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ORIGINAL PAPER

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Guidelines for informed consent in biomedical research involving paediatric populations as research participants

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Abstract To promote and protect the best interests of children involved in biomedical research, paediatricians have to ensure that participating minors and their parents/legal representatives have understood and assented/consented to the research. Therefore guidelines providing child-specific guidance that are compatible with other international guidelines on informed consent are laid down. Special regard is paid to the willingness to participate and the social and cultural background of the patients, the legal conditions of the countries, the capacity of the child to understand and give his/her informed assent, the adequate communication with the child and the parents, the respect of the will of the patient, the understandable written informed consent of legal representatives and to the evaluation of the informed consent/assent process by competent ethics committees.

Keywords Children · Ethics · Informed consent/assent · Research

Preamble

These guidelines are intended to assist European paediatricians in inviting and enrolling children in biomedical research projects by establishing appropriate informed decision and assent/consent procedures. Each paediatrician 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.

The vocation of the paediatrician lies in promoting and protecting the health of children. The paediatrician's knowledge and conscience are dedicated to the fulfillment of this vocation. It is the duty of the paediatrician to ensure that the diagnostic, prophylactic, and therapeutic care are of the highest standard and appropriate to the health needs and concerns of each child. Paediatricians share a responsibility to ensure an 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 in order to advance knowledge in paediatric medicine.

Biomedical 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 models, animals, or adult persons. Paediatricians 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 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.

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These guidelines provide specific guidance for the paediatrician regarding informed consent for research on children. This guidance should be understood as additional and complementary to existing national 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 the Council of Europe, Convention on Human Rights and Biomedicine. Particular attention should be given to the UN Convention on the Rights of the Child, EU Draft Charter of Fundamental Rights of the European Union, EMEA (CPMP) Note for Guidance on Clinical Investigation of Medicinal Products in Children, ICH Clinical Investigation of Medicinal Products in the Paediatric Population, CESP Report Research in Children, and the Proposed EU Directive on the Implementation of Good Clinical Practice.

Guiding principles for requesting the informed consent of a (potential) child-participant in biomedical 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 paediatrician in the informed consent process that invites a child to participate in a biomedical research project.

Safeguard the best interests of the child-participant

All biomedical research involving child-participants must promote and protect the best interests of the child in the research. The paediatrician 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 paediatrician has a responsibility to protect the child-participant from harm beyond what might arise from the reasonable risks associated with research. These may include physical, psychological, spiritual and social abuse.

Assure and respect the privacy of the child-participant

The privacy of the child-participant must be fully respected and assured throughout the research project. This includes the physical, psychological, and social privacy of the child. The paediatrician 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 course of the research or in connection to the research. The paediatrician has the obligation to assure this confidentiality 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. Biomedical research should never be carried out in a paediatric population if it can be carried out in an adult population. However, paediatricians 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. Such investigations will often require research in the paediatric population.
2. Children in particularly vulnerable situations (e.g. children in institutions, homeless children, refugees) should only be invited to participate in biomedical research projects if their particular condition is an object of the research. In such cases, paediatricians 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 immigrant families and families with different cultural backgrounds, 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 biomedical research project should not be dependent upon the child's nationality, race, gender, or religion, except in cases where one or more of these attributes are relative to the objective of the research.
4. The informed consent process for including children in biomedical 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 paediatrician in

inviting and accepting the participation of the child-participant.

5. The paediatrician 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 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 for informed consent should be in conformity with the laws and regulations of the country, and the accepted practices for consent and assent should be considered.
9. Separate information sheets and consent/assent forms should be developed for the parents/legal representatives and for the child. The information sheets and 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 consent form 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 paediatrician 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 paediatrician or parents/legal representatives.
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, as far as 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 biomedical 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 not involved in the proposed research.

Approved by the CESP, May 4th 2002.

Further reading

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