SUBMISSION TO THE AUSTRALIAN HEALTH ETHICS COMMITTEE (AHEC)

RE

DRAFT GUIDELINES ON THE USE OF REPRODUCTIVE TECHNOLOGY IN CLINICAL PRACTICE AND RESEARCH

by

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Introduction

In view of the short time available to make this submission we will adopt the following strategy. We will address only those issues in reproductive technology (RT) which we consider to be essential and able to be improved in the current climate, providing where possible alternative wording. It does not follow that we in any way approve of any or all of the practices which the Guidelines seek to regulate.

PART A Ethical guidelines for clinical practice

4 General principles

While 4.2.2 specifically requires consent, consent is not referred to in 4.2.4, 4.2.5 and 4.2.6, which are not strictly 'treatments' applied to patients but rather laboratory procedures.

It is recommended that section 4.2.2 be amended to make it clear that consent is also required for laboratory procedures. Thus:

4.2.2 information giving, counseling and obtaining consent to treatment and the laboratory procedures carried out to support treatment;

It is recommended that the word "and" at the end of 4.2.5 be deleted and the following three extra principles added:

4.2.7 the treatment of the best interests of any children conceived by reproductive technology as paramount, specifying how that principle is instantiated within the clinic's operational procedures;

4.2.8 the full disclosure of any risks to the patient that may be of significance to that patient as well as any risks to a child conceived through reproductive technology which may be of significance to the person or persons involved in the infertility treatment; and

4.2.9 procedures necessary for the protection and safety of human embryos generated by reproductive technology and which await opportunity for implantation.

5 Clinical decision making

5.2 recommends that procedures be carried out in ways that "take account of" the interests of the people who may be conceived. In our view the best interests of people who may be conceived by RT are paramount since they are more vulnerable than the prospective parent or parents. This principle is a governing principle in the SA Reproductive Technology Act 1988.

It is recommended that 5.2 be recast thus:

5.2 Clinical decisions about the provision of reproductive procedures should be applied only if they do not offend the principle that in RT the best interests of the child to be conceived are paramount.

6 Information giving, counseling and consent

It is not clear in 6.2.2 to whom the significant risks apply, to the mother, to the mother and unborn child, or to the unborn child. Moreover, we doubt that this section would meet the requirements of *Rogers v Whitaker* where consent is concerned.

It is recommended that 6.2.2 be recast thus:

6.2.2 an accurate account of any risk to the mother or child involved in the proposed procedures that would be of significance to the mother and her partner if there is one.

6.2 provides that all potential participants be provided with adequate information about the proposed procedures. It would seem to be important that it be made clear that such information delivery be interactive, with participants being given every reasonable opportunity to have their questions answered.

We recommend an additional point under 6.2, namely 6.2.5 thus:

6.2.5 opportunity to seek and receive answers to their questions about the information provided from those best qualified to provide those answers.

Moreover, sensitivity to "cultural diversity" seems not to be sufficient.

It is recommended that 6.6 be amended to take account of the religious beliefs of participants:

6.6 The information should be given with sensitivity to cultural diversity, including the religious beliefs of participants, accessibility …

The use of the term "personal and social implication" in 6.7.2 seems vague.

It is recommended that 6.7.2 be amended by adding the word "health" after "personal", thus:

6.7.2 exploration of the short – and long-term personal health and social implications …

If AHEC agrees with what we have proposed as a new 6.2.5, then 6.17 will need to be amended consequentially.

It is recommended that 6.17 be amended thus:

6.17 It is the responsibility of the clinician to ensure that participants are informed of the implications of proposed reproductive procedures, and have been given ample opportunity to have their questions answered, before obtaining …

A further consequence of a new 6.2.5 would be the need to amend the written consent forms by adding a new 6.18.3, with the subsequent parts of that section being renumbered accordingly.

It is recommended that the following new 6.18.3 be added and changes made to the numbering of the subsequent parts:

6.18.3 a statement that the participants have had ample opportunity to ask questions and that their questions have been satisfactorily answered;

8 Pre-implantation genetic diagnosis

While the intention of this section is to restrict the use of PGD to obtain information about "serious genetic conditions or diseases", the determination of what is serious remains open to interpretation. 8.2 makes seriousness "a matter for discussion between the people seeking testing and the clinical team". But if in the course of such discussions, and as more genetic tests come on line, people seeking testing wished to exclude embryos with, say a genetic predisposition to breast cancer, heart disease or even alcoholism, what guidance can be offered about the appropriateness of exclusion criteria? In the final instance will the clinic just accede to those who want and can afford any given test? The problem with the term "serious genetic condition" is that it covers both a disease (both late onset and immediate) and a predisposition to a disease which may never in fact eventuate.

It is recommended that 8.1 be modified so that "serious genetic condition or disease" becomes "seriously debilitating disease".

Furthermore, the question arises in response to the bracketed proviso in 8.1, that is, "including serious chromosome abnormalities not associated with a known condition or disease", as to how one can determine whether a serious chromosomal abnormality exists without first conducting PGD. And why would PGD be carried out if there were not some reason to test based upon the parents' carrier status of a seriously debilitating disease condition? This seems to imply that PGD would become a routine procedure on embryos which is contrary to the stated intent of the first section of 8.1. In addition, to include the phrase "not associated with a known condition or disease" implies the possible rejection of embryos that are, by any current measurement, healthy.

It is recommended that the bracketed section of 8.1, that is, "including serious chromosome abnormalities not associated with a known condition or disease", be deleted.

8.2.1 is vague. There are risks to the embryo. Could there also be risks to the parents by way of (say) false negatives, ie the embryo is not affected when in fact it is? If there are risks to the parents then 8.2.1 should reflect that. There will be expertise available to AHEC to say whether or not this is a factor.

It is recommended that, if there are risks to the parents, 8.2.1 be reworded thus:

8.2.1 the risks of the procedure to the embryo and to the participants;

9. Storage of gametes and embryos

9.7 refers to the disposal of embryos in terms of "remove them from storage and allow them to die". Many clinics simply take the embryos and place them on the laboratory bench where, as has been pointed out to us, this rapid thaw will see the embryos burst apart. This encourages the idea of "destruction" of embryos. If the embryos are to be treated with respect then the life support system, ie cryopreservation, should be gradually removed. In other words, the thawing process should be no different than that used when the embryo is to be transferred to the woman's uterus. At the very least, the participants should be given the choice of method.

Moreover, the second sentence in 9.9 is very imprecise. What happens if there is nothing in the consent protocol or that item hasn't been attended to. Either 9.7 could

be reworded to be more explicit about what is meant by removing from storage and allowed to die, or a new 9.11 could be drafted which makes the same point, or 9.9 could be redrafted.

It is recommended that 9.9 be amended thus:

9.9 Each clinic must have protocols in place describing the procedures to be followed in the disposal of embryos. The protocols must provide the option of gradual thawing, used when embryos are to be thawed and transferred to the woman, and then allowing the embryos to succumb. The procedure preferred by the persons for whom the embryos are stored is to be followed. In the absence of consent for any procedure, then those embryos are to be gradually thawed and allowed to succumb.

If this amendment is accepted there would need to be a further amendment to the last sentence in 9.13.

It is recommended that 9.13 be amended as follows:

9.13 … If there is no such directive, or it cannot be complied with, the embryos should be removed from storage and allowed to die as described in 9.9 above.

10 Use of donated gametes in reproductive treatment programs

In 10.13 we wonder whether the term "cadaver" is the right one. It carries an implication of a "very dead" person. Perhaps the word cadaver should be replaced with a term such as "a dead or unconscious dying person".

It is recommended that 10. 13 be amended as follows:

Either

10.13 Gametes should not be obtained from a dead person for use in reproductive technology programs.

Or

10.13 Gametes should not be obtained from a dead person or from an unconscious person who is dying for use in reproductive technology programs.

Missing - Eligibility Criteria

It seems to us that reference to eligibility criteria is a major issue not dealt with by the draft Guidelines. Given that certain matters related to eligibility are still being dealt with by the Courts and ultimately by the Parliament, one can understand the reticence of AHEC to prescribe. However, apart from the issue of whether or not RT should be available to single women and same sex couples, there remain the issues of whether or not infertility treatment is for the infertile only, or whether it is also for the fertile and those women who are peri-menopausal or post-menopausal. There are several really important ethical issues involved in providing RT to women who are peri- or post- menopausal (as distinct from those who are prematurely menopausal), not least being a consideration of the purposes of medicine in general and reproductive medicine in particular. Without wearying members of AHEC with detailed

argumentation with which they will be already familiar we simply draw to your attention that there are issues connected with the best interests of the child that, in our view, override the desire of couples (or singles) to have a child by RT.

It is recommended that there be a new section drafted which deals with eligibility criteria to be included in section 5, and which might look like this:

5.1 Reproductive technology should only be made available to:

5.1.1 those who are infertile, whether the infertility is due to their partner being infertile or themselves being infertile. Infertility is to be understood to mean all infertility (including premature menopause) except that due to being outside of the ordinary age range for fertility.

5.1.2 those who might otherwise transmit a major congenital disease.

Part B Ethical Guidelines for Research.

The Southern Cross Bioethics Institute considers any research on human embryos that is detrimental to the embryo, to be unethical. Therefore, our recommendations are submitted in this context and intended to limit the extent of harm to human embryos.

14 Research on participants in clinical practice.

14.3 states that risks to participants should be minimal. This raises two issues. First, what is "minimal" may be open to interpretation. But the law requires that there be a disclosure of all risks which would be of significance to the participant. That is, what the participants consider to be minimal must be the guide rather than what researchers consider to be minimal. Second, even though 14.4 recognises the possible relevance of research to third parties such as the "people conceived using reproductive procedures", there is no explicit statement indicating that risks to people conceived using reproductive procedures should be minimal.

It is recommended that a definition of consent be provided in then Key Definitions section. Such a definition could look like this:

Consent **Agreement to a procedure or procedures after full disclosure of all risks of the procedure or procedures which are of significance to the one giving consent. The disclosure of all risks must be given by one competent to do so, in plain language, and in a situation where the one considering consent is able to have his or her questions answered.**

It is recommended that 14.3 be amended thus:

14.3 "For research undertaken solely to develop new knowledge, any risks to the participants and "third parties" (as defined in 14.4), should be minimal."

15 Research on gametes

Research on gametes before fertilisation

A major concern with this section is that it effectively represents scientific research on human beings who are destined to be born and live with the consequences of that research. There is always the possibility that if adverse health effects arise, these people may wish to take legal action for what was done in a state sanctioned industry and in the context of the consent being given, and the research undertaken, in ways that were not concordant with the best interests of the one born of the procedure being paramount. Even though the research is upon precursor cells, that is, sperm and eggs, any effects may be manifest during the development of an embryo formed from those gametes, or even later in life.

Furthermore, this section is an example of the difficulty in separating clinical procedures from scientific research. Participants in clinical procedures directed at infertility treatment will be presented with information on the advantages of research on their gametes prior to fertilisation, implantation, and development of their child. The risk here is that they will accede to such research that carries with it some risk for their child because of the dominant interests of science and society. We consider this to be undue interference in a medical procedure.

The main title of this section ought to express the reality that what is being addressed is research on gametes that will then be used to conceive an embryo intended for implantation and subsequent birth.

It is recommended that the subtitle be changed thus:

Research on gametes prior to their use in infertility treatment.

Given that the long-term health effects of RT on children born from these procedures are a) unknown, b) presently under investigation, but c) with early indications of significant concern, we doubt that there can be a rational evaluation of the risks of adverse effects referred to in 15.1.3. Given that the risks involved with research on gametes prior to infertility may be additional to existing risks, and in many cases unknown or even unknowable, then it would seem that the guidelines are authorizing a life-long experiment with human beings. In our view this is, to say the least, problematic.

15.1.4 does not specify whether the number of eggs used and embryos formed are cumulative (across many couples) or specific to only one couple. It further implies that the number of embryos formed should be limited only by defined scientific aims of the project thereby making the production of human embryos subject to external goals. Rather the number of embryos formed ought to have nothing to do with research or other goals but only the interests of the children to be conceived by RT and the participants.

It is recommended that 15.1.4 be amended thus:

15.1.14 The number of eggs and embryos formed from any one couple in the research programme is to be limited strictly to the number determined on clinical grounds to be in the best interests of participants and "third parties" (as defined in 14.4). The total number of eggs used and embryos formed for the whole experiment is limited to the number necessary to achieve the scientific aims of the project.

16 Research and other activities involving embryos

Our comments in the previous section about adverse health consequences for persons born following research, as well as the numbers of embryos created also apply here.

In the illustrative example at footnote 4, described as therapeutic research, the reality may be that if embryos develop poorly in one culture medium, they will not be implanted. Currently, morphologically "good quality" embryos are implanted, while morphologically "poor quality" ones are not. If one or the other treatment produces an excess of morphologically "poor quality" embryos, the dilemma will be to either follow the scientific protocol and implant these morphologically "poor quality" embryos, or to modify the protocol and discard these embryos. Either way, the outcome of this sort of experiment cannot be described as therapeutic.

16.2.9 states that embryos used in research should not be allowed to develop beyond 14 days. This choice of time limit is basically arbitrary and about 7 days beyond the normal time at which a human embryo will implant in its mother's uterine lining. Furthermore, given that the current debate about the use of human embryos has all been about the extraction of stem cells for medical treatment, and this occurs at about 5-6 days of age, why is it necessary to go beyond this time.

We therefore recommend that 16.2.10 be amended thus:

16.2.9 The embryo is not allowed to develop beyond 7 days.

Appendix 1

The Appendix allows research that could in no way be described as "reproductive technology in clinical practice and research." It would allow, for example, toxicological testing, pharmaceutical testing, and studies in genetic modification of embryos where the intention is that the embryos be destroyed. The latter might be justified by claims that it would provide basic knowledge of human disease.

We recommend that the Appendix be amended to limit the scope of destructive or harmful research on human embryos to issues relevant to "reproductive technology in clinical practice and research" as the title of the document stipulates. The issues connected with research involving the destruction of, or harm to, human embryos for purposes unconnected with RT will be dealt with by State legislation and the Committees set up to provide licenses for those activities under those Acts of Parliament.

A1 Evidence that shows that the knowledge sought will improve understanding of human infertility.

B1 Evidence that improvement in technologies will result in improved treatments for human infertility.

Conclusion

We present these suggested amendments for consideration by AHEC. We acknowledge with appreciation the enormous amount of work that members of AHEC have put into this project and that the guidelines have had to be developed within existing social, political, and cultural parameters.