Advisory Committee on Assisted Reproductive Technology

Advice to the Minister of Health on the Use of In Vitro Maturation in Fertility Treatment

July 2010

Subject:	**USE OF IN VITRO MATURATION IN FERTILITY TREATMENT**	
Date:	22 July 2010	**File Ref:** AD20-86-11-2
Attention:	HON TONY RYALL, MINISTER OF HEALTH	

PURPOSE OF REPORT

This report contains advice to you from the Advisory Committee on Assisted Reproductive Technology (ACART) that the use of in vitro maturation (IVM) in fertility treatment should become an established procedure. An established procedure is a fertility treatment that can be undertaken by fertility clinics without having to seek ethical approval.

The Human Assisted Reproductive Technology (HART) Act says in s.6(2) that when ACART gives you advice on whether a procedure or treatment should become an established procedure, we must report to you with:

- information about the procedure or treatment
- an assessment, drawn from the published and peer reviewed research, of the known risks and benefits to health of the procedure or treatment
- advice as to whether, in ACART's expert opinion, the known risks to health of the procedure or treatment fall within a level of risk that is acceptable in New Zealand
- an ethical analysis of the procedure or treatment
- advice as to whether, in ACART's expert opinion, you should recommend that the procedure or treatment be declared an established procedure.

EXECUTIVE SUMMARY

IVM is a fertility treatment process that is a variation of conventional in vitro fertilisation (IVF). Conventional IVF involves stimulating patients' ovaries with large doses of hormones to release numbers of mature eggs which are then fertilised in the laboratory. With IVM, immature eggs are obtained, with little or no ovarian stimulation, and the eggs are then matured in the laboratory before being fertilised.

The main benefit of IVM is that it is a safer treatment option for women who are at risk from the high doses of hormones used in conventional IVF. Women with polycystic ovary syndrome (around 20 percent of subfertile women) have an increased risk of ovarian hyperstimulation syndrome, a condition that can be life threatening. IVM avoids this risk.

Another benefit of IVM is as a fertility preservation opportunity for women who wish to store their eggs before starting medical treatment (such as chemotherapy or removal of ovaries) that will impair their fertility. In these cases, there may not be time for a hormone stimulation cycle, or the use of hormones may be contraindicated because of the type of cancer.

The use of IVM is growing internationally. Most countries treat IVM as a variation of IVF. An international survey found only one country - New Zealand - that does not allow IVM.

Pregnancy rates from IVM are lower than from conventional IVF. However, the available evidence suggests that risks to resulting children are similar to those associated with IVF. We consider that the ethical issues associated with the use of IVM can best be managed in discussion between clinician and patient.

The majority of submitters in public consultation agreed that IVM should become an established procedure.

ACART recommends that the collection of immature eggs and the use of eggs that have been matured by IVM become an established procedure for individual and donation treatment purposes. This means (a) IVM could be used in New Zealand and (b) clinics using IVM would not need to seek ethical approval for its use.

If you agree with our advice, the HART Order in Council 2005 would require amendment.

RECOMMENDATIONS

Regulation of the use of in vitro maturation in fertility treatment

ACART recommends that you:

(a)	**Agree** that the collection of immature eggs and the use of eggs matured by in vitro maturation for individual and donation treatment purposes be declared an established procedure pursuant to section 6 of the Human Assisted Reproductive Technology Act 2004	Yes/No
(b)	**Note** that if you agree to (a) above, the decision would be given effect by amending the Human Assisted Reproductive Technology Order in Council 2005 to include in Part 1 the collection of immature eggs and the use of eggs that have been matured by in vitro maturation for individual and donation treatment purposes, and removing Part 2(4) ["a procedure is not an established procedure if it involves the collection of immature eggs or the use of eggs that have been matured by in vitro maturation"]	Noted

Communications

ACART recommends that you:

(c)	**Note** that the Human Assisted Reproductive Technology Act 2004 requires that "Promptly after providing the Minister with a report [under section 6 of the HART Act 2004] the Chairperson of the advisory committee must ensure that the report is published on the Internet"	Noted

(d)	**Note** that ACART intends to publish this report on its website on 2 August 2010	Noted
(e)	**Note** that ACART will send a copy of the summary of submissions to those who requested it, following publication of this report on its website.	Noted

Sylvia Rumball
Chair, Advisory Committee on Assisted Reproductive Technology

Minister's signature:
Date:

IN VITRO MATURATION

What is in vitro maturation?

1. In vitro maturation (IVM) is a fertility treatment process that is a variation of conventional in vitro fertilisation (IVF). IVM is particularly beneficial for women who are at risk of ovarian hyperstimulation syndrome if they use conventional IVF.
2. IVM involves removing from a woman immature eggs that have yet to complete their growth and then maturing the eggs in the laboratory.
3. The process replaces the maturation process the eggs would normally undergo within the ovary. Once matured, the eggs are fertilised and used in the same way as in conventional IVF.
4. The main differences between conventional IVF, and IVF with IVM, are:
    - In conventional IVF the patient's ovaries are stimulated with large doses of hormones to release mature eggs. With IVM, patients receive little or no ovarian stimulation.
    - In conventional IVF eggs mature within the ovaries. IVM eggs are matured in the laboratory for one to two days, before being used in IVF treatment.
5. While the IVM process involves immature eggs, the eggs are removed only from mature women of reproductive age.

Legal status of in vitro maturation in New Zealand

6. New Zealand clinics may not currently use IVM to treat patients. This is because in March 2005 an expert group advised that IVM was relatively novel, with a lack of evidence about health outcomes. For this reason, the expert group recommended that IVM should not, at that stage, be placed on the list of established procedures in the HART Order 2005. Instead, IVM should be monitored.

International use of IVM

7. The first IVM baby was born in 1983 in the United States. During the 1980s and 1990s there were relatively few pregnancies from IVM. Since 2000, many more children have been born, particularly in Asia and Scandinavia.
8. Countries where IVM has been used include Australia, Canada, United Kingdom, United States, Taiwan, South Korea, and China. An expert literature review commissioned by ACART found peer-reviewed evidence of the use of IVM in 16 countries from 1983 to 2008, with other sources identifying further countries and regions.

9. The expert review estimated that around 300 to 400 children have been born from the use of IVM, but noted this was probably an underestimate. There is no central world wide registry of IVM pregnancies and offspring.[1]

10. Most countries do not have any specific regulation of IVM, treating it as a variation of IVF. The journal *Fertility and Sterility,* in its most recent international survey of assisted reproduction[2], noted only one country – New Zealand - that does not permit IVM. The survey also noted that the use of IVM has become more widespread internationally since 2004.

11. The United Kingdom is the only country that has specifically approved the use of IVM as an adjunct to IVF. United Kingdom fertility clinics wishing to use IVM must apply to the Human Fertilisation and Embryology Authority.

If IVM could be used in New Zealand, what is the level of demand and likely cost?

12. New Zealand has four fertility providers. Two of the four say that they will offer IVM to suitable patients, should it be approved. A third provider says it would probably offer IVM in four to five years. The fourth provider indicated during public consultation that it did not plan to offer IVM.

13. The providers planning to use IVM say that at this stage they see IVM being used mainly by women at risk of ovarian hyperstimulation. This group will not be a new cohort of patients: they will be women who have already tried conventional IVF and found it was unsafe for them. Longer term, if pregnancy rates improve, demand may increase because IVM is more "patient friendly", with fewer drugs and blood tests.

14. Based on this information, we have concluded that the cost overall, where patients are eligible for publicly funded treatment, will be no greater than for conventional IVF. According to some projections, the cost of IVM could become cheaper in time than conventional IVF.

DEVELOPMENT OF ACART'S ADVICE

Why did ACART undertake this project?

15. ACART has monitored the international growth in the use of IVM, and is aware of interest from New Zealand clinics and consumers, in light of the benefits for women at risk from the high doses of hormones used in conventional IVF. IVM is also being used internationally for fertility preservation for women with cancer where oncology treatment will affect their fertility, and there is no time to obtain eggs through conventional drug stimulation.

[1] A Finnish researcher, in 2008, estimated that more than 1000 children have been born internationally, based on peer reviewed and non-peer reviewed reports.
[2] *Fertility and Sterility* 2007 Vol 87 No 4 Supplement 1 International Federation of Fertility Societies Surveillance.

Technical report

16. We commissioned an expert review of the literature on IVM from Associate Professor Jeremy Thompson and Dr Robert Gilchrist of the University of Adelaide. The review includes where IVM is practised; outcomes for eggs, embryos, women and offspring; and benefits and risks.

Public consultation

17. We undertook public consultation 12 January to 16 March 2009, through a discussion document *Consultation on the Use of In Vitro Maturation in Fertility Treatment.* The discussion document included the expert review, an assessment of benefits and risks, an ethical analysis, and our preliminary view that the collection of immature eggs and the use of eggs matured by IVM be declared an established procedure for individual and donation treatment purposes.

18. During the consultation period we held a hui and met with representatives of Fertility New Zealand (national consumer group) and staff from fertility clinics. We received 20 written submissions.

What did submitters say?

19. The summary of submissions is attached as Appendix A. Key points are noted below.

Whether IVM should become an established procedure

20. The majority of submitters agreed that IVM should become an established procedure. Themes in submissions from this group were:

- The need for long term monitoring of the parties involved, and particularly of resulting children.
- The need for rigorous informed consent provisions.

21. Where submitters disagreed with IVM becoming an established procedure, this was usually because they did not agree with any use of human assisted reproductive technologies. However, three submitters in this group considered that if IVM were to be allowed, ACART should issue guidelines so that the use of IVM was subject to ethical approval on a case by case basis.

Ethical issues associated with the use of IVM

22. Where submitters agreed that IVM should become an established procedure, they generally agreed with ACART's views on the associated ethical issues.

23. Some submitters who disagreed with the use of IVM held the view that IVM, in common with IVF, undermined the status of the embryo and therefore was morally objectionable. Submitters who disagreed also noted uncertainties about the safety of IVM.

Donation of IVM eggs

24. Most submitters who agreed that the use of IVM in fertility treatment should become an established procedure also agreed that IVM eggs should be available for donation. Submitters noted the importance of all parties being provided with full information about risks to both recipients and donors.

25. Some submitters who disagreed with the donation of IVM eggs referred to the importance of reproduction within a marriage. Two noted that the merits of donating IVM eggs seemed doubtful, given that IVM has a lower live birth rate than conventional IVF.

ACART'S ADVICE ON THE USE OF IN VITRO MATURATION IN FERTILITY TREATMENT

Advice on whether the use of IVM eggs should become an established procedure

ACART recommends that the collection of immature eggs and the use of eggs that have been matured by IVM become an established procedure for individual and donation treatment purposes. Donated eggs matured by IVM would be frozen as matured eggs.

26. At present egg donation is an established procedure under the HART Act 2004. The established procedure does not specify whether the donated eggs may have been matured by IVM. We consider that the use of eggs matured by IVM should not be restricted to a woman's own use. We see no reason to prohibit the donation of eggs matured by IVM for use in fertility treatment, provided that women receiving donated eggs matured by IVM are informed of the risks associated with their use and that the procedure is a relatively new treatment.

If you agree with ACART's advice, the decision would be given effect by amending the HART Order in Council 2005 as follows:

- Part 1 to include in the Schedule of established procedures the collection of immature eggs and the use of eggs matured by IVM for individual and donation treatment purposes
- Removing Part 2(4) ["a procedure is not an established procedure if it involves the collection of immature eggs or the use of eggs that have been matured by IVM"].

27. The reasons for our advice are set out below, as follows:

    - Assessment of the known benefits and risks to health
    - Advice whether the known risks to health fall within a level of risk acceptable in New Zealand
    - Ethical analysis.

Assessment of the known benefits and risks to health

Benefits of IVM

28. The major benefit of IVM is for women with polycystic ovarian syndrome or polycystic ovaries (four to seven percent of women of reproductive age, and twenty percent of subfertile women).

29. This group of women is at particular risk of developing ovarian hyperstimulation syndrome from the hormones used in conventional IVF to stimulate the ovaries into releasing mature eggs. Ovarian hyperstimulation syndrome occurs in approximately five percent of women undertaking a conventional IVF cycle. While the condition is usually mild and self-limiting, in some cases urgent medical treatment is needed. The condition can be life threatening.

30. IVM therefore provides an alternative, safer option for these women if they want to use their own eggs in fertility treatment. If they cannot use their own eggs in treatment, their other treatment options are a donated egg or embryo, or a surrogacy arrangement.

31. An emerging and increasingly important use of IVM is as a fertility preservation opportunity for women who wish to avoid, or do not have time to use, hormone stimulation before starting medical treatment (such as chemotherapy or removal of ovaries) that will impair their fertility. The eggs can then be frozen for later use in fertility treatment.

32. IVM may also benefit couples with male factor infertility where the woman does not need or want to use fertility drugs.

33. Where hormones are not used, or used in lower doses, the cost of drugs in treatment is reduced. However, this is balanced by the impact of other costs. IVM involves more frequent use of anaesthetics than in conventional IVF, because egg collection from immature follicles is more painful. The culture used in IVM is more expensive than the culture used in conventional IVF culture, and an additional day's embryology work is needed with IVM beyond that in conventional IVF.

Risks to eggs

34. IVM eggs mature readily, with fertilisation rates comparable with eggs in conventional IVF. However, IVM eggs appear to have significant levels of spindle (the part of a cell that holds the chromosomes in place ready for fertilisation) and/or chromosomal defects.

Risks to embryos

35. IVM compromises embryo development rates. The reasons for this are complex and not yet fully understood. The best measure of embryo development is the rate at which embryos implant in the uterus. In IVM, the implantation rate is approximately half that of conventional IVF, most likely due to the increase in spindle and chromosome damage noted above. Embryo development rates following IVM of eggs are slowly, but consistently, improving with time.

36. Possibly for the same reason, miscarriage rates appear to be approximately double that of conventional IVF and the live birth rate half that of conventional IVF. However, no adequately controlled studies have been undertaken to robustly determine the miscarriage rate.

37. This topic is the subject of intense research.

Outcomes for children born following IVM

38. There is limited information on obstetric and postnatal outcomes following IVM, as children born from the procedure are still young. There are still too few births to determine absolute risks for specific health abnormalities.

39. There appear to be no major neonatal or infant health complications following IVM, compared with conventional IVF and intracytoplasmic sperm injection (ICSI). Gestational age, growth restriction, Apgar scores, birth weights and sex ratios are all comparable across births resulting from IVM, IVF and ICSI.

40. No major chromosomal abnormalities have been reported in children born following IVM. The rate of congenital abnormalities appears consistent with that of IVF generally. Physical and neurological development in children born following IVM also appear to be normal.

Health outcomes for women

41. An increased incidence of ovarian bleeding is associated with the collection of immature eggs. This is because the collection procedure differs from that used in conventional IVF. With IVM the eggs are usually more embedded in the follicle wall and must be scraped off. There is no publication of an adverse event arising from egg collection during an IVM treatment cycle.

42. Compared to conventional IVF, IVM brings substantially lower risk of major adverse short-term outcomes (such as ovarian hyperstimulation syndrome) or adverse long-term outcomes (such as the risk of cancers). This is because IVM involves reduced amounts of gonadotrophins (hormone that stimulates egg follicles).

43. As part of informed consent, clinics will need to manage patients' expectations of success from IVM, because IVM is associated with reduced rates of pregnancy and live births. There is no published data indicating that patients have increased anxiety over treatment involving IVM.

44. There are no obvious patient exclusion criteria specific to IVM. In general, the same exclusion criteria apply as with conventional IVF. The notable difference between IVM and conventional IVF is for patients with polycystic ovarian syndrome. For them, IVM may be appropriate because they have an increased risk of ovarian hyperstimulation syndrome if using conventional IVF.

Health outcomes for male patients

45. There are no health risks to male patients from using IVM. Procedures for men are identical in IVM and IVF cycles.

Acceptability of the risks associated with the use of in vitro matured eggs

46. There are very few known health risks associated solely with the use of IVM. We consider that the known risks are at a level that would be acceptable in New Zealand, taking into account the benefits. IVM provides a safer treatment option for women with polycystic ovarian syndrome; couples with male factor infertility where the woman does not require fertility drugs; and women who respond poorly to or wish to reduce or avoid the high doses of hormones that are used in conventional IVF.

47. Outcomes for babies appear, at this stage, to be similar to those associated with the use of conventional IVF and ICSI. This is despite IVM having an implantation rate approximately half that of conventional IVF, a miscarriage rate approximately double that of conventional IVF and about half the birth rate of conventional IVF.

48. There has been a reasonable uptake of IVM internationally, with at least 300 to 400 births. This enables a developing picture of outcomes associated with the technology. Allowing IVM to be used in New Zealand would be consistent with the international regulatory approach: no country has banned IVM, the United Kingdom has explicitly approved IVM, and most countries allow it as a variation on conventional IVF.

49. For a small group of submitters and the wider public, any form of assisted human reproductive treatment is ethically unacceptable. Arguments used to support this view include the sanctity of marriage, children should be conceived only through natural means, and the lack of respect and status accorded embryos. This group's views on IVM reflect their general opposition to a central assumption of the HART Act 2004: specific fertility treatments should be permitted under particular, regulated, conditions.

50. As noted earlier, many submitters advocated for long term monitoring, and the need for rigorous informed consent provisions. ACART's monitoring work includes keeping abreast of international evidence about outcomes of various treatments. Our current work programme includes a joint project with ECART to determine further what can and should be monitored by each committee in our respective monitoring roles.

51. We considered the merits of requiring an external audit of IVM information provided by clinics, in order to ensure a robust informed consent process. However, we have concluded that there is no basis for a special requirement in respect of IVM. A rigorous informed consent process is needed for all forms of treatment. ACART's 2009/10 work programme also includes developing advice to you on requirements for informed consent. We anticipate providing that advice to you early in 2011.

52. Three submitters considered that if IVM were to become available, it should become an assisted reproductive procedure, so that its use required ethical approval. Our view is that the current lack of knowledge

about longer term outcomes for IVM children would not be overcome by requiring ethical consideration of individual applications. If IVM becomes an established procedure, its use will be subject to the following regulatory framework:

- The HART Act 2004
- The HART Order 2005
- The Reproductive Technology Accreditation Committee (RTAC) Code of Practice (an Australasian standard for assessing and accrediting fertility clinics)
- Fertility Services Standard (a New Zealand specific code, which will replace the RTAC Code when implemented from 1 October 2010)
- The Code of Health and Disability Services Consumers' Rights.

Ethical analysis

53. ACART considers that the ethical issues associated with IVM are best dealt with in discussion between the clinician and the patient. Our ethical analysis of IVM is linked to the principles of the HART Act.

(a) The health and wellbeing of children born as a result of the performance of an assisted reproductive procedure or an established procedure should be an important consideration in all decisions about that procedure.

54. As noted above, information to date about IVM indicates that outcomes for children are similar to those for children born from conventional IVF and ICSI.

55. There is limited information on obstetric and postnatal outcomes following IVM as the children are still young and, although there has been a reasonable uptake of the technology, there are still too few births to determine absolute risks for specific health abnormalities.

56. From the published data there appears to be no major neonatal or infant health complications following IVM compared with conventional IVF and ICSI. Gestational age, growth restriction, Apgar scores, birth weights and sex ratios are all comparable with births resulting from IVM, IVF and ICSI. No major chromosomal abnormalities have been reported in children born following IVM, and the rate of congenital abnormalities appears consistent with that of IVF generally. Physical and neurological development in children born following IVM also appear to be normal.

57. Reports, therefore, indicate very few obstetric or child health conditions following IVM, and at this stage it appears that outcomes are similar to those for IVF and ICSI babies. However, the data published is preliminary, and ongoing monitoring as more studies are published will be necessary to assess the risks associated with IVM.

(b) The human health, safety, and dignity of present and future generations should be preserved and promoted.

58. ACART's role includes monitoring the application and health outcomes of procedures. We currently do this through monitoring international and local literature and reports, attendance at relevant conferences, and input from expert members, other experts, and fertility clinics.

59. As noted above, IVM (together with other treatment) would sit within a broad regulatory framework which includes protections for consumers and any resulting children.

(c) While all persons are affected by assisted reproductive procedures and established procedures, women, more than men, are directly and significantly affected by their application, and the health and wellbeing of women must be protected in the use of these procedures.

60. IVM provides an opportunity for some women to have fertility treatment involving IVF, in cases where they would be at risk from conventional IVF.

61. We consider that the use of eggs matured by IVM should not be restricted to a woman's own use. ACART sees no reason to prohibit the donation of eggs matured by IVM, provided that women receiving donated eggs matured by IVM are informed of the risks associated with their use and that the procedure is relatively new.

62. The availability of IVM may contribute to more eggs becoming available for donation. Women at risk from ovarian hyperstimulation syndrome may consider donating eggs if their risk is reduced. This opportunity may be particularly beneficial where a woman at risk wishes to donate eggs to help a sister or another family member have a child.

(d) No assisted reproductive procedure should be performed on an individual and no human reproductive research should be conducted on an individual unless that individual has made an informed choice and given informed consent.

63. The Code of Health and Disability Services Consumers' Rights 1996 includes the right to make an informed choice and give informed consent. The Code also includes the right to complain to the Health and Disability Commissioner about a provider.

64. In addition, more detailed requirements for informed consent, specific to assisted reproduction, are set out in the Fertility Services Standard. Clinics must provide full information, in writing and verbally, on all aspects of the treatment.

(e) Donor offspring should be made aware of their genetic origins and be able to access information about those origins.

65. Children born from treatment with donated eggs matured through IVM would have the same rights as all other donor offspring born from gametes or embryos donated since the implementation of the HART Act 2004. Those rights, set out in Part 3 of the HART Act (Information about donors of donated embryos or donated cells and donor offspring),

include access by donor offspring to information about donors kept by clinics and the Registrar-General of Births, Deaths and Marriages.

(f) The needs, values and beliefs of Māori should be considered and treated with respect.

66. As part of its public consultation, ACART held a hui with Māori with an interest in assisted reproduction. The key issues for attendees were similar to those of other submitters who supported IVM being an established procedure: the availability of accessible, appropriate, and up to date information about the procedures, including outcomes for children, and having a monitoring regime that included New Zealand data and which was available to New Zealanders.

67. Knowledge and protection of whakapapa is a key concern for Māori. As noted above, the HART Act requires that information about donors be kept by providers and the Registrar-General of Births, Deaths and Marriages. Ethnicity and any relevant cultural affiliation must be recorded, along with, in the case of Māori donors, the donor's whānau, hapū and iwi affiliations.

68. ACART recognises concerns that whānau may not be included in decision making about IVM and other treatments. The Fertility Services Standard provides for the involvement of whānau in fertility treatment, if patients wish.

(g) The different ethical, spiritual and cultural perspectives in society should be considered and treated with respect.

69. Human assisted reproduction in any or most forms is unacceptable to some individuals and groups. If IVM becomes an established procedure, it would be used to treat only patients for whom its use was ethically acceptable.

70. IVM produces fewer eggs because it uses no or low doses of hormones to stimulate the ovaries. As a result, there are fewer embryos for implantation, thus reducing the potential numbers of surplus embryos to be frozen or disposed of. IVM may therefore provide an acceptable alternative to conventional IVF for people who regard embryo freezing as unacceptable, and wish to avoid as much as possible making decisions about the fate of surplus embryos.

IMPACTS

71. Please note the following impacts, if IVM becomes an established procedure.

    - The use of IVM as an established procedure would not extend to maturing eggs derived from cryopreserved ovarian tissue. ACART has determined that the use of cryopreserved ovarian tissue is an assisted reproductive procedure, and thus its use would require ethical approval on a case by case basis. There are currently no guidelines on the use of cryopreserved ovarian tissue, and the Ethics Committee on Assisted Reproductive Technology (ECART) is therefore unable to consider applications for its use. We will shortly

consider a commissioned expert technical report, received in June 2010, on the use of cryopreserved ovarian tissue. If we then decide there is a case to develop guidelines on the use of cryopreserved ovarian tissue, we will seek your agreement to that work.

- IVM would not contribute to any increase in multiple pregnancies. New Zealand clinics must minimise the incidence of multiple pregnancies. Only one embryo can be transferred if an embryo is created from the egg of a woman who is younger than 35 years, and in other circumstances no more than two embryos can be transferred. Fewer than 10 percent of deliveries as a result of fertility treatment are of multiple births.
- Where IVM was used as part of an assisted reproductive procedure – for instance, surrogacy or donation of eggs or sperm between certain family members – applications to use the assisted reproductive procedure would be subject to the guidelines for the particular treatment and require ECART approval. This is the same situation that applies to assisted reproductive procedures that involve conventional IVF.
- Patients using eggs matured through IVM would not need to meet medical criteria, such as being infertile. There are no medical criteria attached to the use of established procedures such as conventional IVF.
- Eggs matured by IVM could be donated for research. All human reproductive research must be approved by ECART. The former National Ethics Committee on Assisted Human Reproduction developed guidelines on research on gametes and non-viable embryos. The guidelines allow eggs, sperm and non-viable embryos to be donated for research purposes, provided ECART has given specific approval for each research proposal.

COMMUNICATIONS

72. The HART Act requires that the Chair of ACART must promptly, after providing the Minister with a report on whether a procedure should be declared to be an established procedure, publish the report on the Internet. We intend to publish this report on our website on 2 August 2010. We will then send the summary of submissions to submitters who requested a copy.

Appendix A

SUMMARY OF SUBMISSIONS

INTRODUCTION

The Advisory Committee on Assisted Reproductive Technology (ACART) released a discussion document *Consultation on the Use of In Vitro Maturation in Fertility Treatment* on 12 January 2009. The document invited public submissions on ACART's proposed advice to the Minister of Health that the use of in vitro maturation (IVM) in fertility treatment should become an established procedure.

The consultation document was mailed to 125 individuals and organisations with an interest in ACART's work. This included academics, government agencies, non- government organisations, providers of fertility services, consumer groups, and religious groups. The document was also placed on ACART's website

During the consultation period, ACART held a hui, met with representatives of Fertility New Zealand, and also met with staff from fertility clinics. In addition, ACART received 20 written submissions. Consultation ended on 16 March 2009.

OVERVIEW

The majority of submitters (16) agreed with ACART's proposed advice in respect of IVM becoming an established procedure, with slightly fewer agreeing that IVM eggs should be available for donation. The two key themes in submissions from those who supported IVM becoming an established procedure were:

- The need for long term monitoring of the parties involved, and particularly of resulting children.
- The need for rigorous informed consent provisions.

Both concerns were linked to the observation of many submitters that IVM is still relatively new.

Where submitters disagreed with IVM becoming an established procedure, in most cases this was because they did not agree with any use of human assisted reproduction technologies.

Three of the submitters who disagreed with the advice considered that if IVM were to be allowed, ACART should issue guidelines so that the use of IVM was subject to ECART approval.

The next section sets out themes in responses to the questions in the discussion document.

FEEDBACK TO QUESTIONS IN THE DISCUSSION DOCUMENT

Question 1: Given the identified risks and benefits, what is your opinion on ACART's proposed advice to the Minister of Health? Please give reasons for your views.

Support proposed advice that IVM become an established procedure

- Women and partners can make their own decisions if they are given good information about the limited efficacy of IVM and potential risks to the patient and any future children.
- Using one's own IVM eggs is different to donating IVM eggs. Where people use their own eggs, it will be because IVM offers them a chance they might not otherwise have. In the case of donating eggs, there may not be any medical reason to donate immature eggs
- Monitoring outcomes is vital to ensure there are no detrimental outcomes for women and children.
- There are situations where the procedure could be helpful, but the potential long term risks have not yet been identified.
- Long term outcomes for IVF with ICSI are currently unknown, so IVF/IVM comparisons aren't clear cut.
- There are few ethical issues.
- If IVM becomes an established procedure, its status needs to be kept under review to take account of any new information about outcomes.

Do not support proposed advice that IVM become an established procedure

- All assisted reproductive treatments are wrong.
- The benefits relate only to women and children, not to an embryo. IVM poses greater risks for embryos.
- The balance between risks and benefits is still to be defined. Considerably more research is needed.
- Conclusions about risk and outcomes are tentative in nature because there have been a small number if births. ACART should hesitate before recommending the use of IVM.

Position unclear

- The risks appear to outweigh the benefits, though access seems to be improved because IVM reduces cost barriers. There is a question of how many babies need to be born before any evidence about lack of safety is seen as robust.

Question 2: Has ACART identified all the ethical issues relevant to the use of IVM in fertility treatment? Do any of the identified, or any other ethical issues, affect ACART's proposed advice that the use of IVM should be allowed in fertility treatment? Is so, how?

Views of people supporting the use of IVM becoming an established procedure

- All issues have been identified.
- While it is not clear that ACART has considered the possible impacts of donating IVM eggs, this is not a sufficient reason to prohibit IVM of donated eggs. However, impacts should be monitored.
- It is important to have a monitoring framework.
- Factors to be considered should include the age of donors, the purpose for which eggs have been harvested, and the lifetime of eggs in storage.
- Access will be increased, particularly for those who cannot use other forms of fertility treatment.
- Are there issues for the health of a woman's ovaries following IVM?
- The lack of evidence is itself an ethical concern.
- A key issue for consideration is the social acceptability of ART developments.

Views of people opposed to the use of IVM either becoming an established procedure or being available under any circumstances

- The destruction of embryos equates to the destruction of human life.
- If IVM eggs are donated, there is the risk of same sex couples being parents, and a risk of incestuous relationships.
- The approach taken by ACART appears to be to let the buyer beware.
- IVM should be an assisted reproductive procedure. The clinical evidence is still very limited.
- Apart from issues to do with safety, the ethical issues are the same as those already raised by use of IVF. Both IVF and IVM treat embryos in a utilitarian way, even if IVM produces fewer embryos.
- There are few ethical issues only if you accept that there are few ethical issues associated with IVF and ICSI and deny the humanity of the embryo.
- IVM remains a novel procedure. Conclusions about the safety of the procedure can be no more than tentative at this stage.

Position unclear

- This may lead to individualised consumerism, outside whānau decision making.

Question 3: Should the use of IVM in fertility treatment become an established procedure? If not, why, and how should the use of IVM be regulated?

Yes – the use of IVM in fertility treatment should become an established procedure

- It should be an established procedure only if used by a married woman with her husband's sperm, creating one embryo at a time.
- It is a variation of IVF.
- It should be an established procedure if there is:
    - Rigorous informed choice and consent provisions, and ongoing monitoring.
    - Consideration is given to the age of the donor and associated risks, reasons for storage, length of storage.
- It will give access for people who can't use other treatments, such as conventional IVF.

No – the use of IVM in fertility treatment should not become an established procedure

- IVM should not be permitted at all.
- There are too many uncertainties. If it is to be allowed (and it shouldn't be) then it should be subject to ethical approval by ECART.
- It cannot yet be considered as an established procedure. Instead it should be considered as an innovative practice. The HART Act would need to be changed accordingly to allow the Minister to approve under certain conditions and with defined requirements new innovative techniques or clinical practices where there is existing though limited experience overseas.

Question 4: Should the use of in vitro maturated eggs in fertility treatment be limited to the individuals the eggs came from, or should the eggs be able to be donated to others for use in fertility treatment?

Allow in vitro maturated eggs to be donated

- The "owner" of the eggs, with input from her doctor and counsellor, is the best person to decide what should happen to her eggs if they are not required or surplus.
- It would be the same as a donation of normally matured eggs. There needs to be a greater emphasis on associated risks in the informed consent process.

- Recipients may wish to have eggs from a particular donor e.g. a sister. Donors should be fully informed about risks to themselves and also to the recipient.
- If it is a realistic concern that the use of IVM may lead to a possible reduction in the pool of mature eggs for donation, it may be worth considering limiting the donation of IVM eggs to women with a medical condition contraindicating the use of high doses of hormones.
- There is potential commodification of donated gametes, if donation of IVM eggs is allowed. But as egg donation is already allowed, donation of IVM eggs should also be allowed, subject to existing ACART guidelines on donations of eggs or sperm between certain family members.
- It doesn't matter where the eggs come from as long as people are well informed.
- ACART's advice could include recommending to the Minister that clinics obtain specific information from donors of IVM eggs.
- There is interest from potential egg donors, because of the reduced amount of drugs, and the reduced amount of time needed and impact on daily life.

Limit use of in vitro maturated eggs to individuals from whom the eggs came

- It should be used only by a married woman with her husband as the father of any resulting child.
- The Māori viewpoint is that eggs can be used only by individuals from whom they came, otherwise whakapapa is affected**.**
- Most clinicians probably wouldn't recommend that egg donors use IVM because IVM reduces the chance of achieving the end goal of a baby.
- The nature of marriage means couples recognise the right to become parents only through each other.
- Given that the live birth rate with IVM is lower than with conventional IVF, it seems that couples would be ill-advised to use donated IVM eggs.

Other comments

- Whānau should be consulted in decision making about donating IVM eggs
- On the basis that the live birth rate with IVM is significantly lower, it seems that couples would be ill advised to use donated IVM eggs.

Question 5: Do you have any further comments to share with ACART?

Other comments not captured above

- IVM as practised now is different to earlier IVM. It is important to be clear about the type of IVM that may be approved as an established procedure.

- The potential epigenetic effects from culturing in vitro for a longer period aren't all known, though the recent practice of IVM involves only an extra 24 hours in vitro.
- Despite good information about risks, there is a power imbalance between providers and patients because patients have so much invested in wanting a child.
- It would be good to promote follow up research of offspring, not just for IVM but for all ART.
- There are reservations about its proven safety.
- Māori views are negated by saying in the discussion document that they are diverse - this is true of non-Māori also. There is very little real engagement with Māori. Māori could be consulted out, and feel there is little point.
- The Māori perspectives section feels like a Pākehā world view with Māori kupu thrown in. The depth of meaning behind whakapapa and mana is not conveyed.
- The comprehensive literature review can be used as the basis for patient information on risks and benefits.
- The ethical use of limited health resources should be part of consideration about the use and availability of IVM.
- Information needs to be in simple, accessible language. People need to know the right questions to ask.
- Follow up needs to be internationally based, to capture a significant number of cases. Consent could be sought from patients at the time of treatment, to ensure they are available for future research.
- It should be a choice for parents whether they are involved in monitoring.
- Clinics could be required to be part of an international registry that both receives and shares data (e.g. on adverse events).
- Will clinics reduce fees because fewer drugs are used? If success rates are low, then public funding of IVM comes into question.

List of submitters

Individuals

Virinia Luhrs

Paul Clarke

Vanessa Ralph

Dr John France

Paul Elwell-Sutton

Dr Nicola Peart

An individual
Maria Jones
Dr Cordelia Thomas
Lyn Mason

Organisation
Voice for Life, Hutt Valley
Abortion Law Reform Association of New Zealand
Independent Maori Institute for Environment and Health
Fertility Associates
Women's Health Action Trust
Interchurch Bioethics Council
Te Puni Kokiri
Women's Health Action Trust
Nathaniel Centre (New Zealand Catholic Bioethics Centre)
New Zealand Law Society (Health Law Committee)
Family Planning
Fertility New Zealand
Repromed
Fertility Plus

Appendix B

Membership of ACART

Lay Members	**Expertise / Perspective**
Professor Sylvia Rumball (Chair)	Ethics
Professor Ken Daniels (Deputy Chair)	Policy
John Forman	Disability
Dr Ian Hassall	Representative of the Commissioner for Children
Professor Mark Henaghan	Law
Cilla Henry	Māori
Maui Hudson	Māori
Professor Gareth Jones	Ethics
Bishop Richard Randerson	Ethics
Robyn Scott	Consumer
Non-lay members	
Dr Richard Fisher	Assisted reproduction
Associate Professor Andrew Shelling	Human reproductive research