

**Health Research Authority Comments on the International Society for Stem Cell Research (ISSCR) Guidelines for Stem Cell Science and Clinical Translation (Draft June 26, 2015)**

**Introduction:**

1. The Health Research Authority (HRA) was established in December 2011 in England to promote and protect the interests of patients and the public in health research. We strive, with partners, to make sure the UK is a great place for health research. Recognising that many members of the public want the opportunity to participate in research, we aim to ensure that health research involving them is ethically reviewed and approved, that they are provided with the information that they need to help them decide whether they wish to take part, and that their opportunity to do so is maximised by simplifying the processes by which high quality research is assessed. In doing this, we will help to build both public confidence and participation in health research, and so improve the nation's health. Our responsibilities include the appointment and operation of statutory research ethics committees. For more information see: <http://www.hra.nhs.uk/>

**General Comments:**

2. The Health Research Authority welcomes the ISSCR's Guidelines for Stem Cell Science and Clinical Translation as a positive contribution to the promotion of an efficient, appropriate and sustainable research enterprise aimed at the development of stem cell-based interventions that will improve human health.
3. We particularly note and welcome the recommendations (3.3.7.1 and 3.3.7.3) related to registration and publication, which are in line with the HRA's own commitment to improve transparency in health research.
4. It is not clear if these guidelines have been developed with the involvement of patients and the public. The steering group and members of the ISSCR 'Guidelines Updates Task Force' appear to have been drawn exclusively from the academic and clinical community and the (real or perceived) absence of the public and patient 'voice' could be seen as undermining the legitimacy of these guidelines (or indeed any guidelines that make recommendations for public health issues).
5. It needs to be clear as to whether (pluripotent) haematopoietic stem cells are, or are not, included in the focus of these guidelines which are stated as "*pluripotent cells taken from the earliest stages of human development; to the procurement of gametes and somatic cells for stem cell research; and to the in vitro and animal modeling uses of human totipotent or pluripotent cells or human pluripotent stem cell lines where the experiments raise particular concerns*". We assume that such cells are excluded from this guidance.
6. It should be made clearer that compliance with ISSCR guidelines may be fulfilled by adherence to national and international guidelines, regulations and legislation. It would seem superfluous to ask investigators to confirm that they have followed the ISSCR

guidelines if they have followed pertinent national guidelines/legislation which are compatible with the ISSCR guidelines.

### Specific Comments:

7. **Page 4 - para 2: 'Social Justice'**: Whilst we agree with the general statement that "*the costs of uncertainty about clinical utility be minimized and reduced to an acceptable level before novel treatments are applied in healthcare systems*" there are some healthcare systems, of which the NHS in the UK is one, that can be said to have a duty to bear some of the additional costs (as opposed to direct costs) of supporting and hosting research.
8. **Page 5, line 31**: it should be made clearer that within the stem cell research oversight (SCRO) process different people/committees can have roles in different aspects of this process e.g. initial approval, ongoing monitoring etc. Recommendation 2.1.2 could be read as suggesting that only one review committee would provide oversight.
9. **Page 7, Line 30, para (f)**: It is unclear why neural cell transfer, rather than any other form of cell transfer, is singled out for special consideration.
10. **Page 7, Line 39, para 2.1.3.3 'Category 3 (Prohibited Activities)'**: Activities which are considered to be prohibited currently may not be in the future. What mechanisms would be put in place to monitor, review and, where necessary, remove the 'prohibited' status of specific research activities?
11. **Page 13, Recommendation 2.2.6, Line 9**: It is not sufficiently justified why "*Wherever possible, the treating physician or infertility clinician should not also be the investigator who is proposing to perform research on the donated materials*". Whilst we recognise the potential for a conflict of interests, there will be circumstances where a research active clinician will be best placed to conduct research using the donated materials. It may be preferable to include guidance on how the consent process should be managed in these circumstances.
12. **Page 17, Recommendation 2.4.1, Line 22**: The recommendation that papers submitted for publication should state that the research was performed after obtaining approvals following a suitable SCRO review process should not be required where the authors have followed national processes broadly compatible with these guidelines.
13. **Page 26, Recommendation 3.2.3.1, line 42**: Whilst we unequivocally agree with the need for rigorous pre-clinical testing, the conditions set here regarding the burden of evidence may be too onerous. It can often be difficult to definitively establish a mechanism of action or the 'optimal conditions' including dose (as it is not always possible to extrapolate cell numbers from animal models to humans in order to 'establish' the dose).
14. **Page 29, Recommendation 3.3.1.2, line 24**: We would make the minor observation that experts involved in peer review are rarely "*disinterested*". This term might be helpfully revised or removed.
15. **Page 31, Recommendation 3.3.2.6, line 19**: States that "*Reconsent of subjects is warranted if substantial changes in risks or benefits of a study intervention or alternative treatments emerge over the course of investigation*" but does not explain what is meant by the term "*warranted*" i.e. does this mean it "should" happen or "must" happen? We would suggest that reconsent *must* occur in these circumstances.

16. **Page 31, Recommendation 3.3.2.8, line 41:** In the section heading “*Research teams should make strong efforts to preserve the privacy of study subjects*” the word “must” is to be preferred to “should”.
17. **Page 34, Recommendation 3.3.4.2:** Whilst we recognise the widespread use of the word “sham” in this context we feel that it can be seen as a pejorative and misleading term inferring that some deception of the participant is occurring. However, where a participant in research is fully informed as to the possibility of being randomised to either the group who receive placebo treatment or the investigational intervention; this ‘deception’ is no more problematic than clinical trials involving a placebo medicine or psychological research where the use of deception (followed by debriefing) is widely used and considered to be acceptable provided it is justified by the social and scientific value of the research and an appropriate risk management and harm alleviation strategy is in place.
18. **Page 42, Section 4 “Public Communications”:** This section is primarily concerned with communications aimed *at* the public and it would be helpful to include statements on the need for public engagement and communication *with* (i.e. *to* and *from*) the public on these issues with recommendations for best practice.

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