Specific Ethical Issues in Pediatric Nutrition Trials

Joerg Hasford
Department for Medical Biometry and Epidemiology
Ludwig-Maximilians-Universität München
Munich, Germany
Email: has@ibe.med.uni-muenchen.de
Research with Children / Minors

**Past:** Children as vulnerable subjects were protected / excluded from research.
  ➔ no evidence-based healthcare for children

**Present:** Pediatric research has become a kind of ‘moral imperative’.
Research Ethics – General Principles

• Autonomy
• Beneficence
• Non-maleficence
• Justice
Research with Humans – General Provisions

• The interests and welfare of the human being participating in research shall prevail over the sole interest of society and science.

• Research on human beings may only be undertaken if there is no alternative of comparable effectiveness.

• Research shall not involve risks and burdens to the human being disproportionate to its potential benefits.

• In case there is no potential for direct benefit (PDB) to the health of the research participant, such research may only be undertaken if it entails no more than acceptable risk and acceptable burden for the participant.

Council of Europe: Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research
Research on Minors – General Provisions

• Research on minors may only be undertaken if there is not an alternative of comparable effectiveness.
• The research is essential to validate data obtained in trials on individuals able to give informed consent.
• Such research either relates directly to a medical condition from which the minor concerned suffers, or is of such a nature that it can only be carried out on minors.
Research on Minors – General Provisions

- The clinical trial has been designed to minimize pain, discomfort, fear and any other foreseeable risk in relation to the disease and developmental stage, and both the risk threshold and the degree of distress are specifically defined and constantly observed.
- Some direct benefit for the group of patients is obtained from the clinical trial.
- The informed consent of the legal representative has been obtained, whereby consent shall represent the minor’s presumed will.
Research on Minors - General Provisions

- The minor has received all relevant information in a way adapted to his or her age and maturity, from physicians trained or experienced in working with children, regarding the trial, the risks and the benefits.

- The explicit wish of a minor, who is capable of forming an opinion and assessing this information to refuse participation in or to be withdrawn from the clinical trial at any time, has to be taken into consideration by the investigator in accordance with the minor’s age and maturity.
Impact of ‘Potential for Direct Benefit (PDB)’

• In case there is a PDB the risks have to be *proportionate* to the risks of the medical condition
• In case there is no PDB the research should entail *no more than* minimal risk and minimal burden.
Informed Consent / Assent in Research with Minors

• The legal representatives have to be fully informed (nature, significance, implications and risks of the research) and need to provide written informed consent.

• Minors, starting at an age between 6-8 years, have to be informed in an age- and maturity-appropriate manner and provide assent.

With increasing age and maturity the assent achieves the relevance of consent, in particular in research without PDB.
Informed Consent / Assent in Research with Minors

- Consent can be withdrawn at any time, without the need to provide reasons and without any resulting detriment.
- Informed consent shall be written, signed and given freely.
**Informed Assent Form Template for Minors from the WHO**

**Part I: Information Sheet**

**Introduction**

This is a brief introduction to ensure the child knows who you are and that this is a research study. Give your name, say what you do and clearly state that you are doing research. Inform the child that you have spoken to their parents and that parental consent is also necessary. Let them know that they can speak to anyone they choose about the research before they make up their mind.

[www.who.int/rpc/research_ethics/InformedAssent.doc](http://www.who.int/rpc/research_ethics/InformedAssent.doc)
Informed Assent Form Template for Minors

• Purpose: Why are you doing this research?
• Choice of participants: Why are you asking me?
• Participation is voluntary: Do I have to do this?
  ✔ I have checked with the child and they understand that participation is voluntary ____(initial)
• Information on the Trial Drug [Name of Drug]: What is this drug and what do you know about it?
Informed Assent Form
Template for Minors

• Procedures: What is going to happen to me?
  ✓ I have checked with the child and they understand the procedures ________(initial))

• Risks: Is this bad or dangerous for me?

• Discomforts: Will it hurt?
  ✓ I have checked with the child and they understand the risks and discomforts _____(initial)
Informed Assent Form Template for Minors

• Benefits: Is there anything good that happens to me?
  ✓ I have checked with the child and they understand the benefits_____ (initial)

• Reimbursements: Do I get anything for being in the research?

• Confidentiality: Is everybody going to know about this?

• Compensation: What happens if I get hurt?
Informed Assent Form
Template for Minors

• Sharing the Findings: Will you tell me the results?
• Right to Refuse or Withdraw: Can I choose not to be in the research? Can I change my mind?
• Who to Contact: Who can I talk to or ask questions to?
• If you choose to be part of this research I will also give you a copy of this paper to keep for yourself. You can ask your parents to look after it if you want.
I have read this information (or had the information read to me) I have had my questions answered and know that I can ask questions later if I have them.

I agree to take part in the research.

OR

I do not wish to take part in the research and I have not signed the assent below.__________(initialled by child/minor)

Only if child assents:
Print name of child ___________________
Signature of child: ___________________
Date:____________
   day/month/year

If illiterate:
A literate witness must sign (if possible, this person should be selected by the participant, not be a parent, and should have no connection to the research team). Participants who are illiterate should include their thumbprint as well.

I have witnessed the accurate reading of the assent form to the child, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness (not a parent)______________ AND Thumb print of participant
Signature of witness ______________________
Date ______________________
   Day/month/year

I have accurately read or witnessed the accurate reading of the assent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given assent freely.

Print name of researcher_________________
Statement by the researcher/person taking consent
I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the child understands that the following will be done:
1.
2.
3.
I confirm that the child was given an opportunity to ask questions about the study, and all the questions asked by him/her have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this assent form has been provided to the participant.