



The role of Enpr-EMA in facilitating paediatric research and the results of the Ethics Working Group activities

TEDDY - European Network of Excellence for Paediatric Clinical Research, General
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Disclaimer

- The views expressed in the following slides are those of Pirkko Lepola and should not be attributed directly to Enpr-EMA (European Network of Paediatric Research at the European Medicines Agency)
- Information of the Enpr-EMA have been provided by courtesy of; Irmgard EICHLER, MD, Co-chair Enpr-EMA, Senior Scientific Officer, Paediatric Medicines, Product Development Scientific Support Department, EMA.

Enpr-EMA & Goals



European Network of Paediatric Research at the European Medicines Agency

Enpr-EMA

European Network of Paediatric Research
at the European Medicines Agency

Mission statement

- Enpr-EMA **will facilitate studies** in order to increase availability of medicinal products authorised for use in the paediatric population

Enpr-EMA - Key operational goals

- To link together existing networks
- To provide expertise and access to infrastructure for industry to conduct studies in children
- To define consistent and transparent quality standards
- To harmonise clinical trial procedures
- To define strategies for resolving major challenges
- To communicate with external stakeholders

Enpr-EMA - Main Stakeholders

- Pharmaceutical Industry
- Patients, parents and patient organisations
- National Competent Authorities
- Ethics Committees
- Medical devices industry
- CRO's
- Hospital pharmacists

Enpr-EMA Mandate for working groups

- In June 2013 ad hoc working groups (WG) – tasked to;
 - > **address some of the most important needs identified**
 - > **make the best use of networks** to develop medicines for children
- The number, composition and tasks of the WGs are reviewed every year following the annual face to face meeting

Purpose

- **to develop pragmatic responses to some of the needs** relating to paediatric medicines research that can be implemented within six months (*or so...*).
- **The focus is on stating what networks can do, or what networks need to do**, rather than developing comprehensive guidance.

Ethics Working Group (WG) 4

WG4 –Ethics 2018

WG Topic	Dialogue and interaction with Ethics Committees (ECs)
Objectives	<ul style="list-style-type: none"> • To gather examples of good practice when ECs consider trials relating to children and young people. • To develop proposals to disseminate examples of good practice to ECs. • Contributing work to support the implementation of the Regulation with the view that these efforts will create a more favourable environment to speed up high quality Paediatric Research.
<p>WG Chair / Co-Chairs</p> <p>WG Members</p>	<p>Pirkko Lepola</p> <p><u>Primary members (drafting documents):</u> Peter Sallabank (RegulinX, UK, CRO), David Neubauer (Chairman of the Ethics Working Group of European Academy of Paediatrics), Martine Dehlinger-Kremer (EUCROF), Viviana Giannuzzi (Gianni Benzi Pharmacological Research Foundation), Heidi Glosli (NorPedMed, Oslo University), Geraldine Boylan (INFANT), Maxine Kindred (Janssen R&D, UK), Harris Dalrymple (PRA HealthSciences, UK)</p> <p><u>Co-members (reviewing documents):</u> Christina Manfredi (CVBF-Consortio per Valutazioni Biologiche e Farmacologiche, Pavia, Italy), Jo Mendum (PRA HealthSciences, UK), Diane Hoffman (retired/Janssen R&D,US)</p>

WG4 Deliverables 2013-2017

Year	Deliverable	Publication / Actions
2013	Plan Report for Implementation – Identification of problems & challenges and needed actions & proposed actions	<ul style="list-style-type: none"> Recommendations (12), published in December 2013 for Enpr-EMA (only).
2015	1. Deliverable; "Tool Kit" - Informed Consent and Assent for Paediatric Clinical Trials in Europe	<ul style="list-style-type: none"> Published on Enpr-EMA web-site on 18 December 2015; updated by the Enpr-EMA secretariat
2016	1. Article: "Informed Consent for Paediatric Clinical Trials in Europe"; Authors: Pirkko Lepola, Allison Needham, Jo Mendum, Peter Sallabank, David Neubauer, Saskia de Wildt	<ul style="list-style-type: none"> Published on 25 May 2016, Archives of Disease in Childhood
2016	<p>2. Deliverable; Public Consultation of the "Ethical considerations for clinical trials on medicinal products conducted with the paediatric population" (2008), open June-August 2016</p> <p>Contributed by EFGCP CMWP (European Forum for Good Clinical Practice, Children's Medicines Working Party; WP 1, In collaborating with a small group of EMA PDCO members, submitted 30 August 2016.</p>	<ul style="list-style-type: none"> Revision 1 of the document published on 18 September 2017 on EudraLex Vol.10. Clinical Trial Guidelines, Chapter V - Additional information

Year	Deliverable	Publication / Actions
2016	<p>I. Contribution to PROPOSED CHANGES TO THE U.S. COMMON RULE Implications for Pediatric Research (Federal Policy for the Protection of Human Subjects) Included comments on two points relating to paediatric research: 1) the value of taking an international perspective when revising the Common Rule 2) Informed Consent. Comments submitted on January 2016 by Mark Turner, the behalf of the Enpr-EMA</p> <p>II. Collaboration with the European Network of Research Ethics Committees (EUREC)- Enpr-EMA started</p>	<ul style="list-style-type: none"> The revised Common Rule becomes effective on January 19, 2018 in US EUREC presentation in Enpr-EMA Annual WS, May 2016 1st Enpr-EMA WG4 presentation in EUREC meeting, 08Sep2016, Helsinki

Tool Kit – 2016 (up-dated 2017)



European Network of Paediatric Research at the European Medicines Agency

15 May 2016

The toolkit is available for all those involved in paediatric clinical trials and ethics committees, providing a new platform for proactive feedback on informed consent requirements.

Informed Consent for Paediatric Clinical Trials in Europe 2015ⁱ

Pirkko Lepola, Allison Needham, Jo Mendum, Peter Sallabank, David Neubauer, Saskia de Wildt

	Consent / assent from child		Consent from parent(s) / guardian(s)	General informed consent information	
Country	Legal age of consent	Mandatory / suggested age ranges defined for assent (or consent if assent not used)	Number of required signatories	Official language requirements	IC template(s) / guidelines / information sources
Austria ¹	18 years	8-13 years EC may require younger assents	One parent	German	http://www.medunigraz.at/ethikkommission/Forum/index.htm http://www.ethikkommissionen.at/ http://www.uibk.ac.at/strafrecht/scheil/scheil-einfuehrung-in-die-arzneimittelpruefung-bei-kindern-und-jugendlichen---kks--kids-ip.pdf For clinical trials with an IMP: AMG §42 applies. Legal age of consent is 18. One parent has to sign ("Erziehungsberechtigter"). For clinical trials with an MD: MPG §51 applies. Legal age of consent is 18. One parent has to sign ("Erziehungsberechtigter").

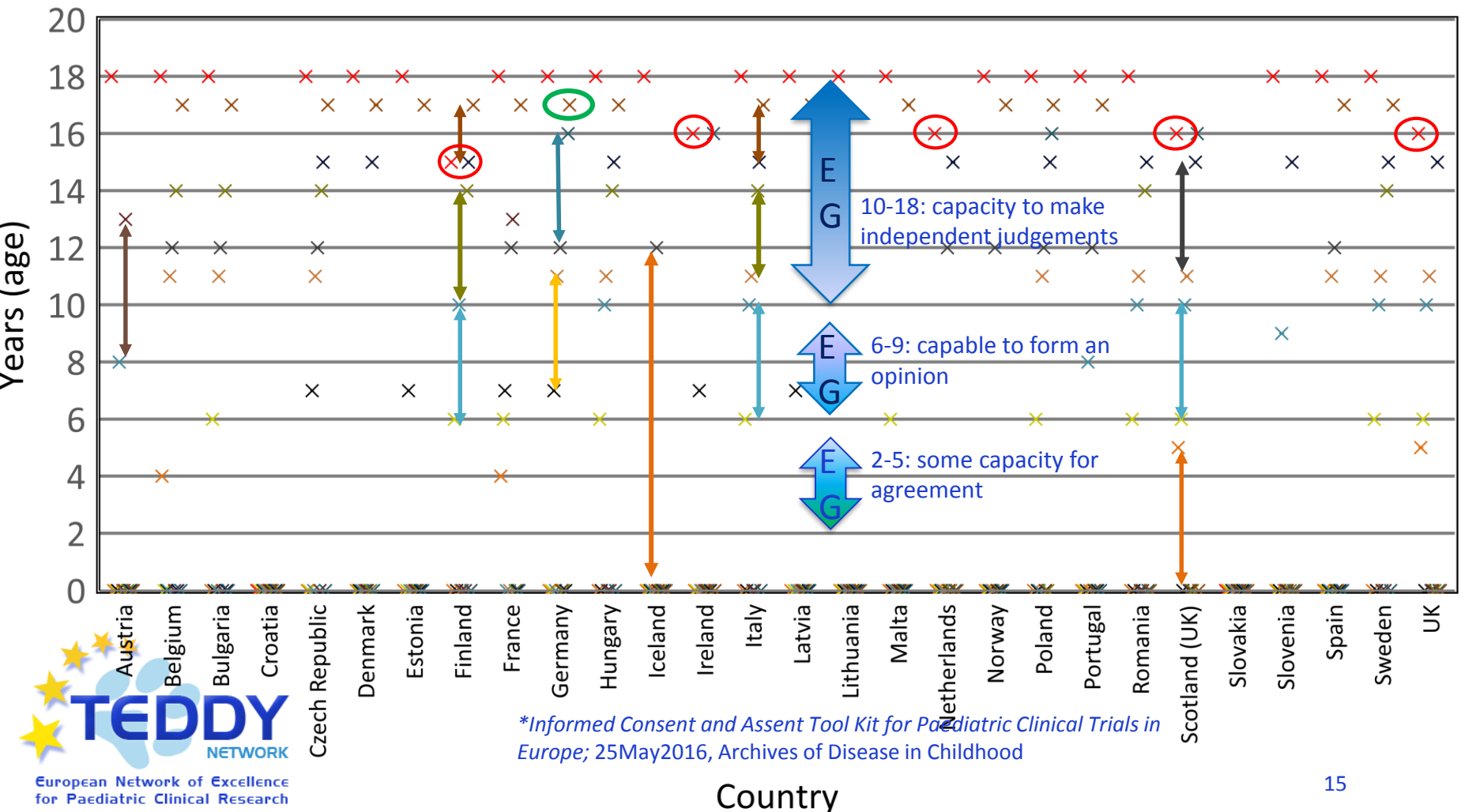
http://www.ema.europa.eu/docs/en_GB/document_library/Other/2015/12/WC500199234.pdf

Statistics – differences in age groups*

Tool Kit Data: Mandatory / Suggested age ranges defined for assent (or consent if assent not used)

- Legal age of consent for CTs
- Lowest age (0-5)
- Until - I (6)
- Until - II (7)
- Until - III (8-10)
- Until -IV (11)
- Until -V (12)
- Until -VI (13)
- Until -VII (14)
- Until -VIII (15)
- Until -IX (16)
- Until -X (17)

EG= Ethics
Guideline R1
(2017)



*Informed Consent and Assent Tool Kit for Paediatric Clinical Trials in Europe; 25May2016, Archives of Disease in Childhood

Number of required legal (parental) signatories

~ 50 % / 50%
distribution in
required nr. of
signatories



*One parent at recruitment, but both parents at some point for signatures

**Both parents. Only by one parent if the other parent is not listed in the child's birth certificate, has died or is younger than 18 years

***Both parents . Exception - no parents if aged 15-17 and non-interventional no risk study (EC dispensation required)

WG4 Challenges & Next Steps

Conclusions -> Challenges in 2019

- New EU CT Reg. (impl.approx.1Q/2019) will harmonise the clinical trial application (CTA) process, but IC/Assent issues remain with each Member State.
- There are noticeable differences between national IC and assent requirements in Europe due to national laws and regulations (See: Tool Kit data)
- These discrepancies can present challenges for multicentre paediatric CTs

Next Steps 2018->

In paper
format
-> 2019:
e-format ?

Year	Deliverable	Publication / Actions
2017 2018	3. Deliverable: "Harmonized General Informed Consent / Assent template – document for European Paediatric CTs" Based on: <ul style="list-style-type: none"> ➢ identification of all similar elements across assents / consents of publicly existing templates ➢ Comparison of the review responses with the EU Ethics Guideline (Revision 1); published in October 2017 ➢ Identification of any conflicting elements across template ➢ Correcting the template according to EU CTR ➢ Include all important elements from eYPAGnet Reports ➢ Including EAP Ethics WG comments 	<ul style="list-style-type: none"> • 1. version published on Enpr-EMA Annual Workshop, 16 May 2017, IC/Assent template model – Version 3.0 (2017) <ul style="list-style-type: none"> • <i>For all stakeholders: to be placed publicly available on Enpr-EMA web-site, plan; -> by 06/ 2018</i> • <i>Publication in 2018 ?</i>
2017	III. Collaboration European Network of Research Ethics Committees (EUREC)- Enpr-EMA Cont.; <ul style="list-style-type: none"> • Enpr-EMA WG4 presentation in EUREC-ANCEI Congress in Barcelona, 18 May 2017 • Discussion, "brainstorming" TC, 03 Oct 2017 • 1st Meeting in London 13th November 2017, EMA 	<ul style="list-style-type: none"> • 4 Action points agreed; 2018 <ol style="list-style-type: none"> 1) Map currently available "ethics" -training programmes for investigators – both e-based and f-2-f 2) Compile available guidance documents (e.g. GRIP placemat, Ethical considerations for clinical trials in minors, etc.) and prepare a template / material package, including involvement of PPGs/YPAGs for PDCO 3) Share UK experience with documentation of patient/young people involvement 4) Ensure inclusion of paediatric research aspects in EUREC training boot camp planned in April 2018 in Helsinki

Thank You !



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