Dear Sirs,

With regard to the above document, I submit the following in the hope it has merit.

Q1: The table of Annex 3 (previously Annex 4) has not been changed. Is the proposed categorisation of these procedures still adequate? Yes. Add urine collection via urosheath and pinprick glucometer testing to minimal risk.

Q2: Which insights may lead to changes in categorisations (in particular those indicated in yellow)? Move Hypoglycaemia test (if this is pinprick) to minimal risk. Move PET scanning from high risk to medium risk.

With regard to minors in emergency situations;

There needs to be some reference to anticipation of Adverse Events.

Whilst later in the document reference is made to pregnant adolescents, it has to be accepted that with the increased maturity and sexualisation of children, there is a real possibility that adolescents aren't the youngest category of children who may present with a pregnancy. This needs to be acknowledged in this document.

Other General Comments;

1. There is capacity for competencies for consent to change during the course of a trial. There needs to be a more specific guidance about how this is to be managed.

2. Where there could be a burden of disruption to educational development during the course of a trial, distinction should be made between whether that change would have occurred within the normal progression of the disease and treatment as usual, or whether there could be a direct cause link with the trial. Whilst this comes under Adverse Events, it would be wise and helpful for researchers to have some guidance within this document as to how this should be managed.

3. Re 8.3 Opinion on the application dossier. There is no reference here to obtaining PPI (Public/Patient Involvement). PPI should be encouraged at every level of the Research Cycle, and here it is most wanting.

4. Developing Age Appropriate documents or tools should be developed with PPI contribution.

5. No reference is made about the possibility that there may be State interference in clinical trials. Whilst this is unlikely, within this set of guidelines it would be wise to anticipate that at some future date a governing body of the State may wish to interfere into the outcome or development of a trial. A guideline to address this would be wise.

6. Re Annexe 2; Information for informed consent; "They should be designed with input from participants, affected children and parents". This should also read, "and/or PPI".

7. Lay summaries should be developed with the support of PPI.

8. The document makes no provision for when there could be disagreement between the wishes of parents. If a mother or father wishes, with the child's agreement, to be entered into a trial, and the other mother/father disagrees, to whom should the researcher pay attention? If the consent document only require the signature of one parent, should the expressed disapproval of the other parent be a factor for not entering the child into the trial? Should both parents consent be the Gold Standard of consent?

9. There is nothing in the document to address the matter of anonymity and security of confidential data.

10. There is nothing in the document to address the disclosure of unexpected diagnoses discovered during the course of the trial.

11. There is nothing in the document to address the matter of competency, especially the competency of a child who is made even more vulnerable through mental handicap. EG. If a trial is proposed to assess a drug the target population for which would be principally, or might include, a child with Downs Syndrome, what is the guidelines for dealing with such a situation, especially if such a child is in the care of an institution or local authority?

12. I am concerned especially that the guidelines fail to address the ethical dilemma of professional carrying out procedures where they could be falsely accused of inappropriate behaviour. I would like to see some recommendation that would protect clinicians from being exposed to the risk and made vulnerable to the possibility of malicious and vexatious complaint.

I hope this is helpful. Please come back to me if I can be of further assistance.

Best wishes,

Jeremy Dearling