16/05/2017

WORKING GROUP 4:

DIALOGUE AND INTERACTION WITH ETHICS COMMITTEES

Pirkko Lepola

EnprEMA WG 4 - Ethics

Current WG4 members 2017:

- Pirkko Lepola, Chair (Finnish Investigators Network for Pediatric Medicines, Helsinki, Finland)
- Maxine Kindred, (Janssen Research & Development, Buckinghamshire, UK) –*Consent group*
- Diane Hoffman, (Janssen Research & Development, Philadelphia, U.S.A.) –*Consent group*
- Martine Dehlinger-Kremer (SynteractHCR Deutschland GmbH, Munich, Germany)
- Jo Mendum (PRA HealthSciences, Reading, UK) –*Consent group*
- Peter Sallabank (RegulinX, Surbiton, UK)
- David Neubauer (University Children's Hospital, Ljubljana, Slovenia)
- Christina Manfredi (CVBF-Consorzio per Valutazioni Biologiche e Farmacologiche, Pavia, Italy)
- Viviana Giannuzzi (Fondazione per la Ricerca Farmacologica Gianni Benzi, Valenzano, Italy)
- Heidi Glosli (Oslo University Hospital, NorPedMed, Oslo, Norway) –*Consent group*

EnprEMA WG 4 - Ethics

Role:

Develop pragmatic responses to be implemented within six months (approx.);

- **Examples of good practice when ECs consider trials relating to children and young people**
- **Develop proposals to disseminate examples of good practice to ECs**

EnprEMA WG 4 - Ethics

First Report: **Plan Report** - Recommendations (12), published in December 2013 for Enpr-EMA (only)

1. Deliverable; "Tool Kit" - Informed Consent and Assent for Paediatric Clinical Trials in Europe

- Published on Enpr-EMA web-site on 18 December 2015; updated by the Enpr-EMA secretariat
- 1. Article: *"Informed Consent and Assent Tool Kit for Paediatric Clinical Trials in Europe"; 25 May 2016, Arch Dis Child 2016, Pirkko Lepola, Allison Needham, Jo Mendum, Peter Sallabank, David Neubauer, Saskia de Wildt*

2. Deliverable; Public Consultation of the "Ethical considerations for clinical trials on medicinal products conducted with the paediatric population" (2008), open June-August 2016

- 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

Additional WG activities in 2016: Contribution to PROPOSED CHANGES TO THE U.S. COMMON RULE Implications for Pediatric Research (Federal Policy for the Protection of Human Subjects) - Comments submitted on January 2016 by Mark Turner, the behalf of the Enpr-EMA

Too Kit -2016

European Network of Paediatric Research at the European Medicines Agency

15 May 2016

Informed Consent for Paediatric Clinical Trials in Europe 2015[i]

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").

Results

- **Wide variation in paediatric consents and assents presents challenges for multinational paediatric trials in Europe.**

- 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, and may finally lead to a needed harmonisation process, including uniform standards accepted across Europe.

Ethics Guideline Consultation

Tuesday 30 August 2016

Consultation on the revision of "Ethical Considerations for Clinical Trials on Medicinal products Conducted with Minors": a response from Enpr-EMA and partners

Ethics Guideline Consultation

Introduction

The EU Clinical Trials Regulation 2014 (CTRs) offers a great opportunity to improve research involving children. The supporting document "Ethical Considerations for Clinical Trials on Medicinal products conducted with Minors" is crucial to its implementation and achieving the Regulations' aims to facilitate research and promote the health of our children and young people (minors).

This document represents the response from Enpr-EMA, its working groups (including representatives of networks, National Competent Authorities and pharmaceutical industry), and partners. It was led and drawn up by Hugh Davies (European Forum for Good Clinical Practice), Pirkko Lepola (Finnish Investigators Network for Pediatric Medicines, chair Enpr-EMA working group on Ethics) and Martine Dehlinger-Kremer (chair paediatric working group of EUCROF and member of EFGCP Children Working Party); then circulated to Enpr-EMA members and partners for their comments.

It is in two parts:

Part 1: General comments on guidance layout and content

Part 2: Specific comment on the text in the guidance with recommendations at the end of each

Ethics Guideline Consultation

Executive summary

1. This document must be written for all audiences, researchers, regulators, research ethic committees, but more importantly families and children.
2. To improve readability, use of modern technology would allow the text to be layered providing easier reading and increasing detail.
3. This guidance should

- be built around text from the regulations in each section
- offer advice on the interpretation of the regulations.
- seek and include evidence and practical examples wherever possible (we have tried to add some) .

Enpr-EMA WG4 – Task 3

3rd Task: Partly harmonized core IC / Assent template with standard language (English) 2016-2017

Background facts:

1. New EU CT Reg. (impl.approx.10/2018) will harmonise the clinical trial application (CTA) process, but IC/Assent issues remain with each Member State.
2. There are noticeable differences between national IC and assent requirements in Europe due to national laws and regulations (See: Tool Kit data)
3. These discrepancies can present challenges for multicentre paediatric CTs

3. Deliverable: "Partly harmonized of Informed Consent / Assent template -document": *Consent group*

- Based on identification of all similar elements across assents / consents of existing templates
- 1. version 16 May 2017; Enpr-EMA WS

Enpr-EMA WG4 – Mini Group

3. Task: Executed by a ”Mini-Group of Consents”

- **Diane Hoffman :** Johnson & Johnson Pediatric Center of Excellence (Chair)
- **Maxine Kindred :** Johnson & Johnson Operations (Operational producer)
- **Heidi Glosi :** Oslo University Hospital (support)
- **Jo Mendum :** CRO, PRA (support)

3.Deliverable: Comparison of Assents from WHO, MCRN and Finland

- Guidance template provided January 2017

- Identification of all similar elements across assents
- Prepared to include all elements
- Items included in the WHO template was added to the guidance as they were deemed important to the assent

Enpr-EMA WG4 - Elements

1. Identification of all similar elements across assents / consents

TYPES OF ASSENTS	INSTITUTIONAL NAME	INFORMATION SHEET:	PURPOSE:	CHOICE OF PARTICIPANTS:	PARTICPATION IS VOLUNTARY:	INFORMATION ON THE TRAIL DRUG DRUG NAME:	PROCEDURES:	RISKS:
		Introduction	Why are you doing this research	Why are you asking me?	Do I have to do this?	What is this drug & what do you know about it?	What is going to happen to me?	Is this bad or dangerous for me?

	DISCOMFORTS:	BENEFITS:	REIMBURSEMENTS:	CONFIDENTIALITY:	COMPENSATION:	SHARING THE FINDING:	RIGHT TO REFUSE OR WITHDRAW:	WHO TO CONTACT:	PROVIDE A COPY?
Finland Template	Will it hurt?	Is there anything good that happens to me?	Do I get anything for being in the research?	Is everyone going to know about this?	What happens if I get hurt?	Will you tell me the results?	Can I choose not to be in the research? Can I change my mind?	Who can I talk to or ask questions to?	
MCRN Template									

	CERTIFICATE OF ASSENT			IF ILLITERATE:	NAME AND SIGNATURE OF WITNESS:	NAME AND SIGNATURE OF RESEARCHER:
	Read it and agree.	Does not agree.	Signature of child:	Thumbprint of participant:		

Assent / Consent – Model template - includes instructions

Version 3.0 Enpr-EMa WG4 Ethics

Italics – instructional text.

Blue – example text

Study Title

Institution Name / Sponsor of the research

Include information about the institution, investigator that is conducting the research and also the name of the sponsor/organisation funding the research.

Document version and date

Specify the version and the date of the document

Model template cont.

Language and supporting visual materials

The language used for using this document and addressed to potential participants, parents and legal guardians, must be commonly understood by the addressees and presented in a way, that all age groups and persons with limited capacity to read and write, or to comprehend (e.g. due to medical condition or low age), can reasonably understand the information. All difficult medical (professional) terms and language should be avoided and all possible aid materials (e.g. pictures, videos, practical equipment etc.) should be used to visualize the given information, depending on the age and capacity to understand.

Time

The addressees, i.e. potential participants, parents and legal guardians, should have reasonable time to receive (read and listen) and understand the given information and have time to pose questions based on that information. The medical professionals responsible for the given information, should be fully trained and informed about the details of the trial, and able to give answers to those questions of the addressees. In case of emergency situations, the information to addressees should be given in a best possible way as a short version to enable fast decisions for study participation, and later again without undue delay with more details and with the possibility to deal additional questions of the addressees.

Template cont.

Version 3.0 Enpr-EMa WG4 Ethics

Introduction

A brief introduction to ensure the child knows that this is a research study. The person obtaining consent should give their name, explain who they are and clearly state they are doing the research.

We would like to invite you to participate in our research study. Please read this information carefully and talk to your mum, dad, carer or anyone else you feel comfortable talking to about the study. There may be some words you don't understand or things you would like explaining in more detail because you are interested or concerned. Please ask us if there is anything that is not clear or if you want to know more. Take all the time you need to decide if you want to take part.

NOTE: Avoid giving too much information at the time. The addressees / potential participants / legal guardians must not feel overwhelmed by the given information. Severe medical conditions and unusual situations may increase the pressure and stress, and decrease the capacity to understand.

Template cont.

The Purpose of this Research

Explain the purpose of the research in clear simple terms.

- *Include information about what research is*
  - Research is a careful experiment to find out the answer to an important question.
- *Include information about the purpose of the trial.*
  - We want to try and find out if/why.....
- *Include information to confirm that an ethics committee (and regulatory authorities) has reviewed the planned research and has given their approval for it to take place in [region/country]*
  - Before any research can take place it has to be checked by a Research Ethics Committee. This is a group of people who look at the planned research and decide if it is OK to do or not. This study has been looked at by XXXXXXX and they have given their approval for the research to take place in [region/country].
- *Who is organising and funding the research*

Template cont.

The Investigational Product

Include information about the trial drug, the reason for its development, how much is known about it and whether it has been studied in children before. Provide as much information as is appropriate and understandable.

Choice of Participants

Include information explaining:

- *why they are being invited to participate / why they are suitable for the trial*
- *number of participants globally / in their country*
- *that they do not have to participate and they can change their mind at any time*
    - You do not have to be in this research. It is your choice. You can think about it and tell us later if you want. You can say yes now and change your mind later and it will still be OK.
- *that no-one will be cross or angry if they decide they do not want to participate at any time. They can say No at any time.*
    - No-one will be mad or disappointed with you if you say no.

Template cont.

- *regardless of their decision the doctors and nurses will still take care of them in the best possible way.*
    - Whatever you decide, the doctors and nurses will still take care of you in the best possible way.
- *that the researchers will also talk to their parents/guardians to get their permission for the child to participate*
    - We will also talk to your parents/guardians who will also have to give their permission for you take part.
- *If new information becomes available the doctors / nurses will discuss this new information with them and they will be asked if they would still like to continue to participate in the study.*
- *The doctors may decide at some point that the child is no longer suitable for participation and they will be informed if this is the case. The doctors and nurses will still take care of them in the best possible way.*
- *The research personnel should stress the importance of responsibilities of compliance and honesty, and open discussions by all parties, and valuing the real partnership; by both the research personnel and potential participants / legal guardians / families. Usually families know best their child and other daily routines, and medical personnel about health care issues. Good collaboration based on trust guarantees reliable and valid research results and high quality health care – even in case of discontinuation.*

Template cont.

Procedures

Include information about what is going to happen to the child during the trial and how the trial will be carried out. Including:

- *How many times they will be seen, for how long*
- *The procedures that will take place*
- *What is considered "extra" to what would normally happen*
- *Length of Trial*
- *Anything specific the child will have to do (or not do)*
- *Clear information about any samples to be taken during the study and what will happen to them*
- *Clear information on any genetic tests to be done, if appropriate – and explanation what that means*

Template cont.

Risks/Discomforts/Benefits

Include information about possible side effects, discomforts, risks of the procedures and any potential benefits (to the participants or maybe other children in the future with the same disease). Tell the participant that if they feel different in any way they should tell their parents/guardians and the doctor. Address any worries you think a child may have (eg, missing school or holidays).

NOTE: Provide information of the availability of all methods to ease the discomfort; e.g. professional personnel with good experience (knowledge to do certain procedures), use of local anaesthetic skin batches (for needle punctures), other products / methodologies to decrease the fear and worries.

Template cont.

Compensation

Include information about what happens if something goes wrong or they get injured during the trial

If something goes wrong, you become ill or get injured during the research we will look after you. We have given your parents / legal guardian´s information about who to contact – with contact details.

Reimbursements

Include information about whether the patients will get anything for their participation or if they (or their parents) will be reimbursed for expenses. Some children may worry that their parents will have additional financial burden by them participating in the study (eg, if the trial site is much further away from their home)

NOTE: *Usually in many European countries, the participation to clinical trial must be free of charges; the health care (doctor/nurse visits, hospital stay), tests and study medications should be free of charge. All extra costs (daily allowances, parking, meals etc.) should be reimbursed to participants / parents / legal guardians according to national law by the study sponsor.*

NOTE: CT Regulation (EU/No 536/2014); Chapter V, Articles 31: 1.(d) and 32: 1.(d): *no incentives or financial inducements are given to the subject or his or her legally designated representative except for compensation for expenses and loss of earnings directly related to the participation in the clinical trial.*

Template cont.

Confidentiality

Include information about who will know the child is taking part in the trial and arrangements for making sure they cannot be identified by anyone else (eg, their name and address will not be used).

Information about you that will be collected from the research will be put away and no-one but the researchers will be able to see it. Any information about you will have a number on it instead of your name. Only the researchers will know what your number is and that information will be locked away so no-one else can see it.

Template cont.

When The Trial Is Over

Tell the child:

- *what will happen to them when the trial is over or if the research is stopped prematurely*
- *what will happen with the results*
- *whether you will make arrangements for them to be informed about the results*
- *what will happen to all the information and data collected during the trial*

Contact Information

Include details for people who the participant can contact to talk to, find out more information, ask questions to or complain about something.

You can ask questions now or later. Below are some names and numbers of people you can contact for more information, to ask questions to, to complain to or even just to chat to. If you want to talk to someone else that you know that's OK too.

Template cont.

Thank-You

Thank them for taking the time to read the document and consider participation in the trial.

Certificate of Assent / Consent

NOTE: Especially for small children, the signature page of the assent / consent should be preferably integrated version; together with the patient information sheet, not exceeding the length of one page (all information included – both the patient information and signatures).

Inclusion of signatures for assent /consent will be based on country/site specific requirements according to local regulations and age range.

- Read & Agree / Disagree
- Signature of Child
- Signature of Researcher obtaining assent
- Other

Please note the new EU Ethics Guideline when it´s coming into force (2017) including new recommend age limits for consents and assents.

WG4 collaboration with EUREC-
European Network of Research Ethics Committees

Further planning of collaboration;

- **Discussion in Enpr-EMA meeting 17May2017**

EUREC-ANCEI Congress in Barcelona 17.-19.May2017

- **Presentation – Enpr-Ema/WG4 on 18may**
- **Discussion with YPAGs**

Future tasks ?? – YPAGs & e-consents

Using digital multimedia to improve parents' and children's understanding of clinical trials

Alan R Tait,[1,2] Terri Voepel-Lewis,[1] Robert Levine[3,4]

Arch Dis Child 2015;**100**:589–593. doi:10.1136/archdischild-2014-308021

Conclusions Results demonstrated the importance of providing information regarding clinical trial concepts to parents and children. Importantly, the ability of interactive multimedia to improve understanding of clinical trial concepts and satisfaction with information delivery, particularly among children, supports this approach as a novel and effective vehicle for enhancing the informed consent process.

THANK YOU!