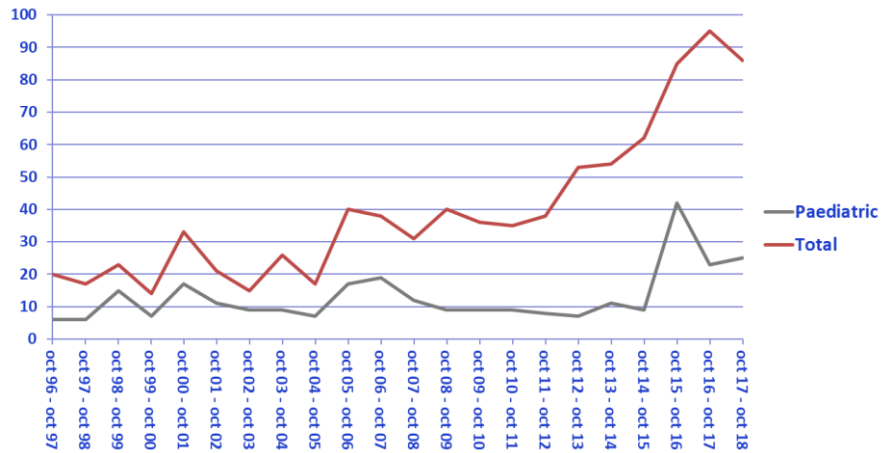
When and how off-label use could be permitted

Availability of paediatric medicines:

- The number of new medicines for children and the new paediatric indications for already authorised products increased in EU *(European Commission, 10-year report, 2017)* after the entry into force of the Paediatric Regulation
- Relevant achievements in some therapeutic areas: e.g. rheumatology *(Ruperto et al, 2013).*

- Among the centrally-authorised active substances in EU, 32% are approved for paediatrics *(TEDDY EPMD, 2018)*
- In some subsets (e.g. rare diseases) and for some patients group (neonates) the lack of paediatric medicines is very high *(Giannuzzi et al, 2017)*
- Also in US paediatric labelling is still unsatisfactory *(Sachs et al, 2012)*



(TEDDY EPMD, October 2018)

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When and how off-label use could be permitted

Off-label ≠ off-evidence!

(Bonati M, Jacqz-Aigrain E, Choonara I., 2016)

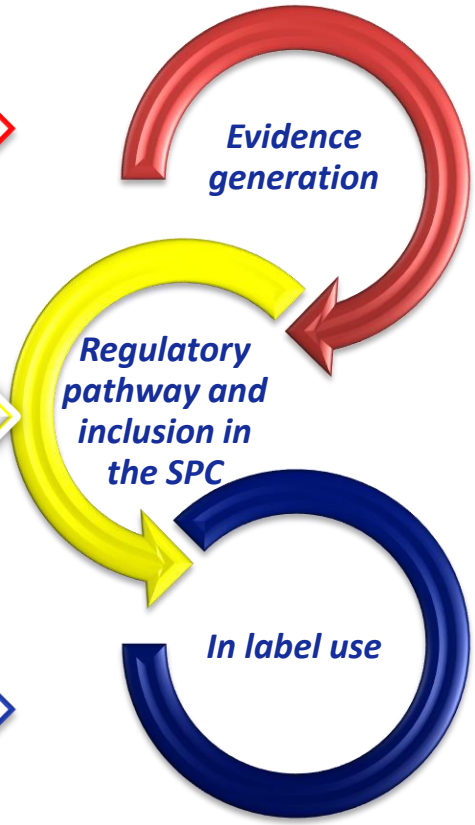
Not all type of off-label use carry the same level of risk

(…)

Quality/quantity of available evidence and need to generate new data

Type of information required and accepted by regulatory agencies

Promptly availability of medicines for children



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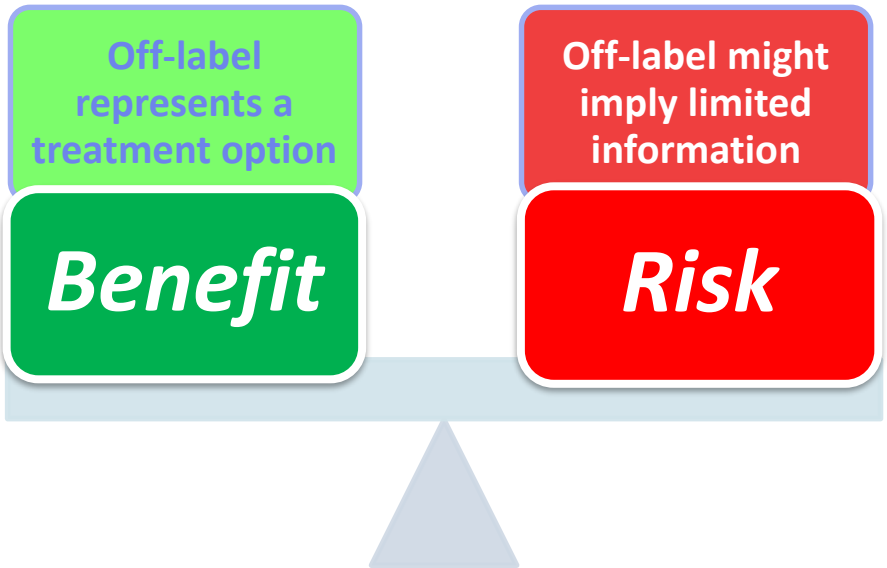
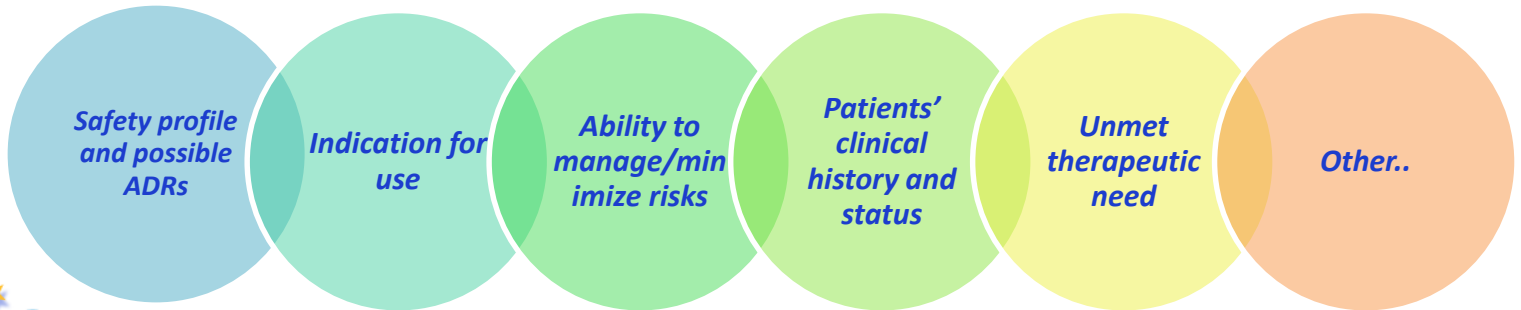
Qualitative and quantitative ***evaluation*** *of benefits and their uncertainties towards the risks and their limitations*





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Safety profile and pharmacotherapeutic follow-up

European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

October 2004
EMEA/126327/2004

Evidence of harm from off-label or unlicensed medicines in children
EMEA

Uncertainties about the relation between off label and adverse drug reactions

- Underreporting of the cases in paediatric population
- Scarce information of the physicians
- Lack in paediatric labelling
- Undervaluation of the crucial differences in PK/PD
- Dosing adjustment errors

Need for further research on this field, in particular with large cohort of patients in order to have statistically significant analyses

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Lack of age-appropriate formulations

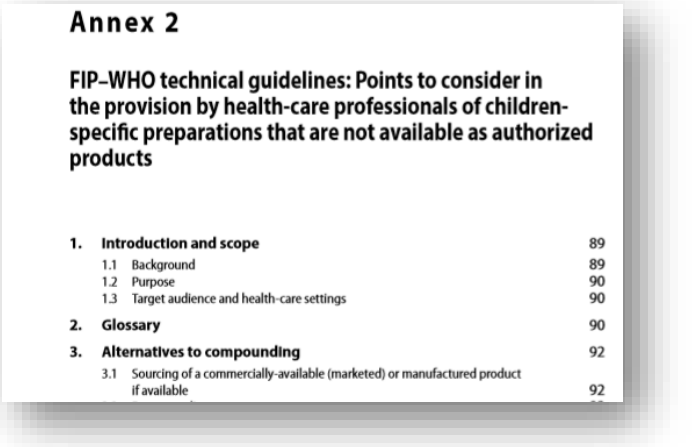
Lack of age-appropriate formulations is a for off-label medicines use and route of administration is a very common relevant off-label category

Development of age-appropriate formulations

Need for safe medicines manipulation

EMA-PDCO Therapeutic Needs lists included the need for a new pediatric formulation for more than 200 Active Substances

(D'Andria et al, 2016)



Annex 2

FIP–WHO technical guidelines: Points to consider in the provision by health-care professionals of children-specific preparations that are not available as authorized products

EuPFi

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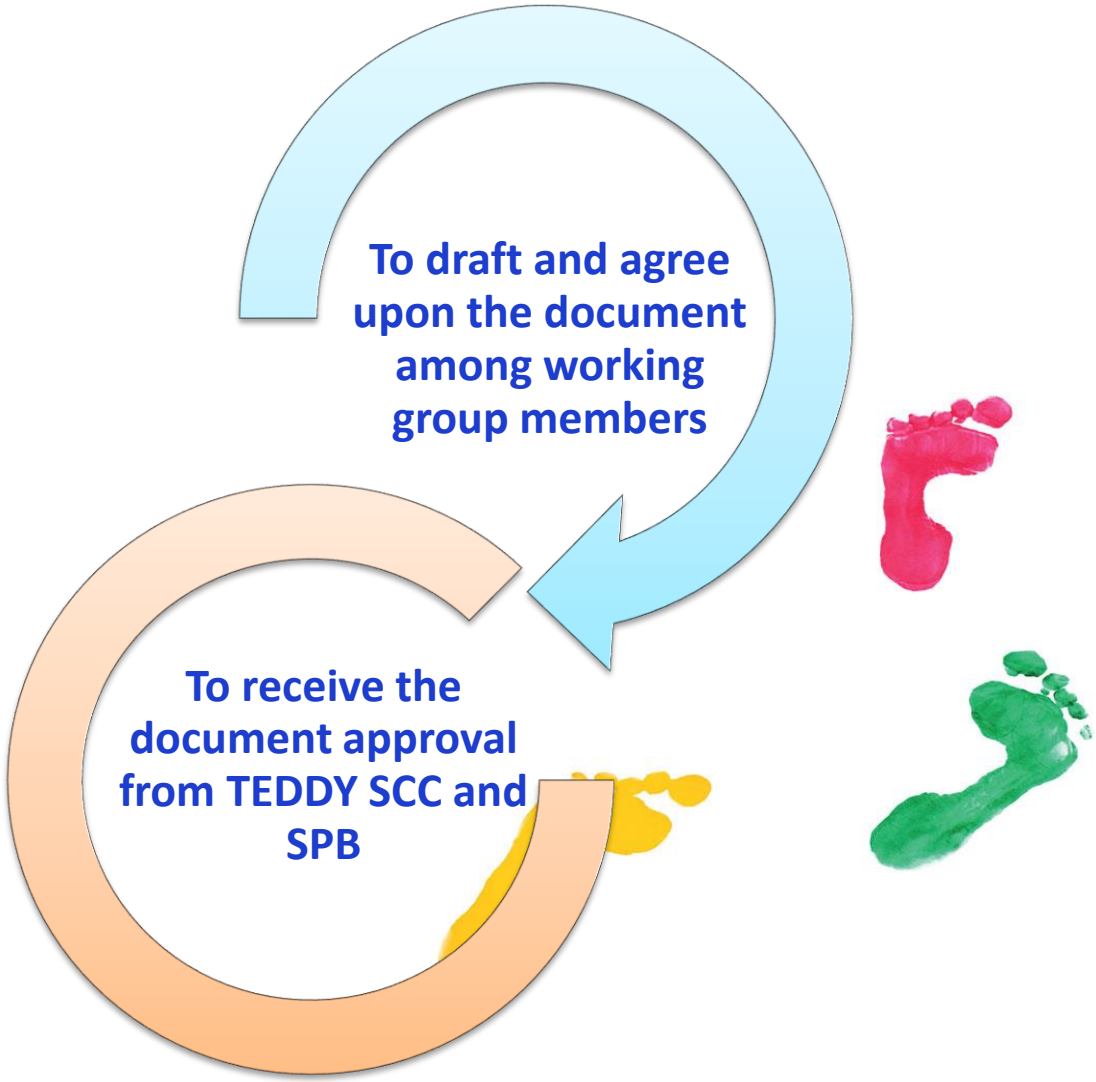
NEXT STEPS



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PROPOSED ACTIVITIES

- ***Development of collaborative project proposals***
- ***Collaboration with other TEDDY Working Groups***

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COLLABORATION

Collaborations with other TEDDY WGs

PAEDIATRIC CLINICAL STUDIES METHODOLOGIES AND PROCEDURES

To integrate the European Paediatric Medicines Database with information about off-label status.

To discuss:

- *methodology for data collection*
- *source(s) of information*
- *data validation*
- *possible selection of therapeutic areas for a pilot phase*

ACTIVE ENGAGEMENT OF CHILDREN AND ADOLESCENTS

- **Information to patients and families (which type of information and in which format?)**
- **Awareness and feelings about the off-label medicines use (are they aware? What they know?)**

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OTHER POSSIBLE ACTIVITIES

- ***Consultations issued by EMA, European Commission and other relevant stakeholders***
- ***Scientific events at national/international levels***
- ***Creation and periodic update of an internal common literature database on the matter***

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Who we are?

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