Paediatric Clinical Trial Site Standards

Work Group 1

Defining what quality of paediatric sites means

Enpr-EMA Annual meeting

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Co-Chairs WG1

9 October 2023

Background Information

- **On Oct. 3, 2022:** Workshop on paediatric site quality requirements co-organised by Enpr-EMA and conect4children (c4c) ➔ Identified Action Points
  - Definition of quality of paediatric trial sites: how can conduct be optimised, what matters to different stakeholders, including children, young people and their families
  - Identification/mapping of existing quality standards
  - Implementation of the recommendations for quality criteria/standards: Roadmap – how to? Publication of a recommendation document.

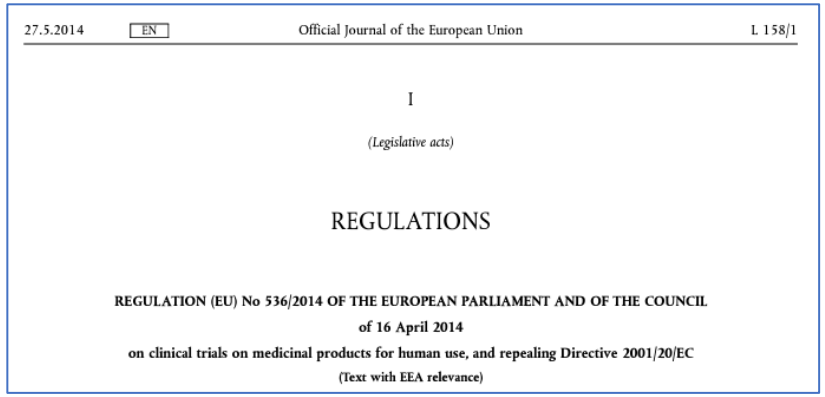
- **On Jan. 26, 2023:** Follow Up Meeting ➔ Discussion Points
  - Groups aiming to define and identify quality standards for paediatric clinical trials could start their work in parallel, at a later stage merge, and work together in the implementation phase.
  - After the definition/identification of general criteria, specificities for specific cases could be defined.
  - Considerations were given to de-centralised clinical trial elements, innovation and digitalisation
  - Need to avoid duplication of work of other ongoing initiatives

- **Two Enpr-EMA Work Groups formed**
  - WG 1: Defining what quality of paediatric sites means
  - WG 2: Identifying/mapping existing quality criteria/standards for sites

WG1 Members

Name	*Affiliation*
Arianna Bertolani	CVBF
Begonya Nafria Escalera	eYPAGnet
Breanne Stewart	MICYRN
Carmen Rodríguez-Tenreiro	GENVIP
Collin Hovinga	Critical-Path Institute
Ensio Norjavaara	AstraZeneca
Eva Degraeuwe	c4c, BPCRN
Fernando Cabanas	Red Samid, PDCO
Holly Huntington	I-ACT
Ivan Foeldvari	JSWG of PRES - Juvenile Scleroderma Working Group
Jorge Alonso	JNJ
Laura Persijn	C4c, BPCRN
Lionel Tan	Viiv Healthcare
Martine Dehlinger-Kremer	ICON plc (CRO)
Mark Sorrentino	ICON plc (CRO)
Melissa Walsh	c4c, IN4KIDS
Nicola Ruperto	PRINTO
Pavla Pokorna	C4c, Czech PharmNet
Sabrina Pierre	c4c; INSERM
Sarah Zaidi	FDA
Tessa van der Geest	Pedmed-NL
Thierry Lacaze	MICYRN

Starting points:
some documents & Initiatives of interest…



27.5.2014 EN Official Journal of the European Union L 158/1

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(Legislative acts)

REGULATIONS

REGULATION (EU) No 536/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 16 April 2014
on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC
(Text with EEA relevance)

23 May 2022
EMA/298712/2022

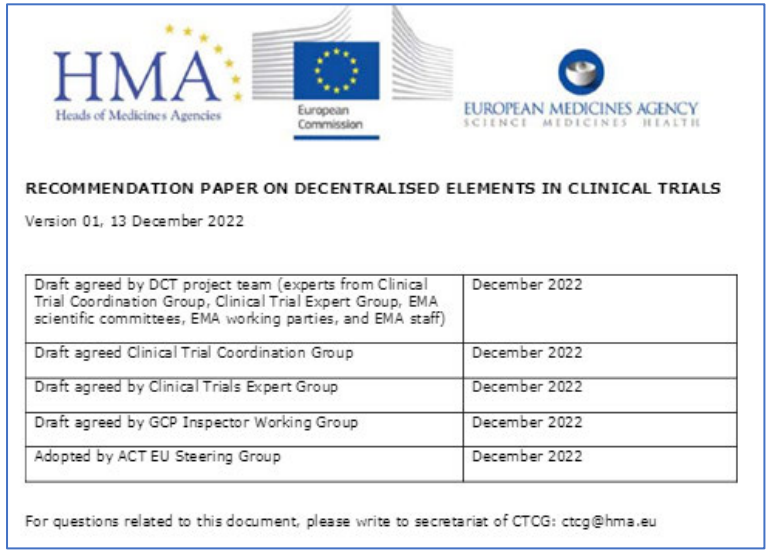
Complex clinical trials – Questions and answers

Version 2022-05-23

Draft agreed by Drafting Group experts (from EMA scientific committees, EMA working parties, EMA staff and Clinical Trials Coordination Group)	May 2022
Draft agreed by Clinical Trials Coordination Group	May 2022
Draft agreed by Clinical Trials Expert Group	May 2022
Adopted by ACT EU Steering Group	23 May 2022

Keywords	Clinical trial; complex clinical trial; clinical trial authorisation application; marketing authorisation application; trial design; trial analysis; Clinical Trials Regulation; master protocol; platform trial; biomarker; adaptive design; modifications; Bayes; control data; transparency

For questions related to this document, please write to ACTEU@ema.europa.eu.



RECOMMENDATION PAPER ON DECENTRALISED ELEMENTS IN CLINICAL TRIALS

Version 01, 13 December 2022

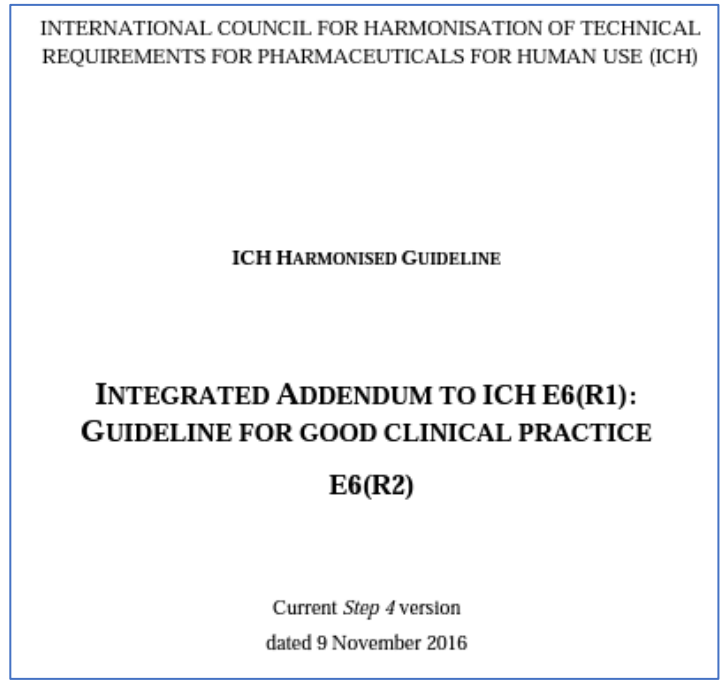
Draft agreed by DCT project team (experts from Clinical Trial Coordination Group, Clinical Trial Expert Group, EMA scientific committees, EMA working parties, and EMA staff)	December 2022
Draft agreed Clinical Trial Coordination Group	December 2022
Draft agreed by Clinical Trials Expert Group	December 2022
Draft agreed by GCP Inspector Working Group	December 2022
Adopted by ACT EU Steering Group	December 2022

For questions related to this document, please write to secretariat of CTCG: ctcg@hma.eu

31 August 2020
EMA/56009/2019

Preparedness of medicines' clinical trials in paediatrics

Recommendations by the Enpr-EMA working group on trial preparedness



INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE (ICH)

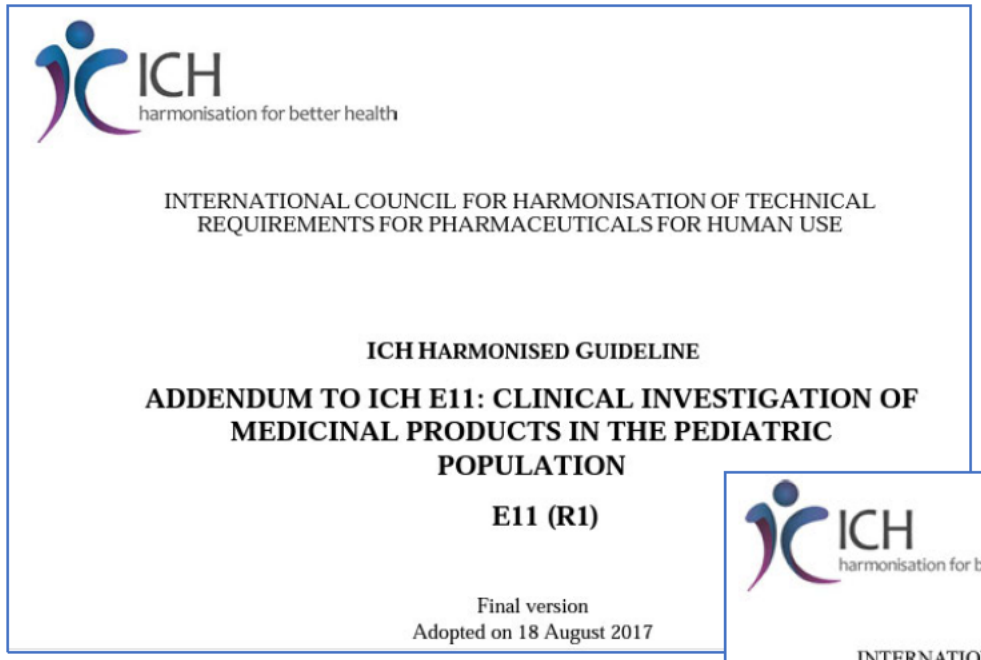
ICH HARMONISED GUIDELINE

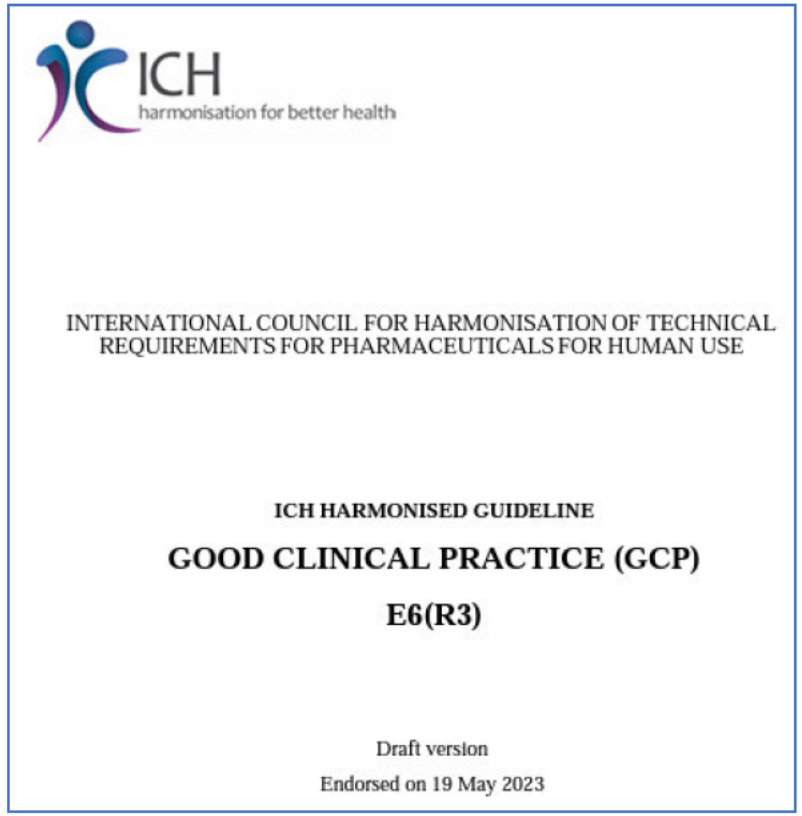
INTEGRATED ADDENDUM TO ICH E6(R1): GUIDELINE FOR GOOD CLINICAL PRACTICE

E6(R2)

Current *Step 4* version
dated 9 November 2016

https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32014R0536&from=EN
https://health.ec.europa.eu/system/files/2023-03/mp_decentralised-elements_clinical-trials_rec_en.pdf
https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf
https://health.ec.europa.eu/system/files/2022-06/medicinal_qa_complex_clinical-trials_en.pdf
https://www.ema.europa.eu/en/documents/other/preparedness-medicines-clinical-trials-paediatrics-recommendations-enpr-ema-working-group-trial_en.pdf





https://database.ich.org/sites/default/files/E11_R1_Addendum.pdf
https://database.ich.org/sites/default/files/ICH_E11A_Document_Step2_Guideline_2022_0404_0.pdf
https://database.ich.org/sites/default/files/ICH_E6%28R3%29_DraftGuideline_2023_0519.pdf

conect 4children
COLLABORATIVE NETWORK FOR EUROPEAN CLINICAL TRIALS FOR CHILDREN

TRIALS @HOME

innovative health initiative

CRITICAL PATH INSTITUTE

PedCRIN

eYPAGnet

EUCT

Enpr-EMA survey & c4c survey

- **Enpr-EMA WG** on international collaboration Regulators and networks in 6 jurisdictions
- Aims: identify requirements from sponsors (industry and CROs) for the clinical sites to participate in paediatric clinical trials.
- Survey conducted April-August 2022, followed up with optional interviews.
- Overall n=33 from 21 countries, and 7 virtual interviews
- Domains: investigator and supporting staff qualifications, site infrastructure requirements, administrative cycle times, and decentralised processes.

- **c4c consortium**, a collaborative network for European clinical trials for children
- Aims: define c4c site standards as a core set of pre-agreed norms or criteria against which the sites could be evaluated
- Questionnaire developed using a structured approach, with input and review by c4c National Hubs and exemplary research sites. Survey conducted August-September 2022.
- Preliminary results: n=116 from 19 countries.
- Domains: Clinical trial experience, scientific competencies and expert capacity; Site organization, relationship and leadership; Contracting and regulatory; Resources and staff; Training; Quality management, assurance and compliance; Data protection and GDPR compliance; Facilities and Technical

WG1 Objectives – Defining what does Quality of Paediatric Site mean

- Aims and scope
  - To develop a common understanding of what quality of paediatric sites means with regards to paediatric clinical trial sites and what matters to the different stakeholders involved in the conduct of a clinical trial, including children and their parents/ caregivers.
  - This work addresses paediatric site standards across jurisdictions, paediatric age ranges, and types of sponsor; inclusive to a diversity of types of sites and site involvement; and is focused on sites delivering regulatory-grade clinical trials.
  - The work intends to drive opportunities for rollout of site standards and improvement of sites, with adequate resources.

WG1 Methods – Defining what does Quality of Paediatric Site mean

- Ways of working
  - Five remote meetings with open discussions, moderated by Chairs
  - Main discussion points, topics with agreement and dissent, and distinct perspectives from various stakeholders were captured
  - Offline work helped focus on specific questions, identify and share supporting evidence (environmental scan)
- Liaised with WG2 for shared alignment, synergy and efficiency
- Interim report on our groups' operational approach, plan and first ideas at the (virtual) Enpr-EMA Coordinating Group meeting in June

What has WG1 delivered?

- A document focusing on 4 questions:
  - What is a paediatric site?
  - Why do we need paediatric site standards?
  - What do we mean by quality of a paediatric site?
  - How to identify a fit-for-purpose paediatric site?

- Align with WG2 ➔ joint document with recommendations

Key findings - What is a paediatric site?

- Core definition of a paediatric site
- Definition can be further expanded to address discussions on site quality
- Concept and definition of a site can consider different levels i.e. legal, organizational, operational, clinical, organizational, setting/level of care, regulatory, ethical or trial design-related.
- The evolving nature of a site across the trial lifecycle should be kept in mind

Key findings - Why do we need paediatric site standards?

- To identify sites that are most likely to deliver a trial on time, on budget and according to the specifications outlined by the sponsor, regulators and GCP.

- *Basic/requested/required* standards to reflect the quality of a site. Further suggested requirements (*aspirational/excellence*) provide a developmental pathway for sites to improve across domains (staff, facilities, etc)

- Paediatric standards should reflect quality of a paediatric site
  - Ensure there is awareness and implementation of existing site standards for high quality regulatory grade trials to paediatric sites
  - Complexity of delivering paediatric trials and gaps in the current paediatric trial delivery enterprise highlight paediatric specific aspects regarding site quality

Key findings - What do we mean by quality of a paediatric site? How to identify a fit-for-purpose paediatric site?

- Quality domains and existing sources, standards and criteria (Enpr-EMA survey, c4c, WG2)

- WG1 considerations and initial proposed recommendations
  - **All sites set out to enrol children and young people, whether they are paediatric-only or also (or mainly) recruit adults, should meet the same specific site requirements**
  - Qualifications and experience rolling into preparedness & performance
  - Facilities
  - Site performance
  - Quality management
  - Patient engagement

Next steps and future directions – for discussion

- To incorporate further input and finalise our WG1 recommendations
- To consolidate with WG2 identified standards and other sources of information
- To plan dissemination and implementation steps, aligned with existing initiatives and target stakeholders