Guidelines for Informed Assent/Consent in Research Involving Paediatric Populations as Research Participants

Ethics Working Group
of the European Academy of Paediatrics (EAP)*

Draft Revision by Francis P. Crawley
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Preamble

These Guidelines are intended to assist the European paediatric researchers in inviting and enrolling children in research projects by establishing appropriate informed decision and assent/consent procedures. Each paediatric researcher engaged, directly or indirectly, in research on a paediatric population must ensure, as appropriate, that the (potential) child-participants and their parents/legal guardians have understood and assented/consented to the research.

These Guidelines address the assent/consent requirements for all research involving paediatric populations. This includes biomedical research, research where children are 'data subjects', research involving children's biological materials, behavioural and social science research, and public health research.

These Guidelines further include all research that makes use of children as 'data subjects' where information on children is collected through health records, social media, online postings, or other electronic means. The same standards of assent/consent apply for research directed at children who are data subjects for health, social science, economic, or financial purposes.

The EAP strongly rejects the use paediatric populations (including children as data subjects) intended to target children for commercial or advertising purposes and considers any attempt to receive assent/consent for such purposes unethical.

The vocation of the paediatrician and paediatric healthcare provider lies in promoting and protecting the health of children. The paediatrician's and the paediatric healthcare provider's knowledge and conscience are dedicated to the fulfilment of this vocation. It is the duty of the paediatric researcher to ensure that the research is carried out according to the highest standards of the profession and that it is adapted to the needs of the paediatric population being studies. Where the paediatric researcher is not a paediatrician or paediatric healthcare provider, it is strongly recommended that a paediatrician or paediatric healthcare provider be consulted on the design of the study as well as on the assent/consent procedures to be used in the study.

All research carried out on a paediatric population should be designed according to the highest standards of the science and appropriately adapted to the specific paediatric population to be studied. The research must always be based on a written protocol where the objectives, methodology, outcomes, and justification for the research are clearly indicated. For biomedical research the diagnostic, prophylactic, and therapeutic care of the child-patient are to be of the highest standard and appropriate to the health needs and concerns of each child-patient.

Paediatric researchers share a responsibility to ensure the ongoing development of the understanding of paediatric medicine that permits an increasing capacity to alleviate suffering and promote health in children. This requires a commitment to research to advance knowledge in paediatric medicine.

Research involving children as the subjects of research is only permissible when such research is necessary to contribute to the healthcare of children and the research cannot be carried out on laboratory or animal models or in adult persons. Paediatric researchers should ensure that the process of inviting and engaging children in proposed research protocols is evaluated according to the best interest of each child, that the potential benefits and risks have been carefully considered, and that the will of the (potential) child-participant plays the paramount role in the decision making. The role of parents/legal representatives in assisting the determination and expression of the will of the (potential) child-participant must be promoted and respected in the process of informed decision-making and assent/consent.

These Guidelines provide specific guidance for the paediatric researcher regarding informed consent for research on paediatric populations. This guidance should be understood as additional to, and complimentary of, existing national, European, and international guidelines on informed consent. In consulting and implementing these Guidelines, consideration should be given to the WMA *Declaration of Helsinki*, ICH and WHO Good Clinical Practice Guidelines, CIOMS *International Guidelines for Biomedical Research on Human Subjects,* WHO *Operational Guidelines for Ethics Committees That Review Biomedical Research*, and Council of Europe, *Convention on Human Rights and Biomedicine*. Particular attention should be given to the UN *Convention on the Rights of the Child*, the *Charter of Fundamental Rights of the European Union*, EMA (CPMP) *Note for Guidance on Clinical Investigation of Medicinal Products in Children*, ICH-E11 *Clinical Investigation of Medicinal Products in the Paediatric Population*, CESP Report *Research in Children*, and the EU *Regulation on Children's Medicine* (2007), the EU Clinical Trials Regulation (2014), and the EU *General Data Protection Regulation* (2016).

Guiding Principles for Requesting the Informed Assent/Consent of a (Potential) Child-Participant in Research

Respect for the dignity of the child-participant
The inherent dignity of each child is no less than that of the adult person, regardless of the age of the child or the child's physical, psychological, or intellectual profile. The inherent freedom and capacity for self-determination of each child must be fully respected and promoted by the paediatric researcher in the informed consent process that invites a child to participate in a research project.

Safe-guard the best interests of the child-participant
All research involving child-participants must promote and protect the best interests of the child in the research. The paediatric researcher has the duty to seek to understand the child's interests and concerns, and to ensure that the child's participation in the research contributes to the pursuit of those interests.

Protect the child-participant from harm
The paediatric researcher has a responsibility to protect the child-participant from harms that are beyond what might arise from the reasonable risks associated with research. These harms may include physical, psychological, spiritual and social harms.

Assure and respect the privacy of the child-participant
The privacy of the child-participant (including that of the child as a 'data subject') must be fully respected and assured throughout the research project. This includes the physical, psychological, and social privacy of the child. The paediatric researcher has the duty to respect and assure the privacy of the child-participant.

Protect the confidentiality of the child-participant
All personal and health-related information of the child-participant must be assured the highest degree of protection. This includes all information collected during the research or in connection to the research. The paediatric researcher has the obligation to assure the confidentiality of the child as a data-subject in the collection and storage of information as well as in any discussion or publication of the research.

The Process and Content of Informed Consent in the Paediatric Population

1. Research should only be carried out in a paediatric population when it addresses a health concern within that population and it has the potential to contribute to an improvement in the health of that population. Paediatric researchers have a responsibility to assure that the diagnostic, prophylactic, and therapeutic methods used in addressing the health of children are first the subject of conclusive investigations that determine their safety and efficacy in the paediatric population. Similarly, behavioural, social, psyschological, or public health interventions in a paediatric population should also be subject to research using methods appropriate to the science and adapted to the paediatric population to be studied.
2. Children in particularly vulnerable situations (e.g., children in institutions, homeless children, migrant children) should only be invited to participate in research projects if their particular condition is an object of the research. In such cases, paediatric researchers have the duty to ensure that the research does not exploit the child-participant by taking advantage of the vulnerability of the child. For children of migrant families and families with a different cultural background from that in which the children live, a cultural mediator experienced in the language, social habits, culture, traditions, religion, and particular ethnic problems should assist in the process of obtaining informed consent/assent.
3. The invitation to a child to participate in a research project should not be dependent upon the child's nationality, race, gender, religion, or statehood status, except in cases where one or more of these attributes are relative to the objective(s) of the research.
4. The informed consent process for including children in research should include all of the information and considerations generally accepted for seeking the informed consent of competent adults. The process should be designed to discover and promote the will of the (potential) child-participant. This will is paramount and must be fully respected and considered by the paediatric researcher in inviting and accepting the participation of the child-participant.
5. The paediatric researcher must ensure that there is no forced or undue influence on the child's decision or parent's/legal representative's consent. Special attention

should be given to ensure that the process of discussion and decision does not take place under duress, nor should the process lead to distress on the part of the (potential) child-participant or parents/legal representatives.

6. The assent/consent process must promote and protect the dignity, privacy, and confidentiality of the child and his or her family. It must also ensure the dignity, privacy, and confidentiality of the child within the family.
7. The laws and regulations of the country where the research takes place must be followed, particularly as they concern the protection of children.
8. The definition of children in research should reflect the legal age definitions for minors in the country where the research is to take place. The process of informed assent/consent should be in conformity with the laws and regulations of the country, and the accepted practices for assent and consent should be considered.
9. Separate information sheets and assent/consent forms should be developed for the child and for the parents/legal representatives of the child. The information sheets and assent/consent forms should be adapted to the different age populations of the child-participants. The parents/legal representatives should be provided with a copy of the information sheet and assent/consent form to be given to the child.
10. Written information alone is not sufficient for assuring the informed assent/consent of either the child-participant or the parents/legal representatives. Adequate time for discussion and reflection must be assured whenever possible. The paediatric researcher must ensure that the child and parents/representatives can sufficiently discuss the invitation to participate in research with the investigator and staff. They should also encourage the child and parents/legal representatives to discuss the invitation among themselves and with other family members or trusted persons.
11. The information (oral and written) to be provided to the (potential) child-participant should be in conformity with the capacity of the child to understand and should be adapted to assist the child at arriving independently at a decision. In particular, the content, language, and mode of communicating the information should be adapted to the child's capacity of understanding and decision.
12. The assent of the child should be sought to the extent possible for the child to express his or her will. If a child is able to express himself or herself in writing, the child should be invited to sign an assent form appropriate to his or her capacity for expression.
13. If the child expresses the will not to participate in the research, or later wants to withdraw from participating in the research, the will of the child should be fully respected provided it is not considered detrimental to the health of the child by the paediatric researcher or parents/legal representative.
14. The information presented to the parents/legal representatives of the (potential) child-participant should completely express the foreseen impact the research would have on the child. The informed consent process for the parents/legal representatives of the child should assist the parents/legal representatives in understanding the health needs of the child and the potential benefits and risks of the research on the child-participant. The parents/legal representatives should confirm their consent by signing a consent form, except in cases where the laws and standard practices do not require written consent.

15. When the child-participant is not legally able to consent, the consent of the parents/legal representatives is required. This consent should reflect both the will of the child as well as that of the parents/legal representatives. The withholding or withdrawal of consent by the parents/legal representatives should be fully respected.
16. In exceptional circumstances (e.g., the investigation of the use of emergency medicines in children), the consent of a relative other than the parents/legal representatives may be sought. In such cases, the (potential) child-participant should be, to the extent possible, fully informed and his/her assent sought. The retrospective consent of the parents/legal guardians should be sought as soon as possible.
17. In general, the consent of both parents should be sought prior to enrolling a child in a research project. However, where the law permits, the consent of one parent may be considered adequate.
18. The written and oral information to be provided to children and their parents/legal representatives, as well as the processes by which this information will be conveyed and discussed, must be reviewed and receive a positive decision from an appropriately constituted and operating ethics committee. The ethics committee must include or seek the advice of a paediatrician or paediatric healthcare provider independent of the proposed research.
19. The assent/consent of children as data subjects in research must be specific, informed, and unambiguous with regard to the purpose for which a child's data is collected and the processing of the child's biological sample or personal data. Children and their parents/legal guardians may also be invited to provide 'broad consent' for unspecified future research on a child's biological materials and/or personal data so long as the parent/legal guardian and the child receive a full explanation of the potential purposes of the future research, the manner in which their biological materials and/or personal data will be further processed, and the rights of the child (including the rights limitations borne by the assent/consent) are also clearly explained.
20. The assent of the child and the consent of the parent/legal guardian are to be considered invalid when the assent/consent is obtained by false, deceptive, hurried, or incomplete means and/or where there is no clear affirmation that the child and/or parent/legal guardian did not reasonably and unambiguously comprehend the purpose or the implications of the assent/consent. The onus is on the paediatric researcher to ensure an informed and unambiguous assent/consent.