Code of conduct relating to expressions of objection by minors participating in medical research

Netherlands Association for Paediatric Medicine

Introduction

The *Medical Research Involving Human Subjects Act* (WMO) came into force on 1 December 1999. Medical research involving human subjects – both healthy subjects and patients – is permitted in the Netherlands only with the approval of an accredited medical ethics review committee. The approval of such a committee depends upon the research meeting certain criteria set out in the act. The WMO pays particular attention to research involving subjects who are not themselves competent to consent to participation: incapacitated adults and minors. With regard to research involving incapacitated subjects or otherwise dependent, such as minors, the act imposes a prohibition with exceptions. The Central Committee on Research Involving Human Subjects (CCMO) is responsible for reviewing protocols for certain forms of research with minors and incapacitated adults. Non-therapeutic medical research (i.e. research in which participation brings no direct benefit to the patient or healthy subject) is permissible only if the risks associated with participation are negligible and the burden is minimal. Furthermore, approval will be forthcoming only for research that cannot be carried out without the participation of people of the category to which the proposed subjects belong (section 4, subsection 1, of the WMO).

If in the context of such research a (prospective) subject objects to a procedure or to behaving in a particular way, that subject's participation in the research must be discontinued (section 4, subsection 2, of the WMO). During parliamentary consideration of the bill enacting the WMO, questions were raised regarding the implications of section 4, subsection 2. What in practice should be deemed to constitute objection and how should an investigator respond to possible expressions of objection? In response to these questions, the Minister of Health, Welfare and Sports (VWS) promised the House that a code of conduct covering such issues would be developed in consultation with the relevant professional associations.

The Netherlands Association for Paediatric Medicine (NVK) has accordingly drawn up the following code of conduct for use in the context of medical research with minors.

Code of conduct

1 Individual children respond differently to diagnostic and treatment procedures and to participation in medical research. Various factors help to determine the nature of the response: the way the child is prepared for what is going to happen, the parent-child relationship, the doctor-patient relationship, the child-friendliness of the environment in which the procedure takes place and so on.
One child will not be unduly disturbed by having an injection (even if he or she winces or makes some other display of pain), while another will find the experience distressing. Although responses vary considerably from child to child, there is a general correlation between the degree of 'invasiveness' of a procedure and the strength of the response. In some cases, fear regarding participation or a particular procedure will prompt a child to object. Patient and understanding explanation and reassurance will generally be sufficient to enable the research or the procedure to proceed without problems. Where a newborn child or infant is concerned, it is much harder to ascertain whether objection has been expressed. As a general rule, however, it is reasonable to suggest that a child may be deemed to object if its behaviour clearly differs in nature or degree from that normally displayed by the child when confronted with situations not encountered in everyday life. In this context, situations not

encountered in everyday life may be considered to include diagnostic or therapeutic procedures.

2 Before seeking consent for a child's participation in medical research, an investigator must fully inform the child's custodial parent(s) or guardian about what is proposed. Information should be provided orally and in writing. The nature of the procedures involved in the research should be discussed with the parents and their views sought on the child's likely response. The possibility of the child objecting to participation and the type of behaviour that should be regarded as an expression of objection should also be discussed. The investigator should also explain what is to happen in the event of the child objecting. The consent obtained from the parents should include agreement to the proposed procedure for dealing with expressions of objection by the child.

3 The consent statement signed by parents should stipulate that, if the child should object to participation in the research, consent for its further participation will be invalidated.

4 If prior to the research there is doubt as to whether a child should participate, consideration may be given to involving the patient in the research for an agreed pilot period.

5 While the research is in progress, the behaviour of the child should be continually assessed at the research location to determine whether the child's behaviour is within the bounds normally associated with the child when confronted with situations not encountered in everyday life. If a child's behaviour is not within these bounds, he or she should be deemed to have expressed an objection in the sense of the WMO.

6 The parents, the investigator(s) and possibly a behavioural scientist should be involved in assessment of a child subject's behaviour. Assessment of a child subject's behaviour should not be a one-off exercise, but should continue through all phases of the research.

7 The parents of a child subject should be able to withdraw their consent at any point during the research. If a child subject expresses an objection, the child's participation should be discontinued.

8 In all medical research involving child subjects, the burden associated with participation should be minimised; where non-therapeutic research is concerned, the law stipulates that it must be negligible. Medical studies often involve the combination of research procedures with diagnostic procedures necessary in connection with the subject's treatment. Where research involves an invasive procedure, such as a finger prick or venapunction, this should if possible be combined with a procedure necessary for diagnostic or treatment purposes, such as blood sampling. If possible, a needle or line that has already been inserted should be utilised, so that the number of 'jabs' is kept to the minimum. The burden can also be reduced by the use of plasters with local anaesthetic. The various steps to be taken with a view to minimising the burden should be detailed in the research protocol and in the information given to the parents and subjects.

9 The following should be noted in the research file or the medical (status) report, as appropriate:

a the outcome of any trial participation;

b the consent of the custodial parent(s) or guardian, including the procedure to be followed in the event of a possible expression of objection;

c an account of the subject's participation in the research, stating whether objection was expressed;

d an assessment as to whether the subject's behaviour constitutes objection, as referred to above;
e the names of the people responsible for assessing the subject's behaviour, as described above;
f an assessment as to whether the subject's behaviour in the course of the study constitutes objection;
g the steps taken to minimise the burden associated with participation.

10 The protocol for a medical research project in which minors are to be used as subjects should state that the NVK's code of conduct for dealing with subjects' expressions of objection in the course of the research will be adhered to.

11 This code of conduct will be evaluated in consultation with the research community two years after its initial publication and amended as necessary.

This code of conduct was approved by the Board of the Netherlands Association for Paediatric Medicine (NVK) on 21 May 2001 and published in NVK Newsletter no. 3, June 2001.