

SUBMISSION OF COMMENTS ON Ethical considerations for clinical trials performed in children. Ref: Recommendations of the Ad Hoc group for implementing guidelines for Directive 2001/20/EC relating to good clinical practice in the conduct of clinical trials

COMMENTS FROM SIOP Europe (European branch of the International Society of Paediatric Oncology) and ICCCPPO Europe (European branch of the International Confederation of Childhood Cancer Parent Organisations)

GENERAL COMMENTS

SIOP Europe represents an established network of experts in clinical trials and management of children with cancer. The majority of children with cancer are enrolled into clinical trials for their first line management. For those who suffer a relapse, fortunately the minority, a substantial proportion will take part in earlier phase trials of new agents for childhood cancer. Our membership and the networks we represent therefore have a broad and long-standing experience of clinical trials in the very vulnerable group of children with a life-threatening condition. Due to the rarity of childhood cancer, we also have a long tradition of collaborating in multinational trials. This has given us many years of experience of working with ethics committees in many countries and with families from a variety of cultural backgrounds.

ICCCPO Europe is the European branch of the International Confederation of Childhood Cancer Parent Organisations (ICCCPO) and represents the European parents of children with cancer. ICCCPPO believes that every child with cancer regardless of financial or social class, race or native origin deserves access to the best possible treatment and medical care and that parents of children with cancer must have access to the information they require to make informed decisions about their child's treatment. ICCCPPO Europe contributes to several European Consortia for innovative treatment in terms of medical-ethical aspects of inclusion of children with cancer in early clinical trials. Having the expertise for judging the acceptability of the expected treatment burden of early clinical trials, ICCCPPO Europe is involved in assessing new proposals for early clinical trials.

SIOP Europe and ICCCPPO Europe are both very supportive of the content of the document produced for consultation. We do not wish to suggest any major changes but do wish to provide further clarification of certain key areas that are mentioned, as below.

SPECIFIC COMMENTS ON TEXT

GUIDELINE SECTION TITLE

Line no¹. + paragraph no.	Comment and Rationale	Proposed change (if applicable)
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¹ Where available

7 Assent from children and 7.1 Assent according to age group	We agree that a number of information sheets should be used in order to provide age appropriate information. However, this needs to be interpreted rationally and in the light of the experience of clinical researchers and the views of the patients and families themselves. It is easy for ethics committees to require a large number of different narrow age bands for information sheets, yet there is little evidence to recommend where these cut-offs should be. Indeed, we note with interest the comment in the penultimate paragraph, page 11 (7.1.2) that “Most children are unlikely to understand randomisation, as indeed are some parents”.	Ethics committees should avoid the creeping tendency to demand large numbers of age-specific information sheets. These should be developed in conjunction with researchers and parent/patient advocates, to ensure they are ‘user-friendly’ and do not cause unnecessary distress at a stressful time, e.g. at time of diagnosis of a life-threatening illness in the child. We would like to recommend that a limited number of standardised age band requirements for patient information sheets be used across Europe. This will facilitate collaborative multinational clinical trials that are essential for rare diseases in children.
8 Ethics committee composition and 8.1.1 Examples of paediatric expertise	We agree completely with the sentiment that “paediatric expertise goes beyond having dealt with children”. We endorse the recommendation that the ‘paediatric experts’ on an ethics committee should “demonstrate at least some years of experience in paediatric care, and direct experience of clinical trials” (our emphasis). We have experience in submitting essentially the same clinical trial protocol through several national ethical approval processes. From this, it has become clear that the evaluation system works most smoothly and consistently in those countries where a single or limited number of ethics committees have develop expertise in assessing clinical trials in a particular childhood condition. It is very difficult for an ethics committee, even one with appropriate paediatric expertise as defined above, to be expert in assessing very complex trials such as are seen in childhood cancer.	Countries should give consideration to the development of specialist or designated ethics committees for the evaluation of complex trial protocols for serious childhood diseases requiring complex treatments, such as childhood cancers.
11 Assessment of risk	We agree that it is important that the potential risk to each participant is considered both in designing and in assessing a protocol. However, it must be borne in mind that for children with life-threatening conditions such as cancer, exposure to an uncertain level of risk that permits evaluation of new drugs in the paediatric age group is essential for progress in treatment of these serious conditions.	Retain a balanced view of the potential benefit of a new drug in the paediatric age group versus the risk of uncertain side effects, in children with life-threatening conditions such as cancer. If too much emphasis is placed on quantifying risk in difficult situations such as relapsed cancer, there is a danger that the very clinical trials that could benefit the patient become impossible to run due to difficulties in obtaining sponsorship and indemnity.

Please feel free to add more rows if needed.

These comments and the identity of the sender will be made public.