Ethical considerations for clinical trials on medicinal products conducted with minors – August 2016

Joint response from Cancer Research UK and the British Heart Foundation

We have an important responsibility to protect children that participate in trials. We also have an ethical obligation to ensure that they receive the best treatment. Like adults, they should be given the opportunity to benefit from the results of research that has been designed specifically for them. However, research in minors poses important challenges with regard to informed consent and assent/agreement, vulnerability and potential conflicts of interest. It is vital that the rules and regulations for clinical research always support patient safety, address ethical concerns and ensure scientific validity. However, unnecessary or inflexible regulations create significant extra costs in running clinical research for funders. We therefore welcome the opportunity to respond to this consultation.

General Comments

We think there are inconsistencies in terminology with the use of minor, child, and paediatric. In some member states a subset of the paediatric population may be old enough to give informed consent, and therefore not considered a minor, or a child. In the UK this is the case for anyone aged 16 to 18 years. Although this is partially covered in the definitions on page 10/11, we felt that the consistency of language could be improved so that it is clear throughout the guidance which population is being referred to.

Comments relating to specific lines:

Lines 482-490

The last sentence in this section states that a translated informed consent form 'could' be an appropriate way to provide trial info to parents/families with a different cultural background. However, earlier in this guidance (and in line with other guidance documents), it is stated that written information 'should' be provided. We therefore suggest that the wording here should be stronger, and require that a translation is provided.

Section 6.5

We felt that this section should be clearer in noting that there could be two parts to withdrawal of consent, for example a patient/parent may withdraw consent for further participation in the trial and trial interventions but may still be happy for trial follow-up to continue or they may withdraw complete consent. If complete consent is withdrawn then the investigator would be unable to complete the obligations outlined in the final paragraph in this section.

Section 7.2.1

Whilst the guidance is well intentioned, it does not accurately reflect clinical practice, since there are very few medical investigations a child of this age will submit to willingly. Clinicians should be relied upon to exercise judgement regarding the severity of resistance or protest in this situation.

Section 16

We suggest some additional guidance in relation to adolescent boys in trials would be appropriate, in line with the tighter requirements, for contraception use for both males and females in our adult protocols.

Lines 1383-1393

If the original informed consent made provision for the use of data beyond the protocol in line with Article 28(2) of the Clinical Trial Regulation, it is not proportionate for re-consenting (after the participant has reached the age of consent) to apply to all re-uses of data; particularly since using anonymous and/or aggregated data many years later is unlikely to be controversial to participants. Re-contacting patients annually would be an unnecessary use of resources, would irritate participants and unnecessarily compromise the completeness of the data.

Section 19.1

The guidance states in lines 1416 – 1418 that this summary should be understandable by the children that will participate in the trial. Further guidance on this, either in this document or in the laypersons summary guidance should be provided.

A summary that will be understandable to participating children may not be possible (due to low age range) or may need to be different to the standard layperson summary. We would appreciate clarification on whether the standard guidance for writing the layperson summary should be followed, or whether a paediatric version of the layperson summary should be produced for paediatric trials. The UK's HRA have produced guidance on producing patient information for children and young people which may prove useful:
http://www.hra-decisiontools.org.uk/consent/index.html

Annex 1

Recommendation 17 should read:
Safety measures including the set-up of a Data Safety Monitoring Board (DSMB), where relevant.

Recommendation 23 should be assessed in the context of assessed in the context of the burden of disease and current standard treatment

Annex 2: List of items recommended to be covered in the information sheets

- Recommendation 3: (Will I have the same doctor or investigator from start to finish?) - in our experience it would be very difficult to commit to having the same doctor or investigator from start to finish. We would recommend this should also include 'research team'.

- Recommendation 7: (what are the compensations?) - the meaning of the word 'compensations' is unclear, are investigators to explain the benefits of taking part, or whether expenses will be compensated?

- Recommendation 18: (Will my taking part in the trial be kept confidential?) - if this also refers to data protection this should be made more explicit.

Annex 3 (Final paragraph)

It is vital that risks are assessed in the context of standard care outside a trial. For example, in the context of oncology, the standard treatment may have high 'risks' due to the side-effects of chemotherapy drugs but they are necessary to treat a life-threatening disease. The side-effects of the new intervention should be assessed in the context of the standard care.

Feedback requested Q1

PET scanning is increasingly used to assess paediatric conditions as standard care so it does need to be considered in this context. We suggest it could be moved to category 2.

Feedback requested Q2

The key point in deciding categorisation of clinical trial procedures according to risk and burden, is that they should always be assessed compared to current standard care and the burden/seriousness of the disease concerned. For example, a bone marrow aspirate should not be considered an increased burden if it is to assess response to a new trial treatment for leukaemia, whereas a bone marrow aspirate for biological sample collection is an additional burden that would need to be fully justified.

For further information, please contact Ed Blandford, Policy Adviser, via Edward.blandford@cancer.org.uk or +44 (0) 203 469 6122.

Cancer Research UK

Cancer Research UK's vision is to bring forward the day when all cancers are cured. Over the last 40 years, cancer survival rates in the UK have doubled. In the 1970s just a quarter of people survived. Today that figure is half. Our ambition is to accelerate progress and see three-quarters of patients surviving the disease within the next 20 years.

Every year more than 25,000 people take part in one or more of over 250 clinical trials supported by the charity. In 2015/16, Cancer Research UK spent spent £432 million on research across the UK, including our £28 million contribution to the Frances Crick Institute. CRUK directly funds over 200 clinical trials. More than a quarter (28%) of these trials involve at least one other EU country. One in three (33%) of CRUK-supported clinical trials have involvement from countries outside of the UK.

British Heart Foundation

The BHF is the UK's leading heart charity. We are working to achieve our vision of a world in which people do not die prematurely or suffer from cardiovascular disease. Thanks to modern treatments built on our research, huge progress has been made in saving lives. Most babies born today with heart defects survive and seven out of ten people survive a heart attack. However, heart and circulatory disease still kills one in four people and affects 7 million people in the UK, so there is so much more to do.

The BHF is the largest independent funder of cardiovascular research and the third largest charitable funder of medical research in the UK. Each year, thanks to the generosity of our supporters, we are able to fund around £100 million of new research across the UK, in all four nations. Our funding portfolio extends from laboratory science to clinical trials and population studies. We fund people from PhDs to professors as well as investing in large programme and project grants.