

Advisory Committee on Assisted Reproductive Technology

Research involving Human Gametes and Embryos

Consultation document

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Contents

Chair’s foreword	1
How to have your say	2
Publication of feedback	2
Official Information Act requests – name and contact details	2
Chapter 1 : Introduction	3
PART I : BACKGROUND.....	5
Chapter 2 : Factors ACART considers when developing guidelines	6
HART Act requirements	7
Legal status of the human embryo and human reproductive research	8
Te Tiriti o Waitangi The Treaty of Waitangi.....	8
Different perspectives	9
Disability perspective	10
Chapter 3 : The origins of this project.....	12
Aotearoa New Zealand’s current human reproductive research guidelines	12
Previous consultations on views of fertility treatment and research	14
Te Ao Māori.....	16
Toi te Taiao, Bioethics Council consultation on embryo research.....	16
Current consultation	17
Chapter 4 : The science of assisted reproductive technology	18
Gametes: definition, collection and storage	18
Embryos: creation, development and storage	20
Chapter 5 : Human reproductive research.....	23
Standard clinical research.....	24
Innovative clinical research	24
Non-clinical research.....	24
Prohibited activities	25
Sources of embryos and gametes used in research	25
General requirements for research	26
Chapter 6 : Ethical and societal views on the embryo	28
The status of the human embryo	29
The 14-day rule	31
Securing the benefits of assisted reproductive technology.....	31
Different religious beliefs.....	32
Using surplus embryos.....	33
Cell line ownership	34
Conclusion.....	34

Chapter 7 : Te Ao Māori and assisted reproduction	35
Whakapapa	37
Consent in Te Ao Māori.....	38
Māori data sovereignty	39
 PART II : QUESTIONS ON TYPES OF HUMAN REPRODUCTIVE RESEARCH.....	 41
Chapter 8 : Introduction to Part II.....	42
Research on viable embryos — a potential policy change from the 2005 guidelines	43
Common considerations	43
 Chapter 9 : Research category 1: standard clinical research	 48
Benefits and risks of standard clinical research	50
 Chapter 10 : Research category 2: innovative clinical research.....	 52
Benefits and risks	53
Additional considerations	54
 Chapter 11 : Research category 3: non-clinical research.....	 56
Benefits	56
A. Non-clinical research with donated gametes and embryos	57
B. Non-clinical research that <i>creates</i> embryos.....	62
C. Non-clinical research with cloned embryos, stem cells, blastoids and human-hybrid embryos.....	66
D. Non-clinical research that genetically edits gametes and embryos.....	79
 Chapter 12 : Currently prohibited or limited research	 85
 Chapter 13 : Use of gametes and embryos for training.....	 87
Benefits and risks	87
Additional considerations	88
 Glossary.....	 91
 Feedback form.....	 95
Questions	96
 Appendix 1: Schedule 1 of the HART Act.....	 97
Prohibited actions.....	97



Chair's foreword

E ngā mana, e ngā reo, e ngā mahana. Tēnā koutou, tēnā koutou, tēnā koutou katoa.
Greetings to all.

Assisted reproductive technology (ART) in Aotearoa New Zealand is regulated under the Human Assisted Reproductive Technology Act 2004 (HART Act). Under the HART Act, the Advisory Committee on Assisted Reproductive Technology (ACART) is required to issue guidelines and advice to the Ethics Committee on Assisted Reproductive Technology (ECART) on human reproductive research. The HART Act defines human reproductive research as any studies that use or involve gametes or embryos.

A key role for ACART is to monitor developments in ART and keep its guidelines up to date. The current guidelines for human reproductive research, titled *Guidelines for Research on Gametes and Non-viable Embryos*, were published in 2005. It is timely to review these now with a view to providing updated guidelines that still enable society to benefit from developments in ART while reflecting the views and attitudes of the day.

This consultation document presents, for public feedback, ACART's thoughts about the matters that will, or might, need to be addressed in updated guidelines for human reproductive research. Based on the outcome of this consultation, ACART will develop draft guidelines that will later be the subject of a second round of consultation.

ACART's intention is that human reproductive research guidelines will only enable research that is likely to benefit society. The guidelines must give clear guidance to ECART on what is expected to safeguard all parties, protect data sovereignty (this may be of particular interest for some iwi Māori) and demonstrate research integrity and benefits.

Fertility treatments in Aotearoa New Zealand are publicly funded for eligible patients, and the combined public and private treatments support about 1,755 children to be born in the country each year, which is about one in 30. ACART believes we must have a robust framework for good-quality human reproductive research to take place and help improve the efficacy of fertility treatments so we can achieve the safest and best outcomes for children and patients.

ACART is interested in hearing public perspectives on:

- the ethical matters associated with research using human gametes and embryos
- what, if any, restrictions should be placed on human reproductive research in Aotearoa New Zealand
- cultural, legal or other matters.

We look forward to receiving your submission and will take all submissions into account.

Nāku noa, nā
Calum Barrett, Chair, ACART



How to have your say

Your feedback can help ACART ensure the updated guidelines for human reproductive research are fit for purpose. ACART welcomes your views on the ethics of human reproductive research.

Please take this opportunity to have your say. You may give feedback on your own behalf or as a member of an organisation. You can contribute your views in any of these ways:

1. completing the Citizen Space link through ACART's or the Ministry of Health's webpage
2. emailing a completed feedback form (at the end of this document) or your comments to acart@moh.govt.nz
3. posting a completed feedback form (at the end of this document) or your comments to:
ACART Secretariat
Ethics team
PO Box 5013
Wellington 6145.

Publication of feedback

We may publish all submissions or a summary of submissions on ACART's website. Please let us know if you do not want your submission published.

Official Information Act requests – name and contact details

In line with guidance from the Ombudsman, standard procedure of Manatū Hauora / the Ministry of Health (the Ministry) is to not release the name and contact details of any submitter who has given feedback in their private capacity (ie, not in a professional capacity or on behalf of an organisation) and who has requested that their personal information not be published by ticking the relevant boxes on the feedback form (or by making such a request in writing).

Where a person has given feedback on behalf of an organisation, the Ministry will release the name and contact details of the submitter and the organisation unless there are other reasons for withholding the information under the Official Information Act 1982. If you consider that we should withhold your or your organisation's name and/or contact details under the Official Information Act 1982, please make this clear on your feedback form, or other method of submitting, noting your reasons.

For more guidance on information released under the Official Information Act 1982, visit the Ombudsman's website at: ombudsman.parliament.nz/resources-and-publications.

The closing date for feedback is 31 March 2023.



Chapter 1: Introduction

1. Every year, thousands of people in Aotearoa New Zealand undergo fertility treatment in the hope that it will enable them to have a child. Since the Human Assisted Reproductive Technology Act (HART Act) was passed in 2004, research worldwide has resulted in significant improvements to the effectiveness of fertility treatments. This research has also led to the development of new treatments that have enabled even more people to conceive children of their own.
2. The Advisory Committee on Assisted Reproductive Technology (ACART) is currently reviewing the guidelines that regulate human reproductive research in Aotearoa New Zealand.¹ The Ethics Committee on Assisted Reproductive Technology (ECART) uses these guidelines to assess applications from researchers who wish to undertake human reproductive research.
3. Under section 36(1) of the HART Act, ACART must consult with the public before issuing guidelines. In particular, ACART must have:

on the basis of a discussion paper or an outline of the proposed guidelines, given interested parties and members of the public a reasonable opportunity to make submissions and taken any such submissions into account.
4. Because ethical, cultural and social perspectives of human reproductive research are likely to vary widely, ACART has decided to undertake its consultation in 2 rounds.
5. In the first round, ACART is publishing this document to consult the public on their views about human reproductive research. ACART invites comments from any interested parties: you can complete the feedback form at the end of this document, make a submission using 'Citizen Space', write to ACART or meet committee representatives in person.
6. Part II presents consultation questions about human reproductive research that ACART has categorised into specific research areas. If you would rather comment generally on human reproductive research, or would like to provide additional information, you can do so in the space for free text in the feedback form or by making a written submission of your own (eg an email or a document attached to an email).

¹ ACART. 2005. *Guidelines for Research on Gametes and Non-viable Embryos*. Wellington: Advisory Committee on Assisted Reproductive Technology. URL: acart.health.govt.nz/publications-and-resources/guidelines-issued/guidelines-for-research-on-gametes-and-non-viable-embryos/ (accessed 3 November 2022).

7. Based on the responses to this first round, ACART will then develop draft guidelines that will be the subject of the second round of consultation. ACART anticipates that these will have extra and more detailed definitions, state the criteria on which ECART may approve or decline research, and set out the range of policies and procedures that researchers must follow if their research is approved.
8. After the second round has been completed and ACART has considered the feedback, its final step will be to advise the Minister of Health on the finalised guidelines as required by the HART Act² and issue the guidelines to ECART.
9. ACART will also decide if it will recommend to the Minister any changes that may require amending the HART Act or the HART Order, along with further related changes to the guidelines.

² HART Act, s 41(2).



PART I: BACKGROUND

Chapter 2: Factors ACART considers when developing guidelines

Summary

- In Aotearoa New Zealand, the HART Act regulates assisted reproductive technology (ART).
- A fertility clinic can only perform an assisted reproductive procedure with ethical approval from ECART, unless the HART Act says that ethical approval is not needed for that specific type of procedure.
- ECART must use ACART guidelines when deciding whether to approve a procedure. If ACART guidelines do not exist for a specific procedure, then ECART cannot grant approval.
- Public consultation is an important part of ACART's process when developing guidelines.

10. The HART Act regulates ART in Aotearoa New Zealand . Under the HART Act, a fertility clinic may only perform an assisted reproductive procedure with approval from ECART,³ unless the procedure has been specifically declared to be an established procedure.⁴
11. Established procedures are those procedures that are considered to have a low level of ethical complexity, and so fertility clinics can perform them without first getting ECART approval. The Human Assisted Reproductive Technology Order 2005 (HART Order) lists the established procedures. Examples of established procedures are the collection of sperm and eggs for donation, *in vitro* fertilisation, and the cryopreservation of eggs, sperm and embryos.⁵
12. For all assisted reproductive procedures that the HART Order does not declare to be established procedures, ECART considers applications on a case-by-case basis, using guidelines developed by ACART. ECART can also consider applications to conduct human reproductive research, using ACART's guidelines.⁶ The current guidelines for human reproductive research, published in 2005, cover research on gametes (ie, eggs and sperm) as well as non-viable embryos. For more on the current guidelines, see Chapter 3.

³ HART Act, s 16.

⁴ HART Act, s 6.

⁵ HART Order, Schedule 1.

⁶ HART Act, s 19(1)(b).

13. Where no guidelines exist for a particular type of procedure, ECART cannot consider the application. For this reason, it is important that ACART monitors developments in ART and keeps its guidelines up to date. This chapter covers the factors ACART considers when developing its guidelines.

HART Act requirements

14. In developing guidelines, ACART must comply with the HART Act. Part 1, section 4 of the HART Act lists the 7 principles that are to guide all people, including ACART members, who exercise powers or perform functions under the Act. The principles are:
 - 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
 - b. the human health, safety and dignity of present and future generations should be preserved and promoted
 - 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
 - d. no assisted reproductive procedure should be performed on an individual and no human reproductive research should be conducted on an individual unless the individual has made an informed choice and given informed consent
 - e. donor offspring should be made aware of their genetic origins and be able to access information about those origins
 - f. the needs, values and beliefs of Māori should be considered and treated with respect
 - g. the different ethical, spiritual and cultural perspectives in society should be considered and treated with respect.
15. In respecting the diversity of views about the ethical status of the human embryo, it is necessary to pay special attention to principles (f) and (g).

Legal status of the human embryo and human reproductive research

16. The HART Act authorises ACART to develop guidelines that enable ECART to consider applications to conduct research on human embryos.⁷ Under the HART Act, it is an offence to conduct human reproductive research without ECART approval.⁸ The current guidelines do not permit research on viable embryos in Aotearoa New Zealand.
17. The *National Ethical Standards for Health and Disability Research and Quality Improvement* do not provide guidance in this area either. Instead, they simply note that all applications for research using human embryos should be submitted to ECART.⁹
18. The Human Tissue Act 2008 explicitly excludes human gametes and embryos from the definition of human tissue. Section 7(2) states, 'A human embryo or human gamete is not human tissue for the purposes of any provision of this Act.' This provision reflects how human embryos have a distinct legal status in Aotearoa, unlike other human tissue, because they have the potential to be used in reproduction and therefore to create people with rights and relationships.
19. The HART Act does not prohibit the use of human embryos in research, except to prohibit the development, *in vitro*, of a human or hybrid embryo beyond 14 days of development.¹⁰ Schedule 1 of the HART Act prohibits certain activities. For discussion of these prohibitions, see Chapter 12.

Te Tiriti o Waitangi | The Treaty of Waitangi

20. As a committee appointed by the Cabinet Appointments and Honours Committee, ACART has a responsibility to help the Crown meet its obligations under Te Tiriti o Waitangi (Te Tiriti) | The Treaty of Waitangi.
21. ACART, within its roles set out under the HART Act, contributes to the Ministry of Health's efforts to ensure good health outcomes for New Zealanders. This includes contributing to the outcome of living longer, healthier and more independent lives.

⁷ HART Act, s 19(2): 'The ethics committee may not give an approval unless it is satisfied that the activity proposed to be undertaken under the approval is consistent with relevant guidelines or relevant advice issued or given by the advisory committee.'

⁸ HART Act, s 16.

⁹ NEAC. 2019. *National Ethical Standards for Health and Disability Research and Quality Improvement*. Wellington: National Ethics Advisory Committee.

¹⁰ HART Act, s 9.

22. Principle (f) in section 4 of the HART Act establishes a principle that confirms the Crown's obligations under Te Tiriti o Waitangi to uphold Māori as Treaty partners. As part of meeting these obligations, the Crown must recognise the 2019 Hauora Report principles of tino rangatiratanga, equity, active protection, options and partnership in designing, delivering and monitoring health and disability services.¹¹
23. ACART works in the spirit of the goals for meeting the Ministry of Health obligations under Te Tiriti. In 2020, ACART published more details about its efforts to meet Te Tiriti obligations,¹² which include a description of its functions and the regulatory and ethical setting in which it operates.
24. In addition, the Waitangi Tribunal has recognised the significance of He W[h]akaputanga o te Rangatiratanga o Nu Tireni (the Declaration of Independence, 1835).
25. The Government of Aotearoa New Zealand has signed the United Nations Declaration on the Rights of Indigenous Peoples (UNDRIP). As a Crown entity, ACART should contribute to advancing those rights. The Government is currently drafting and seeking feedback on a national plan to implement UNDRIP, to be released in 2023.¹³
26. For further discussion of te ao Māori views on assisted reproductive technology generally, and on human reproductive research specifically, see Chapter 7.

Different perspectives

27. Aotearoa New Zealand is culturally and ethnically diverse. Section 4(g) of the HART Act recognises that our society has many perspectives, and that these should be considered and treated with respect in the context of assisted reproduction. The different cultures, ethnicities, religions and backgrounds of the people who hold them can influence these perspectives. Considering these diverse views is an important aspect of ACART's consultation functions.

¹¹ Ministry of Health. 2020. Treaty of Waitangi Principles. URL: health.govt.nz/our-work/populations/maori-health/he-korowai-oranga/strengthening-he-korowai-oranga/treaty-waitangi-principles (accessed 5 November 2022).

¹² ACART. 2020. Summaries of the regulation of assisted reproduction in New Zealand and the legal, ethical and cultural issues often involved in assisted reproduction. Wellington: Ministry of Health. URL: acart.health.govt.nz/publications-and-resources/publications/summaries-of-the-regulation-of-assisted-reproduction-in-new-zealand-and-the-legal-ethical-and-cultural-issues-often-involved-in-assisted-reproduction/ (accessed 5 November 2022).

¹³ Te Puni Kōkiri. UN Declaration on the Rights of Indigenous Peoples. URL: tpk.govt.nz/en/a-matou-whakaarotau/te-ao-maori/un-declaration-on-the-rights-of-indigenous-peoples (accessed 5 November 2022).

28. A further influence on a person's viewpoints is whether they are a researcher, a person using fertility services or an interested member of the public. It is therefore important that ACART's consultations engage a wide variety of interested groups.
29. Different views on the ethical status of the human embryo might include seeing the embryo as a person, or as having potential to be a born person, or as property, or as a group of cells.¹⁴ In some cases, this view may depend on how long the embryo has been developing. For instance, some may believe that from the moment of conception the embryo is a person, while others may believe that personhood is acquired later during pregnancy or at birth.
30. These are just some examples of the many views people could have. For further discussion of different perspectives on the status of the embryo, see Chapters 6 and 7.

Disability perspective

31. When developing guidelines or advice, ACART must consider the perspectives of people with disabilities, including tangata whaikaha (Māori disabled people). As with the regulatory and cultural considerations, ACART has published its consideration of disability matters.¹⁵
32. One consideration is that the guidelines should take into account the need for people with disabilities to have information provided in accessible forms. Another is that they should be able to give consent in ways that suit the individual. For example, if they are not able to give their consent in writing, they should be able to give it orally as long as there is a clear record of that consent.
33. Disabled people may have unique perspectives on individual research proposals, particularly in the area of pre-implantation genetic diagnosis (PGD). PGD is used to identify embryos (for transplantation to the uterus) that do not have genes that would result in a particular medical condition or disability in the offspring. PGD gives parents information and power to decide whether to implant embryos, and which ones to implant and potentially allow to develop in the uterus.

¹⁴ Ethics in Embryo Research Task Force and Ethics Committee of the American Society for Reproductive Medicine. 2020. Ethics in embryo research: a position statement by the ASRM Ethics in Embryo Research Task Force and the ASRM Ethics Committee. *Fertility and Sterility* 113: 2. DOI: 10.1016/j.fertnstert.2019.10.012 (accessed 5 November 2022).

¹⁵ ACART. 2020. Summaries of the regulation of assisted reproduction in New Zealand and the legal, ethical and cultural issues often involved in assisted reproduction. Wellington: Ministry of Health. URL: acart.health.govt.nz/publications-and-resources/publications/summaries-of-the-regulation-of-assisted-reproduction-in-new-zealand-and-the-legal-ethical-and-cultural-issues-often-involved-in-assisted-reproduction/ (accessed 5 November 2022).

34. Some research areas contribute knowledge to the development of potential medical interventions that, in the future, may relieve suffering due to certain illnesses or disabilities. The field of stem cell technologies is one example of an area that hopes to provide cell or organ replacement treatments in future. For further discussion of stem cell technology, see Chapter 11.

Chapter 3: The origins of this project

Summary

- Aotearoa New Zealand's current human reproductive research guidelines were first published in 2005. These guidelines limit research to gametes and non-viable embryos — they do not permit research on viable human embryos.
- The guidelines have not been updated since they were published nearly 2 decades ago. ACART has an obligation to keep its guidelines up to date.
- As a result of the restrictive scope of the current guidelines, little human reproductive research actually occurs in Aotearoa New Zealand.
- Permitting research on non-viable embryos only has some practical limitations. It is difficult to identify whether an embryo is non-viable, and non-viable embryos are unlikely to produce useful data. Clinical research (ie, research involving patients) also cannot occur.

Aotearoa New Zealand's current human reproductive research guidelines

35. The then National Ethics Committee on Assisted Human Reproduction (NECAHR) first published interim research guidelines in 2005.¹⁶ These guidelines were based on extracts from the ethical guidelines for research that the Australian Government published in 2004.¹⁷

¹⁶ Minister of Health. 2005. Approval of interim guidelines under the Human Assisted Reproductive Technology Act 2004. Gazette notice 2005-go5092. URL: [gazette.govt.nz/notice/id/2005-go5092](https://www.gazette.govt.nz/notice/id/2005-go5092) (accessed 7 November 2022).

¹⁷ National Health and Medical Research Council. 2004. *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research*. Canberra: Australian Government. URL: <https://webarchive.nla.gov.au/awa/20170819171151/https://www.nhmrc.gov.au/guidelines-publications/e56> (accessed 7 November 2022).

36. Shortly afterwards, ACART was formally established to replace NECAHR, and ACART issued the interim research guidelines as 'advice' to ECART in 2007. While the Australian version of the research guidelines has been updated as recently as 2017, the New Zealand guidelines have not been updated since they were first published in 2005.¹⁸
37. Under the 2005 guidelines, titled *Guidelines for Research on Gametes and Non-viable Embryos*, research may only be carried out on non-viable embryos. However, as the HART Act does not provide a definition of a 'non-viable embryo', interpreting the guidelines has been difficult.
38. A scientific definition of a non-viable embryo was published in *Human Reproduction* in 2011.¹⁹ That definition stated that a non-viable embryo is an embryo in which development has stopped for at least 24 hours, or in which all the cells have degenerated or lysed.²⁰ A broader definition, which NECAHR used in 2003, may be that non-viable embryos are embryos 'unsuitable for implanting'.²¹
39. Restricting research to non-viable embryos may avoid some of the ethical issues associated with research on viable embryos (such as questions on when personhood begins). At the same time, it raises other ethical issues (such as the need to destroy surplus embryos rather than donating them to potentially beneficial research). It also limits the usability of Aotearoa New Zealand's research guidelines in the following ways.
40. First, it is not a straightforward process to identify in advance whether an embryo is viable or non-viable. It is not uncommon when using embryos in clinical treatment (or research, in some jurisdictions) to find that they will not grow. Some will not grow due to their inherent potential, no matter how well-suited other factors are for supporting growth. Conversely, some embryos that have been as classified as non-viable based on their appearance are, in fact, viable and have continued to develop.
41. Second, because cells degrade rapidly following death, carrying out research using embryos that have stopped developing for 24 hours or are obviously degenerated or lysed would be unlikely to produce meaningful or useful data. This significantly limits the practicality and efficacy of New Zealand's research guidelines.

¹⁸ Chair, ACART. Guidelines and advice issued to Ethics Committee on Assisted Reproductive Technology. Gazette notice 2007-go8262. URL: gazette.govt.nz/notice/id/2007-go8262 (accessed 7 November 2022).

¹⁹ Alpha Scientists in Reproductive Medicine and ESHRE Special Interest Group of Embryology. 2011. The Istanbul consensus workshop on embryo assessment: proceedings of an expert meeting. *Human Reproduction* 26(6): 1270–83.

²⁰ This is where the outer layer, or membrane, of the cell has broken down.

²¹ NECAHR. 2003. *Annual Report to the Minister of Health for the Year Ending 31 December 2002*. Wellington: Ministry of Health, p i.

42. Third, this restriction severely limits research on clinical practices associated with fertility treatments, rather than research on the embryos themselves. For example, under the current guidelines, ECART could not approve a study on whether it is more effective to implant an embryo fertilised *in vitro* at day 3 compared with day 5 after fertilisation, because the study would necessarily involve the use of viable embryos.
43. With these considerations in mind, ACART is reviewing the guidelines with the aim of providing guidelines that do not unjustifiably prevent research conducted to improve fertility treatments. Currently, where people undergoing ART have surplus viable embryos remaining after fertility treatment, they have 2 options for what to do with the embryos. Namely, they may either donate them to another individual or couple; or decide to allow the fertility clinic to destroy the remaining embryos. While donation of surplus embryos to other individuals or couples occurs, this only accounts for a minority of surplus viable embryos. Donation to research could provide another beneficial way of using viable embryos.
44. However, ACART is also mindful that expansion of the guidelines to include research on and with viable embryos raises some significant ethical issues. Not least is the issue that viable embryos have the potential to be born if transferred to a human uterus. It is against this backdrop that ACART now seeks views on how to balance these 2 important factors.

Previous consultations on views of fertility treatment and research

45. Although Aotearoa New Zealand's human reproductive research guidelines have not been updated since they were first published in 2005, ACART has undertaken several consultations on New Zealanders' views of fertility treatment and research over the last 2 decades.
46. One consultation included a project from 2005 to 2007 where ACART reviewed human reproductive research in Aotearoa New Zealand. Despite making several key findings, ultimately ACART did not revise the guidelines, and several of the matters it identified then still need to be addressed.

47. ACART's key views²² were that:
- a. for embryos
 - i. research should continue to be allowed on embryos,²³ on condition that a) evidence is provided, in each research proposal, of the scientific merit and potential medical benefit, b) the informed consent of the embryo donors is obtained, and c) the research would be subject to guidelines developed by ACART and ethical review by ECART
 - ii. the government should impose moratoria on the creation of embryos, hybrids and clones for use in research, and the genetic modification of embryos for use in research to give time to consult properly on these uses in research, and then develop guidelines for their use (or prohibit them)
 - b. for gametes
 - i. research should continue to be allowed using gametes donated for research, subject to guidelines developed by ACART
 - ii. ACART should develop guidelines to allow the genetic modification of gametes donated for research to continue and that the modification and research would be subject to ERMA²⁴ and ECART approval
 - c. for gametes and embryos
 - i. they should be able to be imported to, and exported from, New Zealand for research purposes from countries which have comparable policies and standards to New Zealand, subject to guidelines developed by ACART, and ethical review by ECART. It would be sufficient that requirements for the import and export of gametes and embryos be set out in guidelines developed by ACART, and subject to ethical review by ECART, rather than in regulations.
48. Following its consultation from 2005 to 2007, ACART considered a review of the guidelines in 2017. However, as that particular review was limited to only research on non-viable embryos, ACART concluded that the review would be of minimal benefit so did not progress the matter at that time.

²² ACART. 2007. *Specific Advice to the Minister of Health in Respect of Human Reproductive Research*. Not published.

²³ At the time, research was only allowed on 'non-viable' embryos.

²⁴ Environmental Risk Management Authority (which the Environmental Protection Authority has since replaced).

Te Ao Māori

49. As part of its responsibilities under Te Tiriti o Waitangi, ACART is recognising and addressing Te Tiriti principles, tikanga Māori and Māori perspectives on human assisted reproductive technologies through its consultations and guidelines. Chapter 7 focuses on te ao Māori views of assisted reproductive technologies and we welcome comments about te ao Māori views in any of the consultation questions in Part II.
50. We also note a wider need for further research into the implications of tikanga Māori for ART.

Toi te Taiao, Bioethics Council consultation on embryo research

51. In 2006, Toi te Taiao, the Bioethics Council commissioned focus groups with a range of participants across Aotearoa New Zealand, using ‘deliberative dialogue’²⁵ to consider the use of embryos in research. The Council found that ‘there is very little awareness of what human embryo research consists of, and only very faint notions of what medical purposes it might serve’.²⁶ For example, most participants wanted to know where embryos come from and how they are cultured *in vitro* (in a laboratory).
52. Toi te Taiao reported that people’s views on whether to use embryos in research could be categorised as: strongly opposed, strongly supportive, oscillating (between opposition and support, depending on information presented and others’ opinions) and detached (uninterested).
53. The strongly opposed were in the smallest minority. They remained opposed throughout the discussion, largely due to religious and cultural perspectives, or fear and scepticism of science (delivering benefits).
54. At the start of the focus groups, most people felt generally opposed to embryo research, and even other aspects of human assisted reproductive technology, like *in vitro* fertilisation (IVF) and embryo freezing or storage. Yet once people became more informed, more of them supported the ideas, including research using pre-implantation embryos. The ‘oscillators’ supported research when they saw its potential benefits — for example, when it could achieve new or safer medical treatments. Some also supported the use of embryos to create stem cell lines, and studies to better understand pre-implantation development, that is, the biology of early stages of life in humans from conception to implantation in the uterus.

²⁵ Deliberative dialogue is a process that recognises people’s limited knowledge and uses discussions so that people can become better informed and then be able to form and re-form their views.

²⁶ Toi te Taiao, Bioethics Council. 2006. *Human Embryo Research Qualitative Research Report*. Wellington: Toi te Taiao, Bioethics Council.

55. The Council's report stated that participants reached a consensus that human reproductive research should meet the following fundamental criteria.
- a. Embryos used in research should be from fully informed, consenting adult donors.
 - b. Tight controls ensure the overall medical, scientific and ethical integrity of the research.
 - c. Only research that is of undoubted benefit to society should take place.
 - d. Cloned human beings must not result from this research.
 - e. Eggs (oocytes) and sperm donated for the purpose of creating embryos for research must not be not implanted and allowed to become human beings.
56. Focus groups with Māori revealed that achieving benefits within whānau was important to them. For example, they supported research using embryos to create stem cell lines to benefit whānau, or specific projects within whānau. These views were consistent with concerns about the implications for whakapapa if gametes were donated outside their whānau.
57. Perspectives on cloning (for use in non-clinical research only) suggested that when people understood the potential medical benefits of the use of stem cells, such as regenerative medicine, they supported it. For this reason, they considered cloning was an acceptable source of embryos when the conditions in paragraph 55 applied.

Current consultation

58. ACART's current consultation includes considering human reproductive research involving gametes and involving embryos (both viable and non-viable). As discussed above, the consultation will be conducted in 2 rounds. The first round (this round) is on the ethical, cultural, legal and social issues associated with human reproductive research generally. The second round will focus on a proposed set of guidelines.

Chapter 4: The science of assisted reproductive technology

Summary

- Modern medical techniques allow sperm and eggs to be collected from men and women, and used to create an embryo in a laboratory. This is known as ***in vitro* fertilisation** (IVF).
- The benefit of IVF over other methods of conception is that the sperm can be directly introduced to the egg, increasing the chances of achieving fertilisation.
- Embryos that have been created using IVF can be implanted into a woman's uterus, in an attempt to establish a pregnancy.
- Any sperm, eggs or embryos that are not immediately needed can be frozen and stored at -196°C . These can be thawed and used if needed at a later time, without any impact on the quality of the sperm, eggs or embryos.

59. This chapter describes the key definitions, ideas and processes that are involved in assisted reproductive technology and human reproductive research.
60. First, it presents an overview of how embryos are formed and develop. It then summarises how fertility clinics collect and use human reproductive tissue for the purpose of fertility treatment.
61. In this document, the terms 'man/male' and 'woman/female' refer to biological sex. ACART acknowledges not all people have a gender identity that falls within the binary categories of male and female and that people may have gender identities that differ from their biological sex.

Gametes: definition, collection and storage

62. The word 'gamete' is a collective term for sperm and eggs.
63. The HART Act has a wide definition of a gamete: '(a) an egg or sperm, whether mature or not; or (b) any other cell (whether naturally occurring or artificially formed or modified) that (i) contains only one copy of all or most chromosomes; and (ii) is capable of being used for reproductive purposes'.²⁷

²⁷ HART Act, s 5.

64. In Te Ao Māori, one perspective is that sperm and semen have a whakapapa to Tāne Māhuta. The origins of human fluids began with his feelings for Hine-Ahuone, who is the deity of female gametes. From this perspective, as one source of life gametes are considered tapu.

Collecting and storing sperm and testicular tissue

65. The usual method of collecting sperm from semen is through masturbation. Sperm are then separated from the semen in the laboratory. Another method of collection is testicular aspiration, where a surgical procedure extracts sperm directly from the testicle. Sperm are used in IVF treatment to fertilise eggs in a laboratory, or in insemination cycles, where they are injected through the cervix into the uterus and fertilisation then happens in the body. Testicular tissue can be surgically removed and used clinically, including for fertility treatment, at a later date.
66. Sperm, semen or testicular tissue are cryopreserved in liquid nitrogen at -196°C . Sperm or tissue can be stored indefinitely at this temperature.

Collecting and storing eggs and ovarian tissue

67. When eggs are in the ovary, they are normally in an 'immature' state and only one normally 'matures' each month in a natural ovulation cycle. The egg grows in a bubble-like 'follicle' filled with fluid and supporting cells.
68. A woman can be given synthetic hormones to stimulate the ovaries to produce, or mature, more than one egg at one time.²⁸ It typically takes 1 to 2 weeks of ovarian stimulation before eggs are ready for retrieval.
69. Collecting the eggs involves an ultrasound guided procedure. Here, an aspiration needle is inserted into each ovary through the vaginal wall.
70. The next options are to place eggs with sperm to allow fertilisation (IVF) and embryo development, or freeze them for future use.
71. Ovarian tissue can be removed from an ovary using laparoscopic surgery and frozen. It is possible to graft (transplant) ovarian tissue back into the human body to replace follicles, eggs and hormones that have been lost, such as because chemotherapy has caused ovarian damage. This is a newer technology but has now resulted in the successful birth of a number of babies worldwide.
72. Eggs and ovarian tissue can be cryopreserved at -196°C indefinitely.

²⁸ This process may involve one of several medications, such as medications for ovarian stimulation or for egg maturation. When the follicles are ready for egg retrieval — generally after 8 to 14 days — the patient will take human chorionic gonadotropin (HCG) or other medications to help the eggs mature. Medications can also be used to prevent premature ovulation and to prepare the lining of the uterus.

Embryos: creation, development and storage

73. IVF is a common fertility treatment that creates embryos by introducing sperm to an egg in a laboratory setting. The benefit of IVF over other methods of conception is that the sperm can be directly introduced to the egg, increasing the chances of achieving fertilisation.
74. If the semen sample is of good quality, a large number of sperm can be placed with each egg and one sperm should penetrate each egg and fertilise it. When the semen sample is of poor quality, intracytoplasmic sperm injection (ICSI) is used. This involves injecting a single sperm into each egg. ICSI is used to treat a large number of male²⁹ fertility problems.

Developing embryos in the laboratory

75. Following fertilisation, the fertilised egg starts to divide to form the cells of the embryo. Two days after fertilisation an embryo usually has 4 cells, and 3 days after fertilisation it usually has 6 to 8 cells.
76. On or around day 4 after fertilisation, the embryo compacts to form a 'morula' (a compact cluster of cells). The embryo forms a blastocyst on day 5. This is a fluid-filled ball of cells, with an inner cell mass that will become the fetus, while the outer cells (trophoblast) will become the placenta. On day 6, the blastocyst 'hatches' and is ready to implant into the uterine wall (endometrium) on day 7.

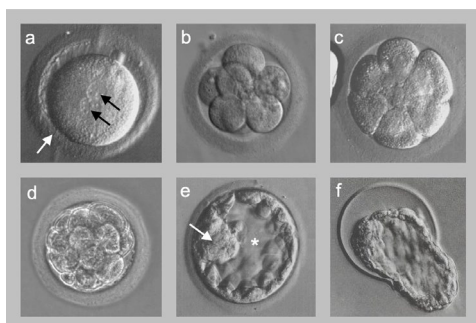


Figure 1: Photos of human IVF embryos. a) Fertilised egg with two pronuclei; one from the egg and one from the sperm (black arrows) surrounded by the zona pellucida (white arrow). b) Embryo three days after fertilisation with eight cells. c) Embryo starting to compact four days after fertilisation. d) Embryo at morula stage four to five days after fertilisation. e) Blastocyst five days after fertilisation showing inner cell mass (white arrow) and fluid filled space or blastocoel (asterisk). f) Blastocyst hatching from the zona pellucida six days after fertilisation.³⁰

²⁹ Human Fertilisation and Embryology Authority. Intracytoplasmic sperm injection (ICSI). URL: [hfea.gov.uk/treatments/explore-all-treatments/intracytoplasmic-sperm-injection-icsi/#:~:text=ICSI%20is%20an%20effective%20treatment,to%20be%20surgically%20extracted%20first](https://www.hfea.gov.uk/treatments/explore-all-treatments/intracytoplasmic-sperm-injection-icsi/#:~:text=ICSI%20is%20an%20effective%20treatment,to%20be%20surgically%20extracted%20first) (accessed 8 November 2022).

³⁰ Niacin KK, et al. 2012. Human pre-implantation embryo development. *Development* 139(5): 829–41. doi:10.1242/dev.060426.

Using and storing embryos

77. Embryos are transferred into the uterus most commonly after 5 days of development when they are blastocysts. This transfer is done by injecting the embryo, along with a small amount of fluid, through the cervix into the endometrial lining of the uterus.
78. Usually just one embryo is transferred at a time so that, if it keeps growing and becomes a pregnancy, it is a single pregnancy that results in just one baby. If 2 or more embryos are transferred at the same time, there is a chance of a multiple pregnancy developing. Any multiple pregnancy is at higher risk of complications than a single pregnancy.
79. Any good-quality embryo resulting from an IVF cycle that isn't transferred into the uterus is frozen. Embryos are frozen and stored in the same way as eggs and sperm. Freezing embryos is an important part of IVF treatment as it allows only one embryo to be transferred at a time (resulting in mainly singleton pregnancies). As a result, it is possible to make a number of attempts at pregnancy using the frozen embryos from one round of ovarian stimulation and egg collection.
80. Some people will decide that they no longer want to keep their frozen embryos. They usually do so when they have completed their family and have additional embryos still frozen. They can choose to donate these embryos to other people or to have them destroyed. Currently they cannot donate such embryos for research as the embryos are still considered to be 'viable' but if ACART issues revised guidelines that allow research on embryos, these surplus embryos would be the main source of embryos for research.

Developing embryos after the blastocyst stage

81. At first, the cells of the inner cell mass of the blastocyst are pluripotent. That is, they are all the same and able to become any type of cell or tissue in the body. These cells multiply and differentiate into cells that form the 3 main layers of the body:
 - ectoderm — skin and nerves
 - endoderm — organs such as digestive tract, lungs, liver and pancreas
 - mesoderm — bone, cartilage, muscle and connective tissue.
82. At around day 14 after fertilisation, the embryonic cells (epiblast) form a groove called the primitive streak. The cells move through this groove as they multiply and differentiate to form the different layers of the body tissue.

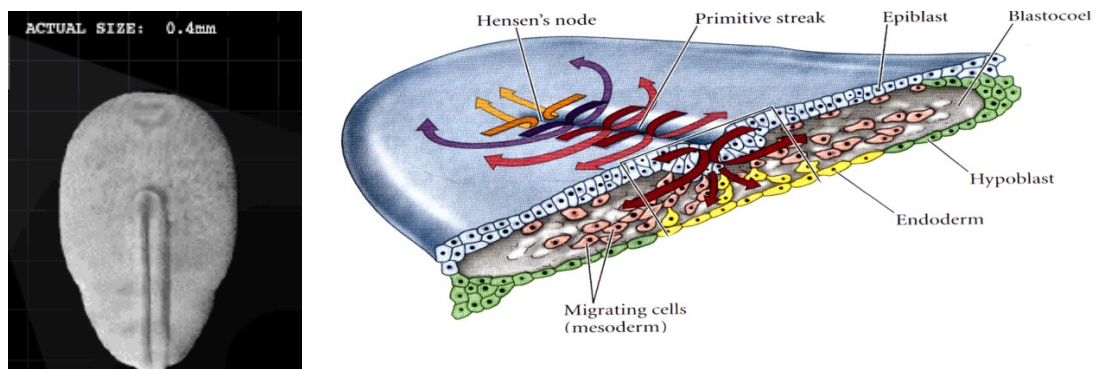


Figure 2. Left shows a microscope image of the primitive streak (groove) in a human embryo at around 14 days after fertilisation. Right is a diagram showing how the cells move through the groove as they multiply and form the different cell types and layers of the developing fetus.

83. Days 14 to 28 see the development of the neural tube (which will form the spinal cord and brain) and somites (which will become the connective tissues, muscle and bone). Other organs such as the heart also begin to develop. At 4 weeks after fertilisation the basic body plan is in place and the heart begins to beat.
84. By 8 weeks after fertilisation the initial formation of the organs has been completed. These organ systems and the structures of the body continue to grow and develop extensively up until the time of birth at around 38 weeks after fertilisation.

When an embryo starts to feel pain

85. Some people have asked when an embryo or fetus can start to feel pain, because it affects how they feel about research using viable embryos.
86. To perceive pain, an embryo/fetus needs to have developed the following structures:
 - structures that can sense pain (sensory receptors)
 - chemicals that can signal pain to the nerves (neurotransmitters)
 - nerve fibre connections to the spinal cord

31

88. Therefore, scientists consider that the earliest the embryo can start to detect any form of pain is 12 weeks after fertilisation. The developing brain will only subconsciously detect pain at around 20 weeks after fertilisation.

³¹ Bellieni CV. 2019. New insights into fetal pain. *Seminars in Fetal and Neonatal Medicine* 24(4). DOI: 10.1016/j.siny.2019.04.001.



Chapter 5: Human reproductive research

Summary

- Before any human reproductive research can be conducted in Aotearoa New Zealand, ECART must provide approval for it, based on ACART's guidelines.
- Human reproductive research can involve a wide range of different methods and techniques. Some research might simply focus on validating existing techniques used regularly in fertility treatment. Other studies may be designed to understand the basic biology of early embryonic development, cell biology, genetics or stem cell research.
- Research can occur either in a clinical setting (involving real patients undergoing real fertility treatments) or in a non-clinical setting (patients are not involved, and any gametes or embryos used in the research will not later be used for reproductive purposes).
- An application to ECART to conduct human reproductive research would have to contain adequate information on a range of matters. This includes the purpose and methods of the research, the method of gaining consent, and evidence of the value and importance of the research.
- It is important to make public the information that comes from research. In Aotearoa, researchers can only publish the results of any research on gametes or embryos if ECART has approved the research.

89. Human reproductive research can involve a wide range of methods and techniques. Some research might simply validate existing techniques that are used regularly in fertility treatment after making minor changes to them, such as testing new commercial products or comparing commonly used procedures. Other research may aim to learn more about how gametes and embryos develop in different situations in order to increase the rates of successful pregnancies.
90. Some research may not be intended for fertility services, but instead be designed to understand more about the basic biology of early embryonic development, cell biology, genetics and stem cell research. This research could build knowledge of what causes fetal abnormalities or miscarriages, how cells grow, divide and differentiate into tissue types, and use of stem cells for regenerative medicine. The goal of this research can be to improve health treatments.

91. It is important to make public the information from research. Researchers can only publish the results of any research using gametes or embryos in Aotearoa New Zealand if ECART has approved the research. As stated earlier, ECART can only approve research based on guidelines ACART has issued.

Standard clinical research

92. Standard clinical research is research that occurs during normal clinical treatment that people are receiving to create offspring. It may involve comparisons of various established procedures to find the most effective interventions for creating successful pregnancies. An example is a study to determine the most effective day following fertilisation to transfer embryos to the uterus. Another example is research to test new culture media (the substance in which embryos develop in the laboratory) that has been approved for use, with randomised controlled trials.
93. Because this type of research is occurring in a clinical setting, with real patients who are seeking real treatment, the Code of Health and Disability Services Consumers' Rights applies. This means that the treatment the patient receives must be safe and effective.

Innovative clinical research

94. Innovative clinical research is any research or clinical practice that is not yet standard. Innovative research is particularly important for developing new and better ART procedures.
95. Any new treatment must be safe. It will be tested in cell culture and/or animals first to establish it is safe and effective before it can be used in clinical treatment.
96. Both standard clinical and innovative clinical research would involve the transfer of embryos to a woman's uterus with the intention of producing offspring. As innovative clinical research still involves patients who are seeking real treatment, the Code of Health and Disability Services Consumers' Rights still applies. These clinical trials must have clear consent processes so patients understand the trial nature of their clinical treatment and what the risks and benefits might be.

Non-clinical research

97. Non-clinical research is research with gametes or embryos that will not be used for a patient's reproductive needs. That is, such research will not involve transferring the embryo to a woman's uterus. Non-clinical research could be about the biology of early human embryonic development, or the biology of gametes and could include development of embryonic stem cells. For more detail on this type of research, see Chapter 11.

98. By the end of most non-clinical research, the embryo is not viable because of the techniques involved, such as fixing and staining to identify protein or gene expression. It is expected that guidelines for non-clinical research would prohibit any transfer to the uterus of any reproductive material (gametes or embryos) used in the research whether it survives the manipulations or not.
99. Although non-clinical research presents very little risk to patients and will not result in offspring (embryos or gametes are disposed of after use), it still raises many ethical matters that must be considered. Chapter 11 explores these matters further.

Prohibited activities

100. Schedule 1 of the HART Act (see Appendix 1) sets out the human reproductive activities that are prohibited in Aotearoa New Zealand. These include (but are not limited to) transferring (ie, implanting) cloned embryos, hybrid embryos, and animal embryos or gametes (eggs or sperm) into a human. Schedule 1 likewise prohibits implanting a human embryo or human-hybrid embryo into an animal.
101. Culture (growth) of human embryos beyond 14 days after fertilisation is also prohibited.³²
102. While ACART is not proposing to amend the prohibited activities in Schedule 1 or section 9 of the HART Act, it is still interested in hearing if people believe any currently prohibited activities should be permitted. Part II includes a question on this point.

Sources of embryos and gametes used in research

103. If ACART publishes guidelines that allow research using viable embryos, some of these embryos will have originally been created for intending parents to use. Other embryos could be created specifically for use in non-clinical research if the guidelines allow it.
104. If embryos are a by-product of research on gametes or are created specifically for non-clinical research, they would be cultured for no longer than necessary (up to the 14-day limit). As this is non-clinical research, the embryos could not be transferred to a uterus.
105. ACART is also interested to hear views on creating embryos specifically for research and using artificial gametes or embryos for research. Chapter 11 presents the questions on these issues.

³² HART Act, s 9.

Consent requirements

106. In clinical research, the research is part of people's treatment. The patients will have the option to consent to participating in the research during their treatment, just as patients in other fields of medicine may agree to participate in clinical trials.
107. In non-clinical research, donors would donate embryos or gametes to the research, with their informed consent.

General requirements for research

108. For research using human participants or tissue in Aotearoa New Zealand either a Health and Disability Ethics Committee or, in some cases, an ethics committee at the university where the study is being undertaken must consider and approve it.
109. However, for any research that uses gametes or embryos, ECART must first provide approval, based on ACART's guidelines. The HART Act sets this requirement for scrutiny, because research using gametes and embryos is more complex ethically than using other human tissues.

Information required in research applications

110. Similar to any research involving human participants or human tissue, an application for human reproductive research would have to contain adequate information about each of the following (where applicable) before ECART could consider the application:
 - a. the purpose — evidence that the research is likely to add to knowledge
 - b. the methods
 - c. whether the research is intended for reproduction or not (ie, clinical or non-clinical research)
 - d. the information and consent process and forms
 - e. evidence that previous studies have shown the safety and efficacy of the research (for clinical research)
 - f. evidence of the value and importance of the research (eg, the benefits, such as improving fertility treatment outcomes, improving health of offspring, understanding an area of biology, developing a cure for a human disease or establishing a stem cell line or model)
 - g. how researchers will report the results
 - h. who will own the data
 - i. how researchers will keep records and secure patient data

- j. whether gametes and embryos will be stored for unspecified future use
 - k. variations to approvals
 - l. whether the research is using gametes and/or embryos from people who are deceased.
111. Details of these requirements would be part of the guidelines that ACART will consult on in the second round of consultation.

Chapter 6: Ethical and societal views on the embryo

Summary

- People hold many different views on the status of the embryo. They may form their views based on their cultural background, spiritual beliefs or life experiences, and may hold them as an individual or share them as a member of a wider group.
- Some people may believe embryos are entitled to human rights and protections (whether on legal or ethical grounds, or both) from fertilisation onwards. Others believe that prenatal life is not entitled to full legal rights and protections until a much later point, such as at birth or an advanced stage of fetal development.
- Regardless of what an individual's belief about the status of embryos is, it is highly likely that the belief includes some recognition that embryos can have a special status and that this status should be respected.
- ACART recognises that people hold a wide range of views. While it is unlikely that any single approach will satisfy everybody completely, it is important that we establish some common core values from which Aotearoa New Zealand can develop an acceptable framework for ethical decision-making in human reproductive research.

112. In 1982, the United Kingdom established a Committee of Inquiry into Human Fertilisation and Embryology, known as the Warnock Committee. Its purpose was to investigate a number of emerging techniques to overcome infertility (many of which are now commonplace), as well as to determine whether scientific research on human embryos should be permitted in the United Kingdom.
113. From the Warnock Committee came the Warnock report, which was published in 1984.³³ One of its recommendations was that research on human *in vitro* embryos should be permitted in the United Kingdom under licence. Recognising that the public held a wide variety of views on the moral status of human embryos, the report aimed to maintain public trust by also placing a strict limit on how far through an embryo's development research could be conducted.

³³ Committee of Inquiry into Human Fertilisation and Embryology. 1984. *Report of the Committee of Inquiry into Human Fertilisation and Embryology*. London: Department of Health and Social Security. URL: hfea.gov.uk/media/2608/warnock-report-of-the-committee-of-inquiry-into-human-fertilisation-and-embryology-1984.pdf (accessed 8 November 2022).

114. In the 4 decades since the Warnock Report was published, great strides forward have been made in our understanding of embryology, and in our ability to use assisted reproductive technologies to help overcome infertility. However, the debate continues around many of the ethical questions associated with human reproductive research, such as questions about the status of embryos, personhood and the value of research.
115. Earlier chapters have introduced embryology and human reproductive research, which we expand on in Part II. While developments in scientific knowledge have greatly increased the range of research that is possible now, a key question we need to ask is: what human reproductive research should be allowed in Aotearoa New Zealand?
116. To answer this question, ACART must take account of the ethical, legal and societal perspectives on gamete and embryo research. ACART recognises that people hold a wide range of views. While it is unlikely that any single approach will satisfy everybody completely, it is important that we establish some common core values from which Aotearoa New Zealand can develop an acceptable framework for ethical decision-making in human reproductive research.
117. This chapter introduces some of the key ethical issues, as well as recognising the diverse range of spiritual and cultural perspectives that may influence opinions on human reproductive research. ACART invites feedback on any of the content in this chapter, either generally or in response to the consultation questions in Part II.

The status of the human embryo

118. The people of Aotearoa New Zealand have a wide range of views on what status the human embryo should have. They may form their views based on their cultural background, spiritual beliefs or life experiences, and may hold them as an individual or share them as a member of a wider group.
119. At one end of the spectrum are those who believe embryos are entitled to human rights and protections (whether on legal or ethical grounds, or both) from fertilisation onwards. Here, prenatal life has a strong claim to the protection of its interests, perhaps equivalent to the rights of a human adult. This view can be linked to the belief that human life begins at conception or the belief that an embryo's potential to become a born person gives it full personhood. Consequently, people who hold this position may argue that destroying embryos is unethical or that embryo research cannot be justified.

120. People holding these views may not necessarily believe that all ART should be prohibited, but may want to see more limits on the application of techniques that create human embryos. For example, a person who believes that life begins at conception may think that embryos created through use of IVF must be implanted, so that they have the full opportunity to become born persons. Implanting all embryos would be largely inconsistent with current practices in Aotearoa New Zealand, where fertility treatments create surplus embryos that are not used, fertility clinics dispose of them at the end of storage.³⁴
121. At the other end of the spectrum are those who believe that prenatal life has a much weaker claim to the protection of its interests and is not entitled to full legal rights and protections until a much later point, such as at birth or an advanced stage of fetal development. To some people, the embryo at its blastocyst stage (around 5 days after fertilisation) is a mere collection of cells, lacking any of the rights of born humans. From this point of view, embryos are not capable of experiencing harm or benefit. Using them for research can be justified ethically so long as other issues such as consent are adequately addressed.
122. It is likely that most people in Aotearoa New Zealand adopt a position somewhere between these 2 ends of the spectrum. They may believe that embryos have moral rights and are owed protections due to their potential to become people, but that these rights and protections exist to a lesser degree than those of people who are born. From this perspective, these rights and protections may gradually increase as the embryo develops.
123. Regardless of what an individual's belief about the status of embryos is, it is highly likely that the belief includes some recognition that embryos can have a special status and that this status should be respected.
124. The reason why people believe embryos deserve this respect may be that they believe embryos:
- a. are a scarce and valuable resource (embryo as property), and/or
 - b. have potential to become born people (embryos as potential), and/or
 - c. are a human life or spirit (embryos as people).
125. Within these views, people need to weigh embryos' rights and protections against the potential benefits that may come from using embryos for research. Consequently, the ethical justification of research projects using human embryos will depend on the potential benefits that the research may provide.

³⁴ As creating *in vitro* embryos requires an invasive procedure to collect eggs, it is practical and safer to collect several eggs in one procedure, rather than to repeat the procedure for each pregnancy attempt.

The 14-day rule

126. Although the 1984 Warnock Report recommended permitting research on human embryos, it also proposed restricting the period in which research could be conducted. The report recommended allowing research on an embryo *in vitro* only up until the end of the 14th day after fertilisation. The United Kingdom adopted this policy through the Human Embryology and Fertilisation Act 1990.³⁵
127. The idea behind the 14-day rule was to provide a consistent and measurable limit to embryo research. The rationale for this limit was that 14 days after fertilisation, embryos develop the 'primitive streak', which will later form the spinal cord and nervous system. A concern at the time was that, once neural development started, an embryo might be able to feel pain. The 14-day rule therefore was a pragmatic way of enabling embryo research while acknowledging some arguments in support of the early development of personhood.
128. In Aotearoa New Zealand, the HART Act codifies the 14-day rule, making it an offence to allow embryos to develop *in vitro* beyond the 14th day after they have formed. Some jurisdictions are reviewing their 14-day limit and considering whether it is still appropriate, given current knowledge about development and when an embryo can feel pain (after about 20 weeks of fetal development) (see Chapter 4). Any change to the 14-day rule in Aotearoa New Zealand is outside the scope of this consultation.

Securing the benefits of assisted reproductive technology

129. One of the purposes of the HART Act is to secure the benefits of assisted reproductive procedures, established procedures and human reproductive research.³⁶
130. Embryo research has the potential to improve ART techniques and our knowledge about infertility. These improvements could include, but are not limited to: improving the safety of procedures; creating new, more effective techniques; and/or leading to developments that make ART more accessible. Research may also help further our understanding of developmental biology and provide for new ways to avoid inheritable diseases.
131. Although Aotearoa New Zealand currently has research guidelines, they have limited application to only gametes and non-viable embryos. With these guidelines, therefore, it is highly unlikely that Aotearoa New Zealand can realise the wider benefits of human reproductive research. On this basis, it could be argued that it is necessary to expand the research guidelines to meet the purpose of the HART Act.

³⁵ legislation.gov.uk/ukpga/1990/37/contents (accessed 16 November 2022).

³⁶ HART Act, s 3.

132. Some other key considerations that support research relate to a moral obligation to contribute to the research base on which our health treatments are founded. The Government's Health Research Strategy³⁷ aims to underpin health provision with robust clinical research to achieve both effective treatment and good health outcomes. Without the mechanisms to effectively enable this research, however, Aotearoa New Zealand cannot meet this aim. Improving clinical treatments also means patients and taxpayers are getting better outcomes and value from investments in fertility treatments. Another argument in support of improving fertility treatments is that this could benefit prenatal life and the future people born as a result of ART.

Different religious beliefs

133. Some religions may hold the belief that an early embryo constitutes a person. However, as Neaves' analysis shows,³⁸ this is neither a universally held religious belief nor a universal ethical principle. Different religions may differ in their teachings about when human life begins. For example, they may consider it starts (a) at conception, (b) when an embryo implants into a uterus, (c) after a certain number of weeks of gestation, or (d) at birth. Neaves concluded that several religions appear to reject the idea that an embryo, before implantation in a uterus, is a 'person' and so are more supportive of research into human embryology. It is important to note that views within a given religious tradition will also differ.
134. The official position of Roman Catholicism is that life begins at conception. Under this position, an embryo is a human individual with a right to life, and any act that restricts its development is immoral no matter what benefit might result. From this viewpoint, research that limits the development of the embryo could not be allowed. Other Christian views on the use of embryos and gametes in research are likely to be diverse. Although the Vatican does not approve the use of embryos in research, other Christian churches may accept many of the applications of assisted reproductive technology. Some branches of Christian thought see full human status as something that an individual gains gradually, and so it might not be present in the early embryo. Consequently, it is difficult to categorise a single Christian view on the use of gametes and embryos in research.

³⁷ Ministry of Business, Innovation and Employment and Ministry of Health. 2017. *New Zealand Health Research Strategy 2017–2027*. Wellington: Ministry of Business, Innovation and Employment and Ministry of Health. URL: health.govt.nz/publication/new-zealand-health-research-strategy-2017-2027 (accessed 9 November 2021).

³⁸ Neaves W. 2017. The status of the human embryo in various religions. *Development* 144(14): 2541–3. URL: researchgate.net/publication/318496133_The_status_of_the_human_embryo_in_various_religions (accessed 9 November 2022).

135. The Jewish faith respects embryos because of their potential to become human beings, but does not give them moral status before 40 days of gestation. As with many religions, the Jewish tradition also places a strong emphasis on healing and saving lives. This view would permit some uses of early embryos for research purposes. An important feature of Jewish thinking in this area is that embryos outside the womb have no legal status unless they gain the potential for life through the parents' intention to create life through implantation and pregnancy. On this basis, an embryo created for IVF treatment and maintained *in vitro* without the potential for implantation could be donated and used for therapeutic research in line with the lifesaving duty of Judaism.
136. Within Islam, there is no central perspective on the moral status of the embryo. However, like Judaism, the religion takes a developmental view and does not give the embryo moral status in its early stages of development. This view would permit some uses of embryos for research purposes.
137. In Hinduism, many believe that personhood begins with conception, as this coincides with reincarnation. Buddhism, on the other hand, teaches that embryos gain personhood after implantation. Even though their views on when personhood occurs differ, however, both religions teach that research on surplus embryos may be undertaken where this may provide a benefit to humankind.³⁹

Using surplus embryos

138. Patients can sometimes face a difficult choice when deciding what to do with any surplus embryo(s) once they have completed their fertility treatment. The options currently are to keep the embryo(s) in storage (up until the end of the 10-year storage limit), to allow the clinic to dispose of the embryo(s) (or return them to the patient), or to donate the embryo(s) to another person or family to use with the aim of creating a pregnancy. Under the current research guidelines, viable embryos cannot legally be donated for use in research.
139. People who have embryos that are surplus to their reproductive needs often want their remaining embryos to be used in beneficial ways. In some cases, they may feel that using surplus embryos for research is a preferable option to donating to other families. This could be because they are not comfortable with the idea of other people using their embryos to have a child, or because they feel they would like to contribute to the field of health care from which they benefited.

³⁹ Ibid, p 2542.

140. Populations can differ in whether they prefer to donate embryos to research or to other families.⁴⁰ A review of literature found that, when thinking about donating for research, the matters people most often considered were trust in science and a feeling of ‘giving back’, rather than thinking about whether embryos have personhood.⁴¹ Permitting the donation of viable embryos to research may provide patients with greater choices when deciding what to do with their surplus embryos.

Cell line ownership

141. The new guidelines may allow researchers to use embryos as a source of embryonic stem cell lines. For more discussion on obtaining stem cell lines from embryos, see Chapter 11.
142. Participants in human reproductive research may have an interest in the ownership and fate of cell lines produced from their own tissue. While the researchers create or modify the cell lines, the original genetic material comes from the participants, or from the materials created from their tissue. The people whose tissue was originally used must consent to the research and to the fate of the cell lines created from their tissue.
143. This is a matter of particular interest to many Māori, in part due to the importance of whakapapa. A Māori cell line has a whakapapa to whānau, hapū, iwi and ancestors and there are many implications for the whakapapa, including for the mana and tapu of the whakapapa. In Te Ao Māori, the cell line is treated in the same way as an embryo. It does not differentiate between the 2 and the associated cultural practices.

Conclusion

144. This chapter has presented some of the ethical and social views on the status of the embryo.
145. Part II presents questions to gain your views on different categories of human reproductive research. This includes some broad questions about whether those types of research should be permitted or not, and what limitations or criteria the guidelines should set out.

⁴⁰ Lyerly AD, Faden RR. 2007. Willingness to donate frozen embryos for stem cell research. *Science* 317(5834): 46–7. Wånggren K, Alden J, Bergh T, et al. 2013. Attitudes towards embryo donation among infertile couples with frozen embryos. *Human Reproduction* 28(9): 2432–9.

⁴¹ Samorinha C, Pereira M, Machado H, et al. 2014. Factors associated with the donation and non-donation of embryos for research: a systematic review. *Human Reproduction Update* 20(5): 641–55. URL: <https://pubmed.ncbi.nlm.nih.gov/24907125/> (accessed 9 November 2022).

Chapter 7: Te Ao Māori and assisted reproduction

Summary

- Principle (g) in section 4 of the HART Act states ‘the needs, values, and beliefs of Māori should be considered and treated with respect’. It is important that ACART applies this principle to its work.
- This chapter offers a worldview from Te Ao Māori, recognising that the western view is not the only view of assisted reproduction.
- Human reproductive research is tapu (sacred) and uses a taonga that involves whakapapa.

146. This chapter introduces some of the key views from Te Ao Māori on assisted reproductive technology, and how these views should be recognised in human reproductive research.

Te Kore (Nothing)
Te Pō (Darkness)
Te Marama (Enlighten)
Papatūānuku and Ranginui.

147. From the womb were created Ranginui and Papatūānuku. From them were created Tāne Māhuta who created the first woman, Hine-Ahuone, with the assistance of his mother and some of his brothers (noting iwi variations such as Ngāi Tahu, who state that Takaroa and Papatūānuku were Tāne’s parents). It was Tāne’s mother, Papatūānuku, who told Tāne where her reproduction organs were in response to Tāne’s feelings that he needed something that he could not explain.
148. Tāne and Hine-Ahuone produce a daughter, Hinetītama. Māui was also involved in the tapu nature of childbirth as it was he who was crushed in the vagina of Hine-nui-i-te-Pō.
149. Hine-te-Iwaiwa, also referred to as Hine-Uri and Hine Keha, is the atua of childbirth. She was and is often recited in karakia associated with conception and birth. Hine-te-Iwaiwa appears to be the atua most commonly seen as the kaitiaki (guardian) for birth.

150. Tiki is an atua that is recognised in Māori and all across Polynesia as the atua of fertility. Many whakataukī state that if you are to have intercourse and to conceive a child, it is not to be with anyone genealogically more closely connected than a second cousin. The tikanga (traditional Māori knowledge) is always clear that this caution and whakapapa must be known and respected and that reproduction must not be with anyone closer than a second cousin.
151. The research on Māori attitudes to assisted reproduction is limited. From the research that is available, Dr Marewa Glover (Ngā Puhi)⁴² identified the following perspectives associated with fertility services.
- There is no single pan-Māori view, but diverse views among people.
 - He puta tātou: ensure the survival of Māori as a tangata (people).
 - He mokopuna, he taonga: children are central to whānau, to relationships, and whānau, hapū and iwi are responsible for making sure the offspring are looked after and provided for.
 - Consider human assisted reproductive technology treatments as a Tiriti right, to restore people's fertility when it has been damaged by impacts of colonisation.
 - Whānau rights and responsibilities are integral, and they should be recognised through consultation, without giving precedence to individual rights.
152. In Te Ao Māori, the belief is that an embryo constitutes a person bound by intergenerational spiritual and physical genealogy, first from Hine-Ahuone to the donor of the embryo and her hapū, iwi and ancestors.⁴³
153. The embryo is tapu (sacred) and should be treated as a human being, with respect, and stored and disposed of in a culturally appropriate manner.⁴⁴
154. Other relevant tikanga Māori with an embryo include: hau (vital essence), kaitiaki (guardianship), mākutu (spells), mauri (life force), rangatiratanga (authority), wairua (spirituality) and whakapapa.⁴⁵

⁴² Glover M. 2008. *Māori Attitudes to Assisted Human Reproduction: An exploratory study*. Auckland: Department of Social & Community Health, University of Auckland. URL: maramatanga.co.nz/sites/default/files/Research%20Report%20-%20Maori%20Attitudes%20to%20Assisted%20Reproduction%20FINAL.pdf (accessed 10 November 2022). See especially pp 13–16, 54 and 119. Glover M, Rousseau B. 2007. 'Your child is your whakapapa': Māori considerations of assisted human reproduction and relatedness. *Sites: A Journal of Social Anthropology and Cultural Studies* 4(2): 117–36. DOI: 10.11157/sites-vol4iss2id76 (accessed 10 November 2022).

⁴³ Māori Genetic Data Ira Tangata Framework (Taiuru 2020), cited in: Taiuru K. 2022. *Tikanga Tawhito: Tikanga Hou: Kaitiaki guidelines for DNA research, storage and seed banks with taonga materials*. URL: taiuru.maori.nz/guidelines-for-dna-research-storage-and-seed-banks-with-taonga-materials/#Maori_Genetic_Data_Customary_Ownership_of_the_Ira_Tangata_Framework (accessed 10 November 2022).

⁴⁴ Ibid.

⁴⁵ Ibid.

Whakapapa

155. The term whakapapa has always been considered the explanatory framework for the world and everything in it. Whakapapa chronicled evolutions from the beginning of time and explained Māori social and political connections to each other and the natural and spiritual world. Whakapapa as an approach, whether it is relevant to genetics, history, education or elsewhere, is inextricably connected to underlying protocols and tribal ethics.⁴⁶
156. Whakapapa has its own tribal-specific and collective politics that seek out connections and inclusivity. These different politics are necessarily exclusive when it comes to exercising and asserting ownership and authority.⁴⁷
157. Māori individuals and their beliefs generally fall into 6 broad groupings.⁴⁸
- Group a. Some Māori are connected with a number of Māori networks. They are involved with their whānau communities and activities, marae, hapū, iwi and Māori organisations. They can speak and/or understand te reo Māori and are immersed in tikanga.
 - Group b. Māori entities and staff such as Government Treaty partners, marae and Māori organisations who have a responsibility to represent their stakeholders.
 - Group c. You identify as Māori, but may have limited knowledge of Māori culture and language. You have limited connections with the Māori community and are integrated into mainstream society.
 - Group d. You previously identified as group c, but have recently identified with your Māori heritage and are on a cultural learning journey.
 - Group e. As a person of Māori descent, you identify as non-Māori and are fully integrated into mainstream society.
 - Group f. As a person of Māori descent, you choose a non-Māori religious or fraternity belief above Māori cultural values.
158. In addition to the points above, each Māori individual has genealogical links to at least one — but likely several — iwi, hapū and marae. Each of these groups has its own epistemologies, ancestors, dialects, protocols and mixed ancestry with other cultures and lived experiences. Therefore, it is important that many Māori viewpoints are represented in public consultation.

⁴⁶ Taiuru K. 2020. *Māori Genetic Data: Inalienable Rights and Tikanga Sovereignty*. PhD thesis, Te Whare Wānanga o Awanuiārangī.

⁴⁷ Mahuika N. 2019. *Rethinking Oral History and Tradition: An indigenous perspective*. Oxford: Oxford University Press.

⁴⁸ Taiuru K. 2021. *Māori Opinions and Views Framework*. Unpublished.

159. Kaupapa Māori research methodologies should be practised when using biological materials that have a whakapapa Māori. Kaupapa Māori research methodologies are grounded in Māori tradition and philosophies, legitimise Māori knowledge, are controlled by Māori and are accountable to Māori expectations and quality standards.⁴⁹

Consent in Te Ao Māori

160. In relation to whanaungatanga (relationships of the individual and communities),⁵⁰ requiring free, prior and informed consent from the participant's whānau, hapū or iwi follows a principle protected by international human rights standards for Indigenous Peoples.⁵¹ The standards state, 'all peoples have the right to self-determination' and — linked to the right to self-determination — 'all peoples have the right to freely pursue their economic, social and cultural development'.
161. This consent process may be especially relevant in embryo research, where the embryo might be seen as a direct link to the creation of the natural world and containing the mauri, wairua and whakapapa of the entire and intergenerational whānau, hapū or iwi. Individual privacy and autonomy might be in tension with collective decision-making and consent if the individual has different views from their whānau, hapū or iwi. This potential for tension should be acknowledged when seeking the views of Māori about the moral status of the human embryo and human embryo research.
162. Under the Code of Health and Disability Services Consumers' Rights, patients have the right to consent to their own treatment. They also have the right to consent to what will happen to gametes and embryos over which they have authority, as long as it is not inconsistent with the HART Act.
163. In assessing proposals for embryo research, it is necessary to consider:
- whether there is a collective consent for research using material with Māori whakapapa
 - governance of research programmes that use Māori data
 - ownership of stem cell lines

⁴⁹ National Ethics Advisory Committee. 2019. *Ethical Standards for Health and Disability Research and Quality Improvement*. Wellington: Ministry of Health. URL: neac.health.govt.nz/national-ethical-standards (accessed 10 November 2022), p 43. Smith LT. 2015. Kaupapa Māori research: some kaupapa Māori principles. In L Pihama, K South (eds), *Kaupapa Rangahau A Reader: A collection of readings from the Kaupapa Māori Research Workshop Series* (pp 46–52). Hamilton: Te Kotahi Research Institute. URL: researchcommons.waikato.ac.nz/bitstream/handle/10289/12026/Kaupapa%20M%C4%81ori%20Research.pdf?sequence=21 (accessed 10 November 2022).

⁵⁰ Law Commission. 2021. *Review of Surrogacy* (Issues Paper 47). Wellington: New Zealand Law Commission, p 55.

⁵¹ *The United Nations Declaration on the Rights of Indigenous Peoples* (UNDRIP).

- d. future profit-sharing if the research is to involve commercial ventures or outcomes, such as for commercial stem cell lines
 - e. how the research outcomes will be communicated with Māori, whānau, hapū, marae and iwi.
164. In cases where patients are donating embryos for training, quality improvement or protocol validation, before they consent they could be asked if they would like to consult their whānau to ensure they have considered any interests or concerns their whānau may raise.

Māori data sovereignty

165. Māori genetic data is connected to Māori and world Indigenous knowledge. The data contains an abundance of knowledge and information that can connect whānau, hapū and iwi to one another and enable people to acknowledge identity of place, personality and history. As such, Māori genetic data should be acknowledged as a taonga.⁵²
166. Te Tiriti recognises that Māori have rights to their taonga. Therefore, ACART acknowledges the Māori data sovereignty principles of 'Rangatiratanga (Authority), Whakapapa (Identity), Whanaungatanga (Obligations), Kotahitanga (Collective benefit), Manaakitanga (Reciprocity) and Kaitiakitanga (Guardianship)'.⁵³
167. Creating opportunities for benefit-sharing with Māori includes acknowledging that Māori have an inherent right to benefit from the use of their taonga. This right has been expressed in He Wakaputanga, Te Tiriti, the Mataatua Declaration and the United Nations Declaration on the Rights of Indigenous Peoples. It also underpins recent discussions on Māori data sovereignty.
168. Article II of Te Tiriti guarantees Māori have rights to data associated with their health and research that uses their biological material (body tissue), as well as an interest in the outcomes of research and applications of their data. Some Māori also believe that their clinical data is personal information. Its use in the public domain, as part of supporting research, is to improve health outcomes for their community. While many recognise that the pathway to delivering such benefits often involves commercial entities, they have concerns about their personal information becoming corporatised through research activities. Many Māori expect that those who contribute to research should receive direct benefits over and above those delivered to the public.

⁵² Taiuru K. 2022. *Tikanga Tawhito: Tikanga Hou: Kaitiaki guidelines for DNA research, storage and seed banks with taonga materials*. URL: taiuru.maori.nz/guidelines-for-dna-research-storage-and-seed-banks-with-taonga-materials/#Maori_Genetic_Data_Customary_Ownership_of_the_Ira_Tangata_Framework (accessed 10 November 2022).

⁵³ Taiuru K. 2022. *Compendium of Māori Data Sovereignty*. URL: taiuru.maori.nz/compendium-of-maori-data-sovereignty/#MAORI_DATA_SOVERIGNTY_PRINCIPLES (accessed 10 November 2022).



PART II: QUESTIONS ON TYPES OF HUMAN REPRODUCTIVE RESEARCH

Chapter 8: Introduction to Part II

Summary

- This chapter introduces the format for Part II.
- Each of the following chapters presents questions that ACART would like feedback on. These questions are also included at the end of the document.
- The chapters are categorised into 3 broad research areas. Each chapter provides an overview of the type of research it is focusing on, the benefits it may provide and key considerations.
- Your answers to these questions will help ACART to draft updated research guidelines. However, if you would prefer to comment generally on human reproductive research, rather than follow ACART's specific question format, a final, free-text question is included at the end of the feedback form.
- This chapter also presents an important question on whether research on viable embryos should be allowed in Aotearoa New Zealand. Currently, research can only be performed on gametes and non-viable embryos. If research on viable embryos continues to not be allowed, many of the examples in the following chapters could not be performed.

169. This part of the consultation document seeks your views on human reproductive research. To help explain the areas that we would like feedback on, ACART has categorised the types of human reproductive research into 3 broad areas:

1. standard clinical research
2. innovative clinical research
3. non-clinical research.

170. Each of the following 3 chapters provides an overview of one of these types of research, the benefits that it may provide and key considerations. Each discussion ends with the questions that ACART would like feedback on about this research.

171. To illustrate the types of research that are possible, each chapter includes several research scenarios. Because the current guidelines limit research to gametes and non-viable embryos, most of these scenarios are hypothetical in Aotearoa New Zealand. They could only be conducted in practice if research on viable embryos was permitted.

172. If you would rather comment generally on human reproductive research instead of responding to the specific questions that ACART presents, or wish to provide additional information, you can respond in the free-text question at the end of the feedback form.
- 173. Note that the following chapters are not proposals. Instead, they are designed to provide context and information so that ACART can understand the public's views on a wide range of types of human reproductive research.**

Research on viable embryos — a potential policy change from the 2005 guidelines

174. As discussed in Chapter 3, because the current research guidelines restrict human reproductive research to only gametes and non-viable embryos, they limit the potential for effective research. They also have practical limitations in that it is difficult to know for sure whether an embryo is non-viable and, even if that can be established, non-viable embryos are generally unlikely to produce useful research data.
175. In addition, the restriction severely limits research on clinical practices associated with fertility treatments, because such research would necessarily involve viable embryos (even though the research is not being conducted directly on these embryos). As a result, Aotearoa New Zealand may not be fully realising the benefits of assisted reproductive technology.
176. As part of this review, ACART is considering changing the human reproductive research guidelines to enable ECART to consider cases of research that involve the use of **viable** human embryos. The research could be part of clinical treatment or non-clinical research.
177. Although updating the guidelines to permit research on viable embryos would likely provide significant benefits in Aotearoa New Zealand (such as improving outcomes for fertility services patients), it is important to also recognise that this change would introduce new ethical considerations for proposed research. For this reason, ACART is interested in hearing your views on whether research on viable embryos should be permitted in Aotearoa New Zealand.

Common considerations

178. As discussed in Chapter 5, ECART must approve any application to conduct human reproductive research that uses gametes or embryos, based on ACART's guidelines. This scrutiny is required because the ethics of using human gametes and embryos in research are complicated.

179. All 3 types of human reproductive research we discuss in the following chapters have some ethical and other considerations in common, which we have outlined below for convenience. Where we believe one type of research has its own specific considerations (for example, cloning in non-clinical research), we have provided additional information in the relevant chapter.
180. Whether approval for human reproductive research needs to come from a Health and Disability Ethics Committee or a university ethics committee, in addition to ECART, will be a question ACART will consider in the second round of consultation on this topic.

Responsibility to gain informed consent

181. Informed consent is an important cornerstone of health care in Aotearoa New Zealand, codified as a patient's right in the Code of Health and Disability Services Consumers' Rights.⁵⁴ This right extends to patients who participate in human reproductive research, either through clinical treatment or by donating their gametes or embryos to research.
182. In order for their consent to research to be 'informed', a patient must receive sufficient information to understand the purpose of the research, what will happen to any donated material, any implications of their clinical treatment (if relevant) including risks, and how they may be informed of results of the research.
183. Ongoing research that uses donated gametes or embryos, or clinical research that involves their participation, must continue to be consistent with a person's understanding of the research that they consented to. For example, researchers would not be able to significantly change their research without getting new consent from participants/donors.
184. Where research could harm the patient or the likely success of their fertility treatment (for example, where it is trialling innovative new methods), it is important that researchers give the patient sufficient information to understand these risks balanced against the potential benefits.

Responsibility not to harm future persons

185. Some clinical human reproductive research could affect any children born from that research. It is therefore important that, where research is in a clinical setting, researchers identify and carefully mitigate any risks to the wellbeing of children born following the research. Principle (b) in section 4 of the HART Act reflects this consideration, in stating that 'the human health, safety, and dignity of present and future generations should be preserved and promoted'.

⁵⁴ Right 6.

186. However, not all human reproductive research will result in the birth of a child, just as not all embryos people create using IVF result in a child. Some embryos may not develop and some surplus embryos may be disposed of when people have formed their family. A distinction could be made between clinical research (which may result in the birth of a child) and non-clinical research (which will not). In non-clinical research, any embryos will be destroyed at the conclusion of the research, meaning that there is no risk of harm to future born persons.⁵⁵
187. As discussed in Chapter 6, people have a wide range of views on the moral status of the human embryo in Aotearoa New Zealand. Some people may consider that embryos that have a chance of developing into a born person if transferred into a woman's uterus have a greater moral status than those embryos that do not. Other people may consider all embryos have the same moral status.

Responsibility to provide effective treatment and avoid risks to health

188. Clinical research usually involves real patients who are seeking fertility assistance. While research may change some aspect of the treatment to investigate its effect, the first priority is to ensure that patients are still receiving safe and effective treatment.
189. People taking part in research should not be subjected to procedures that put them at risk of harm and should not be placed under pressure to participate, by either coercion or undue inducement. Where research involves an increased risk of harm, researchers need to mitigate this risk where possible, clearly disclose this greater risk as part of the consent process and justify it against the possible benefits from the research.

Responsibility to support medical research

190. Aotearoa New Zealand benefits from advances in fertility treatments that result from research conducted overseas. However, under the current guidelines, it is difficult for researchers in this country to contribute in-kind to the pool of knowledge that is generated internationally. This may be seen as unfair, as Aotearoa New Zealand is taking advantage of international research while contributing nothing to knowledge generation.
191. International research on viable embryos has provided the main foundation for developing fertility treatments. For this reason, it could also be argued that Aotearoa New Zealand cannot use fertility treatments without also being implicated in the research that led to their development.

⁵⁵ See: Savulescu J, Labude M, Barcellona C, et al. 2022. Two kinds of embryo research: four case examples. *Journal of Medical Ethics* 48: 590–6. DOI:10.1136/medethics-2021-108038 (accessed 11 November 2022).

192. Some may believe that Aotearoa New Zealand has a moral and ethical obligation to support the social and individual benefits that can be realised from research. Such research may be ethical because it provides opportunities to improve the health of individuals and populations. If using embryos in research could help to create a cure for certain diseases or conditions, it could be argued that preventing such research is unethical in that failing to achieve this social and individual benefit causes harm and deprives people of an important opportunity to improve their wellbeing.

Responsibility to not waste gametes and embryos

193. Gametes and embryos are scarce resources, which require significant time and effort to collect and create. With this in mind, some people may believe that researchers should design and conduct their studies in a way that does not waste these resources. People may also hold this view based on their belief that embryos have a special status.
194. Currently, people with viable embryos that are surplus to their own needs can only donate these to other people, store them for up to 10 years⁵⁶ or have them destroyed. One argument could be that research on viable embryos presents an additional way of making good use of these resources.

⁵⁶ People can apply to ECART to extend this storage for up to a further 10 years.

Questions

Question 1: Research on viable embryos

- a. Do you think that research on viable human embryos should be permitted?

Yes ☐ Yes, but only in certain circumstances ☐ No ☐

Please explain your answer.

- b. What are the possible risks and/or harms that need to be considered with research on viable human embryos? How can these risks and/or harms be addressed?

Comment

- c. Are there ethical issues specific to research on viable human embryos that you would like to comment on?

Comment

Chapter 9: Research category 1: standard clinical research

Summary

- Standard clinical research uses gametes and embryos in clinical treatment to create a child, but with some changes to the treatment protocol.
- The usual aim of this research is to improve the chances of success of the treatment, or to compare another treatment method with the current one to establish which is better.
- Because this type of research involves real patients who are undergoing real fertility treatments, it will involve viable embryos and so is not allowed in Aotearoa New Zealand under the current guidelines.
- ACART is interested in your views about such research.

195. Standard clinical research involves using gametes and embryos in clinical treatment with the intention of enabling patient(s) to have a child, but making some changes to the treatment protocol. The usual aim is to improve the chances of success of the treatment, or to compare another treatment method with the current one to establish which is better.
196. Examples of such research include analysing or testing different brands of embryo culture media⁵⁷ and transferring embryos to the uterus on different days of development.
197. Because researchers usually do standard clinical research involving embryos alongside a procedure that is aiming to create a child, it will by necessity involve viable embryos. Under the current guidelines, which only allow research involving non-viable embryos, many types of standard clinical research cannot be performed in Aotearoa New Zealand.
198. The following 2 scenarios present examples of clinical research activities that would manipulate the gametes or embryos in a way that is not very different from normal treatment. They involve a minor change to the treatment that falls within standard procedures, using products approved for clinical use.

⁵⁷ An 'embryo culture medium' is a liquid solution that embryos are placed in after they have been created, which supports their growth until they are implanted into the uterus. Embryo culture media attempt to mimic the natural environment of the reproductive tract to promote healthy embryo growth. Advances in this area could, for example, result in higher IVF success rates.

199. Scenario 1 demonstrates why the current research guidelines may be overly restrictive.

Scenario 1: Comparing culture media for growing embryos

A media manufacturing company advertised a new embryo culture medium that it claimed helped the embryo to survive and grow before being transferred to the uterus. A clinic in Aotearoa New Zealand wanted to check the company's claims in its own laboratory environment.

However, because the current guidelines prevent 'research using viable embryos', the clinic decided to do a retrospective observational study rather than seek ethical research approval (as it knew the study wouldn't be approved under the current guidelines).

The clinic stopped using the regular medium on a certain date and changed to the new brand. After a time, it looked back through the records to see whether the rates of growth and survival of the embryos had improved.

This type of research is not allowed under the current guidelines.

200. In Scenario 1, the data might not be reliable, because the method was not robust — it did not use a randomised controlled trial. This is because the current research guidelines do not allow research using viable embryos.
201. A randomised controlled trial would be a better research method because it would take into account variables (factors) such as the influence of different embryologists (scientists who work in the laboratories of fertility clinics) doing the work, or the seasonal changes affecting the laboratory temperature. By gaining ECART approval, the researchers would also be allowed to publish the results from the randomised trial. Publication would contribute to knowledge about the media the study was investigating.
202. Scenario 2 is an example of the kind of clinical research that focuses on the fluid (medium or media) in which embryos were grown without manipulating the embryo in any way that is different from normal treatment. As with Scenario 1, this research might not be permitted under the current guidelines as it potentially involves viable embryos (even though the embryos are not directly part of the research).

Scenario 2: Research on ‘spent’ culture media

A researcher wants to collect the media that human embryos have been grown in, after the embryos have been removed for transfer or freezing, to identify markers of embryo quality.

The intending parents would consent to the collection of the media and to telling researchers about their clinical pregnancy and birth outcomes.

The researcher might want to measure the amount of particular proteins or concentrations of gases or other molecules, or cells or DNA released by the embryo, that are now in the media. They could then find out if any of these measures are related to pregnancy success rates.

The goal would be to analyse the media to determine which embryo is likely to be the healthiest and so most likely to result in a successful pregnancy.

This information about the culture media could allow researchers to identify biomarkers of healthy embryos. They could also identify factors that may be altered during culture to improve embryo quality.

It is legally unclear if this type of research is allowed under the current guidelines.

Benefits and risks of standard clinical research

203. Standard clinical research can lead to improvements in treatment for patients in terms of the procedures they go through, or the outcomes of treatment. These improvements could increase the chance of pregnancy for patients, reduce the cost of treatment or make treatment easier in some way.
204. As standard clinical research usually focuses on slight modifications to existing practices, the risks associated with it are likely to be low. Some studies could bring risks of unintended outcomes that reduce the chance of a successful pregnancy or cause other unexpected issues. However, making changes to treatment as part of a robustly designed research project should make it easier to detect any unintended or negative outcomes and stop or modify the project.

Questions

Question 2: Standard clinical research

- a. Should standard clinical research be permitted?

Yes ☐ Yes, but only in certain circumstances ☐ No ☐

Please explain your answer.

- b. What are the possible risks and/or harms that need to be considered with standard clinical research? How can these risks and/or harms be addressed?

Comment

- c. Are there ethical or other matters specific to standard clinical research that you would like to comment on?

Comment

Chapter 10: Research category 2: innovative clinical research

Summary

- Innovative research is research that is not yet standard and is done to introduce new techniques to clinical practice. It could only be allowed with strong evidence of safety.
- Because this type of research involves real patients who are undergoing real fertility treatments, it will involve viable embryos and so is not allowed under the current guidelines.
- ACART is interested in your views about such research.

205. Innovative, or novel, research is research that is not yet standard and is done with the goal of introducing new techniques to clinical practice. If such research were to be allowed, any guidelines would need to ensure that ECART would only be able to approve a proposal that included strong evidence of safety.
206. While standard clinical research focuses on variations to current techniques, innovative clinical research focuses on new practices. Examples include adding a new growth factor to media, or using a completely different kind of culture system (eg, growing embryos in the presence of cells from a uterus).
207. It is important to highlight that any innovative clinical research would first need to have been demonstrated as safe and effective in animals and human cell lines (ie, non-clinical trials).
208. Although standard and innovative clinical research have similarities, it is helpful to distinguish between them for the purposes of this consultation. Innovative clinical research will still need to demonstrate that it is safe before it is granted ethical approval. However, because it is investigating new techniques, it may not be as effective as standard practices.
209. Because clinical research involves real patients who are trying to conceive, innovative research may involve a slightly higher risk of failure. It is therefore very important that researchers minimise the risks, and that patients understand the risks and provide fully informed consent to the research. Any revised guidelines may need to set slightly different criteria for innovative research from standard clinical research.

210. Scenario 3 provides an example of innovative clinical research where a clinic wants to try a new treatment with the aim of improving outcomes for its patients.

Scenario 3: Human chorionic gonadotrophin hormone infusion into the uterus

Researchers and staff at a fertility clinic often have some evidence, from small studies done overseas, about new techniques that might improve the chance of an embryo implanting into a woman's uterus. One such current technique is to inject a small amount of human chorionic gonadotrophin hormone (hcg) into the uterus a few minutes before transferring an embryo into the uterus.

Patients often hear about these new treatment options and are keen to try them. Clinic staff would prefer to do this in a controlled manner so that they can collect good data and then decide whether these treatments are of benefit or not.

In this scenario, a research study is planned to inject a small amount of hcg into the uterus before transferring the embryo and compare the outcome of this with a placebo treatment. Pregnancy outcomes are recorded.

The results could then be used to see whether this 'add-on' to IVF treatment increases pregnancy rates and doesn't cause harm.

This type of research is not allowed under the current guidelines.

Benefits and risks

211. Innovative research is particularly important for developing new and better procedures for ART. New procedures could increase the chance of pregnancy for patients, reduce the cost of treatment or make treatment easier in some way.
212. It could allow researchers based in Aotearoa New Zealand to contribute to international research on gametes and embryos. As a result, people could benefit from changes to treatment methods and protocols that increase the chances of pregnancy, reduce costs or enable other improvements in treatment outcomes.
213. Because innovative clinical research focuses on new or less established procedures than standard clinical research, they may bring a higher chance that fertility treatments are unsuccessful or that some other unexpected consequence occurs. To reduce this risk, any innovative clinical research would need to first prove that it was safe before ECART granted approval. It is also important that participants receive sufficient information to understand this risk, so that they can provide fully informed consent to the proposed research.

Additional considerations

214. Although, compared with standard clinical research, innovative clinical research focuses more on new techniques, it still occurs in a clinical setting and involves one or more patients who are undergoing fertility treatment. The first priority is to ensure that the proposed research does not compromise the patient's treatment and the wellbeing of the resulting child. It is important to provide the patient(s) with sufficient information for them to give informed consent to the innovative clinical research. The research proposal must also provide adequate evidence of safety, particularly for any offspring.

Questions

Question 3: Innovative clinical research

- a. Should innovative clinical research be permitted?

Yes ☐ Yes, but only in certain circumstances ☐ No ☐

Please explain your answer.

- b. What are the possible risks and/or harms that need to be considered with innovative clinical research? How can these risks and/or harms be addressed?

Comment

- c. Are there ethical or other matters specific to innovative clinical research that you would like to comment on?

Comment

Chapter 11: Research category 3: non-clinical research

215. Non-clinical research, by definition, does not involve transferring an embryo or gametes to the uterus, and there are no offspring. It may perform some manipulations of gametes and/or embryos that would not be permitted in people's treatment.
216. The HART Act prohibits the development of human embryos *in vitro* beyond 14 days and, as noted in paragraph PART IChapter 6128, any change to the 14-day rule in Aotearoa New Zealand is outside the scope of this consultation. Consequently, if ACART does publish guidelines that permit research with viable embryos and/or that creates viable embryos, those embryos would not be allowed to develop beyond 14 days.

Benefits

217. Non-clinical research could lead to new methods for clinical treatment that improve the success of ART and the health of resulting offspring.
218. Non-clinical research with embryos and gametes would be useful for a wide range of developmental studies. Researchers could preserve embryos at different stages of growth and examine them to discover any changes to the structure of cells, or where genes or proteins are expressed that control cell development.
219. Understanding early embryonic development is important to understanding things like:
- a. what factors control fertilisation, cell division and the early growth (pre-implantation) of embryos
 - b. how cells of the early embryo change to become the inner cell mass or cells that will form part of the placenta
 - c. why so few embryos implant, even when they are transferred at the right time of the menstrual cycle and have developed to the appropriate stage for making the transfer
 - d. why so many embryos do not continue to grow after a chemical pregnancy is detected (resulting in early embryo loss or miscarriage⁵⁸)
 - e. how to identify the healthiest embryo to transfer to a uterus.

⁵⁸ Miscarriage is the spontaneous loss of a pregnancy before the 20th week. About 10–20% of known pregnancies end in miscarriage.

220. Research could also improve and optimise other assisted reproduction activities such as cryopreservation of sperm, eggs and embryos, or intracytoplasmic sperm injection.
221. This chapter presents 4 types of non-clinical research that ACART would like to hear your views on:
- non-clinical research with donated gametes and embryos
 - non-clinical research that **creates** embryos
 - non-clinical research with cloned embryos, stem cells, blastoids and human-hybrid embryos
 - non-clinical research that genetically edits gametes and embryos.
222. As with the previous chapters, each section introduces the type of research, describes the benefits, risks and any additional considerations, and ends with specific questions for consultation.

A. Non-clinical research with donated gametes and embryos

Summary

- Non-clinical research uses gametes and embryos to contribute to knowledge that may lead to health benefits and improved treatment options.
- The research does not create a born child or a pregnancy: embryos are grown in a laboratory for a maximum of 14 days.
- This type of research is allowed under the current guidelines, but only with gametes and non-viable embryos.
- ACART is interested in your views about such research.

223. This section discusses non-clinical research using donated, surplus gametes and embryos from people's fertility treatment. Permitting this category of research would offer an alternative way of dealing with surplus gametes and embryos, in addition to the current options of donating them to other families or having them destroyed.
224. Scenario 4 is an example of non-clinical research using gametes donated to research. It shows how non-clinical research on gametes can contribute to knowledge that may lead to health benefits and improved treatment options.
225. Having a better understanding of *in vitro* maturation (IVM) of human eggs would be of great benefit to ART. With IVM, it is possible to collect immature eggs from a woman's ovaries without exposing her to hormones to stimulate egg maturation and ovulation. The eggs are matured in culture before they can be fertilised. Developing this technology could help secure the fertility of cancer patients and provide alternative treatments for women with certain fertility issues.

Scenario 4: Research to improve *in vitro* maturation of eggs

Using sheep eggs and sperm, researchers discovered a substance that, when added to IVM culture media, improved the success of egg maturation and increased the number of eggs used in IVF that developed into embryos. Transferring these embryos to the uteri of adult ewes resulted in the birth of healthy lambs.

The researchers wanted to test this new medium on human eggs to find out if it could improve the success rate of human egg IVM. To conduct this research, they would need to collect immature eggs from women who consented to the research. The eggs could come from women having their ovaries removed to prevent ovarian cancer (eg, in patients with a positive breast cancer gene mutation) or from donors whose eggs had not matured following a standard ovarian stimulation and egg collection procedure.

The researchers would culture these immature eggs in the new medium and then examine them to find out if they had matured or not. The eggs would not be fertilised and no embryos would be created.

This type of research is allowed under the current guidelines.

226. While IVM methods are well established for animal species such as mice, sheep and cattle, they are currently less successful in humans. Non-clinical research with donated gametes on IVM is essential to improve its effectiveness.
227. Non-clinical research with donated embryos is also necessary to gain new knowledge to improve fertility treatment methods. Scenario 5 uses donated embryos to study culture media.

Scenario 5: Research to improve embryo development by improving culture media

Similar to Scenario 4, researchers may have discovered a protein or nutrient that, when added to embryo culture media, improves pre-implantation embryo development in animals. They would like to find out if this additive also improves survival and growth of human embryos. Improving embryo culture media could ultimately increase success rates for pregnancies and increase the health of the offspring.

The 14-day rule would apply. That is, the researchers could not culture the embryos for longer than 14 days after fertilisation.

The research would not involve transferring embryos to a woman's uterus and no offspring would be born.

This type of research is not allowed under the current guidelines.

Additional considerations

- 228. Because the research will not lead to a person being born, it could be argued that fewer, or less serious, risks are involved. Such research would also make good use of an existing resource (embryos and gametes that would otherwise be destroyed).
- 229. People who think that all human gametes and/or embryos have personhood or potential personhood might oppose this non-clinical research because (a) the gametes/embryos will not have the opportunity to become a born person and (b) such research could involve risk or harm to the gametes/embryos.
- 230. People opposed to such research might also think that the risk or harm will increase the more the research manipulates the gametes or embryos.

Questions

*Question 4: Non-clinical research using donated **gametes***

- a. Should non-clinical research using donated **gametes** be permitted?

Yes ☐ Yes, but only in certain circumstances ☐ No ☐

Please explain your answer.

- b. What are the possible risks and/or harms that need to be considered with non-clinical research with gametes? How can these risks and/or harms be addressed?

Comment

- c. Are there ethical or other matters specific to non-clinical research with gametes that you would like to comment on?

Comment

*Question 5: Non-clinical research using donated viable human **embryos***

- a. Should non-clinical research using donated viable human **embryos** be permitted?

Yes ☐ Yes, but only in certain circumstances ☐ No ☐

Please explain your answer.

- b. What are the possible risks and/or harms that need to be considered with non-clinical research with viable human embryos? How can these risks and/or harms be addressed?

Comment

- c. Are there ethical or other matters specific to non-clinical research with viable human embryos that you would like to comment on?

Comment

B. Non-clinical research that *creates* embryos

Summary

- If guidelines allowed, researchers could create human embryos specifically for use in non-clinical research. This would be an alternative to using embryos that have been created for fertility treatment and then donated to research because the donors no longer need them.
- Creating embryos specifically for research could be helpful if donated surplus embryos were not available or for studying specific genetic disorders.
- If guidelines allowed, some non-clinical research on gametes could also lead to the creation of embryos.
- The research would not create a born child or a pregnancy. Instead, researchers would grow embryos in a laboratory for a maximum of 14 days.
- The current guidelines do not allow research that creates human embryos specifically for research.
- ACART is interested in your views about such research.

231. Research could potentially gain embryos from sources other than donated embryos in either of the following 2 situations. First, research using human eggs or sperm could result in the creation of an embryo as a 'by-product' of the gamete research. The embryos must be produced as part of the research process but the embryos themselves are not the subject of the research. Alternatively, people might donate gametes for the purpose of deliberately creating embryos for research. In this scenario, it is the embryos themselves that are the subject of the research.
232. ACART is interested in your views about creating embryos during and/or for non-clinical research. The HART Act does not prohibit the creation of embryos specifically for use in research. While some international jurisdictions permit it, others prohibit researchers from conducting IVF for the sole purpose of creating a supply of embryos for research.

Benefits

233. The obvious benefit of creating embryos for research is that, because donated embryos are a limited resource, creating embryos deliberately for research may be a way to provide a reliable supply of embryos for non-clinical research. Creating embryos with the same genetic make-up may also be beneficial for research into specific genetic disorders (for example, carriers of cystic fibrosis gene mutations could create embryos that carry the same mutations).
234. Research using human eggs or sperm could result in the creation of an embryo as a 'by-product' of gamete research. Scenario 6 is an example of a study on gametes that may create embryos as part of the research.

Scenario 6: Gamete research that creates embryos

Researchers might wish to do non-clinical research to improve gamete maturation methods (as in Scenario 4). This research may need an embryo to be created from the gametes to find out if the new method did in fact improve gamete quality and the embryo development that followed.

The researchers could not culture the resulting embryos for more than 14 days or transfer them to the uterus for reproductive purposes.

The embryos are not 'surplus' to reproductive requirements because they are created as a result of the research on the donated gametes.

This type of research is not allowed under the current guidelines.

Additional considerations

235. To some people, creating embryos specifically for research may be ethically different from non-clinical research that uses surplus embryos, as it deliberately creates embryos solely for research rather than for reproductive purposes. People who think that all human gametes and/or embryos have personhood, or potential personhood, might be concerned by this type of research as these embryos will never have the potential to become born people.
236. Creating embryos as a result of research on gametes may involve additional ethical considerations for similar reasons. Although the research would create the embryos for a different reason from the first situation, the effect is the same in that an embryo will be created and will be used in (or be available for) research, but will never have the chance to develop into a born person.

Questions

Question 6: *Non-clinical research on gametes that creates embryos*

- a. Should non-clinical research **on gametes** that **creates embryos** be permitted?

Yes ☐ Yes, but only in certain circumstances ☐ No ☐

Please explain your answer.

- b. What are the possible risks and/or harms that need to be considered with non-clinical research on gametes that creates embryos? How can these risks and/or harms be addressed?

Comment

- c. Are there ethical or other matters specific to non-clinical research on gametes that creates embryos that you would like to comment on?

Comment

Question 7: Non-clinical research with *embryos that were created specifically for research*

- a. Should non-clinical research be permitted with **embryos that were created specifically for** such research?

Yes ☐ Yes, but only in certain circumstances ☐ No ☐

Please explain your answer.

- b. What are the possible risks and/or harms that need to be considered with non-clinical research with embryos that were created specifically for such research? How can these risks and/or harms be addressed?

Comment

- c. Are there ethical or other matters specific to non-clinical research with embryos that were created specifically for such research that you would like to comment on?

Comment

C. Non-clinical research with cloned embryos, stem cells, blastoids and human-hybrid embryos

237. This section discusses activities and terms that may be new to some readers, so the table below explains some key terms briefly. The glossary also includes these terms for your reference.

Name	Definition/description
Blastoid	A blastoid is a model of an embryo based on stem cells. Blastoids look and behave like early, pre-implantation blastocyst. However, they do not support the development of a fetus and so are generally considered to be a cell culture model rather than an embryo.
Clone	A cloned embryo is an embryo that is a genetic copy of (has exactly the same DNA as) another organism. It can be made by removing the nucleus containing the DNA from an egg cell and replacing it with the nucleus from a cell of the animal to be cloned (eg, a skin cell). This process is called somatic cell nuclear transfer (SCNT) and the egg is induced to start to develop into an embryo without fertilisation.
Hybrid	A hybrid embryo is generally defined as an embryo that is formed from a combination of human and animal cells. This can be done, for example, by fusing the nucleus from a human cell into a non-human egg or embryo, or the reverse. Another term for hybrid embryos is chimeras (see the glossary). It is prohibited to transfer a human-animal hybrid to a human or animal uterus.
Stem cells	Stem cells are cells that can be reprogrammed to become different types of cells in the body. Embryonic stem cells have the greatest potential to do this; in scientific terms, they have the greatest 'pluripotency'.

238. The HART Act permits research on cloned embryos and hybrid embryos, under appropriate guidelines and with ECART approval. However, it prohibits research from implanting any embryos created from such research into a human or animal uterus.
239. The HART Act defines an embryo as a zygote, and as a cell or group of cells that have the capacity to develop into an individual. The definition does not include stem cells that come from an embryo.
240. Non-clinical research could use artificial human gametes or embryos. Potentially, if it met the criteria, innovative clinical research could use them as well.
241. ACART seeks your views on whether, and to what extent, non-clinical research with clones, stem cells, blastoids and hybrids should be permitted. Some examples are given in the following sections.

Summary

- If guidelines allowed, non-clinical research could **create** human embryos to obtain embryonic stem cells.
- Stem cells are cells that can be reprogrammed to become different types of cells, such as blood cells, kidney cells, cartilage or organs. These could be transplanted into the patient with less risk of rejection than if cells from another person were used.
- Such treatments are still in the research and development stage, so further research is needed before they can be used routinely.
- The research would not create a born child or a pregnancy: embryos would be grown in a laboratory for a maximum of 14 days.
- This type of research is not allowed under the current guidelines.
- ACART is interested in your views about such research.

Cloned embryos and stem cells

242. The HART Act prohibits cloning humans for reproductive purposes by implanting a cloned human embryo into a woman. It does not prohibit the creation of cloned human embryos for research. A common use of cloned embryos is to create stem cells.

What is cloning?

243. Cloning is a process used to create an embryo that is genetically identical to another organism — that is, it has exactly the same DNA. Clones of mammals, including humans, can be made by replacing the nucleus (containing the DNA) of an egg cell with a nucleus from a somatic cell⁵⁹ of the individual to be cloned. This process is called ‘somatic cell nuclear transfer’. Following this transfer, the egg is stimulated by electricity to undergo cell division to start embryonic growth, without fertilisation by a sperm cell.

⁵⁹ A somatic cell is any cell of a living organism other than the gametes (which only have half the number of chromosomes), for example a skin cell.

What are stem cells?

- 244. Stem cells are cells that can be reprogrammed to become different types of cells. Embryonic stem cells have the greatest potential to do this; in scientific terms, they have the greatest 'pluripotency'.
- 245. Stem cells can divide indefinitely and become a source of identical cells for research in many studies.
- 246. To make stem cells *in vitro*, the embryo is grown *in vitro* to develop into a blastocyst. It will contain pluripotent embryonic stem cells that can be collected, grown, treated and used for a wide range of research and therapeutic purposes. For this reason, they are valuable for medical research.
- 247. At present, in Aotearoa New Zealand, human embryonic stem cells can only be used if they come from an established line of cells imported from overseas. The current *Guidelines for Using Cells from Established Human Embryonic Stem Cell Lines for Research*⁶⁰ do not enable the creation of new human embryonic stem cell lines in Aotearoa New Zealand. The stem cell guidelines may need updating if the barrier to using viable embryos in research were to be removed. If so, ACART would advise the Minister of Health to consider that this work be done.

Benefits: clones and stem cells are useful for health research

- 248. Cloning for the purpose of creating a source of stem cells is useful for individualised health treatments. Stem cells can be created from cloned embryos that have the same genetic make-up as a patient, and they can be programmed to behave like many different kinds of cells, such as blood cells, kidney cells, cartilage or even organs that can be transplanted into the patient with less risk of 'rejection' than if cells from another person were used.
- 249. Many treatments of this kind are still in research and development stages, but there are promising potential health treatments across a wide variety of areas. As the research is non-clinical, the cloned embryos could not be transferred to a woman's uterus for reproduction.
- 250. Another use of stem cells is for studying cell biology. This has potential to expand basic biological knowledge, which can be valuable for a wide variety of health treatments (see Scenario 7).

⁶⁰ Ministry of Health. 2006. *Guidelines for Using Cells from Established Human Embryonic Stem Cell Lines for Research* Wellington: Ministry of Health. URL: [moh.govt.nz/notebook/nbbooks.nsf/0/7D723EE803F89C67CC2576D5006CBBCC/\\$file/guidelines-stem-cell-use.pdf](http://moh.govt.nz/notebook/nbbooks.nsf/0/7D723EE803F89C67CC2576D5006CBBCC/$file/guidelines-stem-cell-use.pdf) (accessed 13 November 2022).

Scenario 7: Embryonic stem cells for cancer research

In order to survive, grow and invade organs in the body, cancer cells often take control of genes that would normally only function during embryonic development. Researchers could study how cancers take control of early developmental genes. The best way to discover these early genetic events is to analyse human embryonic stem cells.

To date, researchers in Aotearoa New Zealand have used imported human embryonic stem cells to discover a number of genes that are expressed only in early development and become reactivated in cancer cells. This research has been restricted due to difficulties in obtaining human embryonic stem cells. Permitting stem cells to be derived from human embryos in Aotearoa New Zealand would enable more of this type of research to be done on cells with our unique genetic make-up.

This type of research is a fast-growing area. It has a lot of potential to provide insights into cancer biology, with the hope of developing new diagnostic and therapeutic targets for invasive cancers.

Developing stem cell lines in Aotearoa New Zealand would give our researchers a ready supply and control over their use. Potentially also Aotearoa New Zealand could receive any economic benefit that comes from such research.

This type of research is not permitted under current guidelines.

251. If the new guidelines permit research on viable human embryos, the research could include collecting human embryonic stem cells from embryos. Those stem cells could then be used for a range of clinical and research purposes.
252. People with rare genetic disorders may want to donate surplus embryos, or create embryos specifically, so that researchers can create human embryonic stem cell lines to conduct research on their particular genetic disorder. This may or may not involve cloning.

Additional considerations

253. Research using embryonic stem cells raises several ethical matters. Importantly, the source of the cells needs to be considered. These sources could be:
 - existing lines imported from overseas, which were originally obtained from human embryos that were later disposed of
 - embryos that were surplus to the reproductive needs of the people who had them created
 - embryos created solely to provide a source of stem cells for research.

- 254. Cell lines can continue to divide and can be grown for any length of time into the future, sometimes with commercial value. Ownership of cell lines is a consideration.
- 255. Similarly, because cell lines contain the genetic make-up of the donor cell (which could be from an embryo) there may be data sovereignty issues around who has access to genetic information that can be connected to living and future relatives.
- 256. The consent process would need to be clear about the potential future uses of stem cell lines.

Questions

*Question 8: Non-clinical research with **cloned human embryos***

- a. Should non-clinical research with cloned human embryos be permitted?

Yes ☐ Yes, but only in certain circumstances ☐ No ☐

Please explain your answer.

- b. What are the possible risks and/or harms that need to be considered with non-clinical research with cloned human embryos? How can these risks and/or harms be addressed?

Comment

- c. Are there ethical or other matters specific to non-clinical research with cloned human embryos that you would like to comment on?

Comment

Blastoids (artificial embryos)

Summary

- If the regulatory setting allowed, non-clinical research could create human blastoids (artificial embryos).
- Creating blastoids could enable research that leads to health benefits and improved fertility treatment options, without having to use human embryos.
- The research would not create a born child or a pregnancy: blastoids would be grown in a laboratory for a maximum of 14 days. Whether blastoids are legally 'human' is yet to be determined.
- This type of research might not be allowed under the current guidelines.
- ACART is interested in your views about such research.

257. A human blastoid is a 'model' of an embryo, made either from embryonic stem cells or cells from other tissues that are induced to become stem cells. During culture in a petri dish, these cells can develop into the different cell types of an embryo and so form something similar to an embryo at the blastocyst stage of development. Blastoids are not the same as embryos but they have some characteristics of embryos that are valuable for studying embryo development. With the technology available to date, a blastoid is not capable of developing into a viable fetus.

Benefits

258. Artificial human gametes or embryos could potentially be used in non-clinical research. They may provide a model for research to improve our understanding of early embryo development or to test the effects of drugs on embryos (see Scenario 8). Blastoids could also be made to replicate only some tissues of the embryo for particular studies on early organ development.

Scenario 8: Research using blastoids to test the effect of medication on embryo development

Many prescription medicines cannot be used during pregnancy because of the risk to the developing fetus. During the first 2 weeks of gestation, embryos are particularly susceptible to damage from environmental factors such as drugs and medicines.

Scientists could create human blastoids (artificial embryos) from reprogrammed human cells (eg, from skin cells or from embryonic stem cells) in culture, which would mimic a human embryo. Researchers could then expose these blastoids to the medicines/drugs in the culture and examine how this affects the development of the embryo cells and early organs.

This research would provide much-needed information on which medicines and what doses may be safe to use during pregnancy.

This type of research might not be allowed under the current guidelines. This is uncertain because it is unclear whether blastoids are legally defined as embryos.

Additional considerations

259. ACART notes that blastoids are probably not provided for in the HART Act because they are arguably not human embryos as they cannot develop into viable fetuses or become born people. This is a significant ethical, legal and operational matter that would need careful investigation.
260. If blastoids are not legally human embryos, they would not be subject to the '14-day limit' on development *in vitro*.
261. The ethical or moral questions might be significant. With blastoids, the question of 'What is a human?' is particularly relevant. Blastoids are arguably not human embryos and cannot develop into viable fetuses, yet they can be potential models for experimentation on early cell organisation in embryonic development. Does the humanness of a human embryo depend on the extent to which it has been modified?

Questions

Question 9: *Non-clinical research using **human blastoids***

- a. Should non-clinical research using human blastoids be permitted?

Yes

☐

Yes, but only in certain circumstances

☐

No

☐

Please explain your answer.

- b. What are the possible risks and/or harms that need to be considered with non-clinical research with human blastoids? How can these risks and/or harms be addressed?

Comment

- c. Are there ethical or other matters specific to non-clinical research with human blastoids that you would like to comment on?

Comment

Human-hybrid embryos

Summary

- If the regulatory setting allowed, non-clinical research could create human-hybrid embryos, which are formed from a combination of human and animal cells.
- A potential future use of human-hybrid embryos is for growing human organs to transplant into a person, using that person's own cells. This may overcome the shortage of organs available for transplant and reduce the risk of organ rejection. However, further research into this area is still needed.
- The research would not create a born child or a pregnancy: human-hybrids would be grown in a laboratory for a maximum of 14 days.
- This type of research might not be allowed under the current guidelines.
- ACART is interested in your views about such research.

262. A human-hybrid embryo is generally defined as an embryo that is formed from a combination of human and animal cells. The HART Act prohibits the implantation of human-hybrid embryos into the uterus of a human or an animal. If any research on these embryos in culture could occur, it would be restricted to the 14-day limit.
263. These hybrids can be made, for example, by fusing the nucleus from a human cell into a non-human egg or embryo, or the reverse. They can also be made by transferring human cells into an animal embryo. The resulting hybrids are also known as interspecies embryos, chimeras or admixed entities.

Benefits

264. A potential future use of human-hybrid embryos is for growing human organs for transplantation into a person, using that person's own cells. This may overcome the shortage of organs available for transplant and reduce the risk of organ rejection.
265. Researchers overseas are experimenting on ways to do this. One method, called 'blastocyst complementation', involves injecting stem cells from one species into an early blastocyst from another species that has been modified to prevent a particular organ from developing. The stem cells then go on to develop into the organ or tissue that is missing in that embryo.
266. This research has created functional kidneys, thymus and pancreas in hybrid mice and pigs. So far in human-animal hybrids, however, only a very low percentage of human cells have survived and the method has not yet been able to produce organs. Therefore, much more research is needed before the aim of producing 'personalised' organs for transplant can be realised. Scientists think that human-pig hybrids may be more successful than human-rodent hybrids.

267. Where the demand for medical technologies is high, there is also an incentive to do research that can contribute to meeting the demand, for example, for organ transplants (see Scenario 9). Aotearoa New Zealand may wish to contribute to the development of such technologies to supply organs for transplant in future.

Scenario 9: Human-hybrid embryos to create human organs for transplantation

In Aotearoa New Zealand, and worldwide, there is a shortage of human organs for transplant. Some countries are researching ways to grow human donor organs inside host animals and potentially use a patient's own cells to develop into an organ, such as a kidney.

Researchers overseas are developing ways to transfer and reprogram human cells, such as skin cells or embryonic stem cells, into mouse or pig eggs to establish embryos that contain human-compatible organs. The embryos are mainly animal cells but have some human cells programmed to create a particular organ.

Currently, the HART Act would only allow the hybrid embryos to be developed for 14 days after creation. If this research occurred, it could only develop the embryos *in vitro* and not transfer them to an animal or human.

It is unclear whether this research would be permitted under the current guidelines.

Additional considerations

268. The creation of human–animal hybrids raises the question of ‘What is a human?’ If a human embryo is modified in some way with animal cells, is it still human? Does the extent of modifications affect how human it is? Does its status as a human depend on how many, or what proportion of, human cells are present?
269. ACART notes that, although research with human–animal hybrid embryos could provide benefits, such research could also present risks, particularly in relation to its social acceptability.
270. Some people may be concerned about the future risk of animal cells getting into humans through transplantation treatments. Others may perceive this as ‘xenotransplantation’ and may oppose it because the treatment comes from animals.

Current regulation

271. The HART Act definition of a hybrid embryo includes this situation: an embryo created by transferring the nucleus of a human cell into a non-human egg or non-human embryo.
272. The HART Act would not allow the hybrid embryo to develop beyond 14 days or after the first appearance of the primitive streak, whichever is earlier, and it could only be developed *in vitro*. Hybrid embryos are prohibited from transfer to an animal or human uterus.
273. Therefore, Scenario 9 would provide benefits only for studying early organogenesis⁶¹ or basic biological knowledge that Aotearoa New Zealand could contribute to the field of research. Researchers could not grow whole animals under current legislation in Aotearoa New Zealand.
274. The research would need approval from both an animal ethics committee and ECART.

⁶¹ Organogenesis is the phase of embryonic development that starts at the end of gastrulation and continues until birth. During organogenesis, the three germ layers formed from gastrulation (the ectoderm, endoderm, and mesoderm) form the internal organs of the organism.

Questions

Question 10: Non-clinical research with **human-hybrid embryos**

- a. Should non-clinical research with human-hybrid embryos be permitted?

Yes ☐ Yes, but only in certain circumstances ☐ No ☐

Please explain your answer.

- b. What are the possible risks and/or harms that need to be considered with non-clinical research with human-hybrid embryos? How can these risks and/or harms be addressed?

Comment

- c. Are there ethical or other matters specific to non-clinical research with human-hybrid embryos that you would like to comment on?

Comment

D. Non-clinical research that genetically edits gametes and embryos

Summary

- Research with human gametes and embryos that have been genetically edited could be useful to study impacts of genetic mutations on early embryonic development, or to develop stem cell lines to understand what genes do in cells to support cell function.
- To genetically edit an embryo, scientists use molecular tools to alter a part of the DNA in the chromosomes of the embryo. Clustered regularly interspaced short palindromic (CRISPR) technology is increasingly used for genetic editing as it is more accurate than older technologies.
- The research would not create a born child or a pregnancy: the gametes or embryos would be grown in a laboratory for a maximum of 14 days.
- This type of research is not allowed under the current guidelines.
- ACART is interested in your views about such research.

275. Genetic editing is a complex topic and this section gives a simplified summary of what it involves. ACART's aim is to provide enough information to help readers understand the key issues relevant to this consultation.
276. DNA is the sequence of chemicals (deoxyribonucleic acid) that are the code providing a cell with 'instructions' for building an organism. Scientists try to discover what those codes (genes) are and what they do in a cell, so we can understand the biological make-up of cells and organisms. This knowledge is useful to create treatments for diseases that are caused by malfunctioning cells or genes.
277. Gene editing is the process of changing parts of DNA in a cell so that its daughter cells (in this case, the cells that form an embryo) all have the same change. The changes usually target a piece of DNA that codes for a particular gene. There are three main reasons for making that change. First, it may be to fix a mutation. Second, it may be to 'add' a gene that will enable the cell to make a protein that is not currently available in that cell. A third reason is to 'knock out' a gene so that researchers can study what happens in the cell if the gene doesn't work.
278. It is important to remember that the HART Act prohibits transferring any cell or embryo that has been genetically modified to a uterus. The potential for research in this area applies only to *in vitro* research — that is, non-clinical research.

279. Gene editing has been used in research for almost 50 years to study how genes work *in vitro* (in cells in the laboratory) or in live organisms (often in mice). Genetically edited mice have genetic changes that can show, in a live animal, what happens if a gene is knocked out (ie, the gene doesn't work) or if a mutation is 'fixed' to make the gene work properly. These tests are very useful for studying genetic diseases that may be caused by single-point gene mutations, such as cystic fibrosis or sickle-cell anaemia. Genetically edited cells are also studied *in vitro* using cell lines that divide and multiply to provide a long-term source of cells with the same genetic information in them.
280. Such research has developed modern understanding of how genes control cell and organ development, as well as diseases such as some cancers. In some cases, the research has led to the development of gene therapies for medical and other treatments.
281. To genetically edit an embryo, scientists use molecular tools to alter a part of the DNA in the chromosomes of the embryo. They may do this at the stage of embryo development shortly after the nuclei of the sperm and egg have fused (at single-cell embryo stage). Alternatively (depending on the goal of the research), they may genetically edit the DNA in the egg or sperm before fusion.
282. Clustered regularly interspaced short palindromic (CRISPR) technology is increasingly used for genetic editing as it is more accurate than older technologies. CRISPR can efficiently make cell lines or embryos with targeted genetic alterations.

Benefits

283. Genetic editing in human gametes and embryos could be useful to study impacts of genetic mutations on early embryonic development. The findings would then increase our understanding of why so few embryos successfully implant after fertilisation.
284. Genetic editing of human embryos could also be used to develop stem cell lines as a way of learning more about what genes do in cells to support cell function. Once a genetically edited stem cell line is created, it can in theory be continued indefinitely and used for a wide range of research.
285. Recent advances in genetic editing have increased the research activity internationally on ways to reduce the disease burden from single gene mutations. Scenario 10 presents an imaginary example of this kind of research.
286. Policy work on a therapeutic products bill for Aotearoa New Zealand is under way. Eventually, if approved, the use of genetically edited cells in human medicine may become a part of effective and safe medical treatment.

Scenario 10: Medical research using genetically edited human embryonic stem cells

Scientists want to study a potential treatment for cardiovascular disease. Earlier evidence indicates that modifying a gene in liver cells can reduce cardiovascular disease indicators (that are normally caused by familial hypercholesterolemia).⁶²

The current gene therapies use either protein or messenger RNA (mRNA)⁶³ regularly injected into the liver. A proposed study⁶⁴ is to use genetically edited human stem cells to create a permanent change in the patient's liver, with the goal of reducing the ongoing treatments needed. The researchers propose to use a supply of genetically edited human embryonic stem cells as the source because they can become any type of cell required.

As the embryo grew, the researchers would study the impacts of the gene editing using microscopes or biochemical analysis, or by fixing the embryo for staining (eg, to see where genes or proteins are found in the cells of the embryo). Currently, the HART Act only permits growth of human embryos *in vitro* up to 14 days, so only early developmental research would be possible on genetically edited embryos.

This research would require scientists to genetically edit human embryos at the zygote stage (just after fertilisation and before the cell begins to divide) and then extract the stem cells to develop a stem cell line for the clinical trials.

The gene therapy does not involve changing the genome of the patient — and will not affect their gametes (sperm or eggs) so there would not be genetic changes in future generations. Rather, the proposed genetically edited cells would only be used in the liver of the patient.

The stem cell treatment must first have been tested for proof of concept and safety in non-human animals such as mice and non-human primates.

This research would need approvals from the Environmental Protection Authority (which regulates genetically modified organisms) as well as ECART.

This type of research is not allowed under the current guidelines.

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- ⁶² Wang X, Raghavan A, Chen T, et al. 2016. CRISPR-Cas9 targeting of PCSK9 in human hepatocytes in vivo: brief report. *Arteriosclerosis, Thrombosis and Vascular Biology* 36(5): 783–6. URL: pubmed.ncbi.nlm.nih.gov/26941020/ (accessed 14 November 2022). Li Z-F, Wu N-Q. 2022. The progression of treatment for refractory hypercholesterolemia: focus on the prospect of gene therapy. *Frontiers in Genetics* 13: 911429. URL: pubmed.ncbi.nlm.nih.gov/35754818/ (accessed 14 November 2022).
- ⁶³ mRNA is a type of single-stranded RNA involved in protein synthesis. mRNA is made from a DNA template during the process of transcription. The role of mRNA is to carry protein information from the DNA in a cell's nucleus to the cell's cytoplasm (watery interior), where the protein-making machinery reads the mRNA sequence and translates each 3-base codon into its corresponding amino acid in a growing protein chain.
- ⁶⁴ This is a made-up scenario simply intended to illustrate why people might want to use genetic editing in human embryos and to highlight the ethical considerations.

Additional considerations

- 287. There may be ethical concerns about using human embryos as a source of stem cells. Some may argue that, instead of using human embryos, liver stem cells (for example) would be a preferable source of cells, to create a liver stem cell line.
- 288. The donors of the human embryos must consent to this use. They must be informed that if a stem cell line is successfully created from their embryos, that cell line may be used around the world for research and clinical treatments.
- 289. It is often impractical to maintain records of specific consents for cell lines that become widely used around the world, so opportunities to share any commercial benefits with donors may be limited.
- 290. The potential ethical risks include whether gene therapy for medical use is socially acceptable, and the general safety issues around use of stem cells for medical treatment.

Questions

*Question 11: Genetic modification of human **embryos** as part of research*

- a. Should genetic modification of human embryos as part of research be permitted?

Yes ☐ Yes, but only in certain circumstances ☐ No ☐

Please explain your answer.

- b. What are the possible risks and/or harms that need to be considered with research that genetically modifies human embryos? How can these risks and/or harms be addressed?

Comment

- c. Are there ethical or other matters specific to research that genetically modifies human embryos that you would like to comment on?

Comment

*Question 12: Should genetic modification of human embryonic **stem cells** be permitted?*

Yes ☐ Yes, but only in certain circumstances ☐ No ☐

Please explain your answer.

Te Ao Māori considerations on genetic editing

Question 13: Does your whānau or hapū or do you yourself have an opinion on genetic editing that you can share?

Question 14: Sir Hirini Mead⁶⁵ created the Tikanga Test to seek solutions for controversial decisions, including genetic modification. If you apply your own tikanga to the test, what are your opinions?

⁶⁵ Mead S. 2003. *Tikanga Māori: Living by Māori values*. Wellington: Huia.



Chapter 12: Currently prohibited or limited research

291. While ECART can approve certain types of human reproductive research that is consistent with ACART guidelines, Schedule 1 of the HART Act specifically prohibits certain activities (see Appendix 1). Without a specific amendment to the Act, ACART cannot include these activities in any guidelines that it develops.
292. The prohibited activities include transferring cloned embryos, hybrid embryos, and animal embryos or gametes to a human being (implantation). Similarly, transferring cloned embryos, hybrid embryos, and human embryos or gametes to an animal is prohibited. For this reason, any research described in previous chapters that creates any of the embryos noted above for research purposes would have to comply with these restrictions in the Act.
293. In addition to the restrictions in Schedule 1, the HART Act states that the *in vitro* development of human embryos must not continue beyond 14 days of development.⁶⁶
294. ACART believes the prohibitions and limits in the HART Act provide a logical limit to the extent to which human reproductive research can be carried out while still allowing researchers to conduct beneficial research. ACART's position is that, given the prohibited activities and the 14-day limit would not unduly restrict useful research, they are appropriate for now.
295. ACART does not propose to recommend to the Minister of Health any changes to the prohibited activities or the requirement to stop the development of *in vitro* embryos at 14 days. However, ACART still welcomes any views on this matter.

⁶⁶ HART Act, s 9.

Question

Question 15: Do you think there should be any changes to the current prohibitions in the HART Act? If so, what are those changes and why are they needed?

Chapter 13: Use of gametes and embryos for training

296. Training staff to handle gametes and embryos is important as the gametes and embryos are very small, delicate to handle and not easily replaceable.
297. One method of training is to use gametes and embryos that are no longer needed for someone's treatment (see Scenario 11). Currently gametes can be used for training purposes in a fertility clinic or other laboratory, but embryos that remain after someone has finished their treatment cannot be used for training as they are potentially viable.
298. In some cases, a research activity might include some training. Research methods may be used to evaluate whether the training has been successful.

Scenario 11: Biopsy training with surplus viable embryos

In some cases, fertility clinics remove cells from (biopsy) embryos that they are going to use in fertility treatment. They then send these cells for testing to identify genetic disorders such as cystic fibrosis and haemophilia. Embryos without genetic disorders can be used to establish pregnancies without the disorders occurring in any resulting children. This technology is known as pre-implantation genetic diagnosis.

To perform a biopsy of these embryos, an embryologist must have a high level of skill. Currently training to remove cells from an embryo is limited to using non-viable embryos. Most non-viable embryos have very few cells, or cells of such poor quality that they don't provide a suitable training experience. This makes it much more difficult for embryologists to train in these techniques. Using viable embryos that are no longer required for fertility treatment would make it easier and quicker for embryologists to develop these skills.

It is unclear whether this activity would be permitted under the current guidelines.

Benefits and risks

299. Using gametes and embryos for training purposes brings benefits. For example, embryologists and other laboratory staff would be able to become proficient at handling and manipulating embryos for clinical work much more quickly than they currently do. Doing many more procedures using cells from embryos during their training would also give them more experience before they deal with embryos that are actually used in treatment.

300. One risk is that a laboratory may not use gametes and embryos for the types of training that it has approval for. This risk could be mitigated by ensuring good processes for getting informed consent from the people donating their gametes and embryos to training, and auditing the laboratories involved. Patients undergoing fertility treatment may also feel under pressure to donate their surplus gametes or embryos for training.

Additional considerations

301. Although training in the use of human gametes and embryos is not a research activity in itself, it is still an activity that needs to be carefully managed.
302. Research guidelines could provide for donating gametes and embryos specifically for training purposes, as distinct from research. Gametes could also be used, or embryos formed, as part of training in clinical practice that is also a research activity.
303. People donating their gametes or embryos would need to consent to donating their gametes or embryos to research or training. The types of training activities that the donor is being requested to consent to would need to be listed by the applicant.
304. If the guidelines included such provisions, ACART expects that ECART would give approval to a particular clinic to use gametes and embryos for training for a specific number of years.

Question

Question 16: Embryos and gametes to be donated for training

- a. Should people be permitted to donate embryos and gametes for training purposes?

Yes ☐ Yes, but only in certain circumstances ☐ No ☐

Please explain your answer.

- b. What are the possible risks and/or harms that need to be considered with training on donated gametes and embryos? How can these risks and/or harms be addressed?

Comment

- c. Are there ethical or other matters specific to training on donated gametes and embryos that you would like to comment on?

Comment

Final question

Question 17: Do you have other general comments on human reproductive research?

Glossary

This glossary is intended to support this discussion document, and should not be relied on as a legal interpretation of the terms listed.

Advisory Committee on Assisted Reproductive Technology (ACART)

The advisory committee established under Aotearoa New Zealand's Human Assisted Reproductive Technology Act 2004. Members are appointed by the Minister of Health. ACART's website is acart.health.govt.nz.

Assisted reproductive procedure

The Human Assisted Reproductive Technology Act 2004 defines an assisted reproductive procedure as a procedure performed for the purpose of assisting human reproduction that involves:

- the creation of an *in vitro* human embryo, or
- the storage, manipulation or use of an *in vitro* human gamete or an *in vitro* human embryo, or
- the use of cells derived from an *in vitro* human embryo, or
- the implantation into a human being of human gametes or human embryos.

Blastoid

A blastoid is an embryoid,⁶⁷ a model of an embryo based on stem cells. Blastoids morphologically and transcriptionally resemble the early, pre-implantation, mammalian blastocyst.

On *in vitro* development, blastoids generate analogues of the primitive endoderm cells, in this way comprising analogues of the 3 founding cell types — the epiblast, trophoblast and primitive endoderm, with aspects of implantation on being introduced into the uterus of a compatible female.⁶⁸

They do not support the development of a fetus and so are generally considered to be a model rather than an embryo.⁶⁹

⁶⁷ Simunovic M, Brivanlou AH. 2017. Embryoids, organoids and gastruloids: new approaches to understanding embryogenesis. *Development* 144(6): 976–85. DOI: 10.1242/dev.143529 (accessed 15 November 2022).

⁶⁸ Rivron NC, Frias-Aldeguer J, Vrij EJ, et al. 2018. Blastocyst-like structures generated solely from stem cells. *Nature* 557(7703): 106–11. DOI: 10.1038/s41586-018-0051-0 (accessed 15 November 2022).

⁶⁹ Clark AT, Brivanlou A, Fu J, et al. 2021. Human embryo research, stem cell-derived embryo models and *in vitro* gametogenesis: considerations leading to the revised ISSCR guidelines. *Stem Cell Reports* 16(6): 1416–24. DOI: 10.1016/j.stemcr.2021.05.008 (accessed 15 November 2022). Hyun I, Munsie M, Pera MF, et al. 2020. Toward guidelines for research on human embryo models formed from stem cells. *Stem Cell Reports* 14(2): 169–74. DOI: 10.1016/j.stemcr.2019.12.008 (accessed 15 November 2022). Rivron N, Pera M, Rossant J, et al. 2018. Debate ethics of embryo models from stem cells. *Nature* 564 (7735): 183–5. DOI: 10.1038/d41586-018-07663-9 (accessed 15 November 2022). Lovell-Badge R, Anthony E, Barker RA, et al. 2021. ISSCR Guidelines for Stem Cell Research and Clinical Translation: the 2021 update. *Stem Cell Reports* 16(6): 1398–408. DOI: 10.1016/j.stemcr.2021.05.012 (accessed 15 November 2022).

Chimera	A single organism composed of cells with more than one distinct genotype. Animal chimeras are produced by the merger of multiple fertilised eggs. In animals, this means an individual derived from 2 or more zygotes, which can include having different blood types, subtle variations in form (phenotype) and, if the zygotes were of differing sexes, then even the possession of both female and male sex organs. Another way that chimerism can occur in animals is by organ transplantation, giving one individual tissues that developed from a different genome.
Clinical research	Research including people who are undergoing clinical treatment. Includes clinical trials, and may include quality improvement or laboratory validation processes.
Clone	A cloned embryo is an embryo that is a genetic copy of (has exactly the same DNA as) another embryo. It can be made by removing the nucleus containing the DNA from an egg cell and replacing it with the nucleus from a cell of the animal to be cloned (eg, a skin cell). This process is called somatic cell nuclear transfer (SCNT) and the egg is induced to start to develop into an embryo without fertilisation (parthogenetic).
Cryopreservation	The process of cooling and storing cells, tissues, or organs at very low or freezing temperatures to save them for future use. Also called cryobanking.
Donated embryo	An in vitro human embryo that is donated for reproductive purposes.
Donor	A person whose gametes or embryos are given to another person for use in assisted reproduction or research. See section 5 of the HART Act. Note that the legal definition under the HART Act means that a person who gives a gamete to their partner is not considered a donor.
Donor offspring	Children born from assisted reproduction in which a donor has been involved.
Established procedure	'Permitted' procedures. Established procedures are declared in the Human Assisted Reproductive Order 2005 (HART Order), and do not require ECART review and approval. The Minister of Health is responsible for the HART Order.
Ethics Committee on Assisted Reproductive Technology (ECART)	The ethics committee established under Aotearoa New Zealand's Human Assisted Reproductive Technology Act 2004. ECART reviews and decides case-by-case: (1) applications to undertake assisted reproductive procedures or human reproductive research; and (2) applications to extend the statutory storage period of gametes and embryos. Members are appointed by the Minister of Health. ECART's website is ecart.health.govt.nz .

Gamete	An egg or sperm, whether mature or not, or any other cell (whether naturally occurring or artificially formed or modified) that (1) contains only one copy of all or most chromosomes and (2) is capable of being used for reproductive purposes.
Genome	All the genetic information of an organism. It consists of nucleotide sequences of DNA that code for proteins, as well as non-coding regions that have other functions.
Hapū	Sub-tribe or group of related families or whānau.
Human Assisted Reproductive Technology Act 2004 (HART Act)	Aotearoa New Zealand's human assisted reproductive technology legislation, under which ACART and ECART were established. The Minister of Justice is responsible for the HART Act.
Human assisted reproductive technology research (human reproductive research)	Any research that uses human gametes or embryos. The term 'uses' includes in clinical research, where the research is studying any aspect of clinical fertility treatment. For clarity, this type of research does not use synthetic 'gametes' or 'embryo-like organoids', unless they are intended for transfer to the uterus and capable of developing into a fetus.
Hybrid	Generally defined as an embryo that is formed from a combination of human and animal cells. A hybrid can be made, for example, by fusing the nucleus from a human cell into a non-human egg or embryo, or the reverse. Another term for hybrid embryos is chimeras (see above). It is prohibited to transfer a human–animal hybrid to a human or animal uterus.
Informed consent	A person's voluntary agreement, based on adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic or preventive procedure.
<i>In vitro</i>	Performed or taking place in a test tube, culture dish, or elsewhere outside a living organism.
<i>In vitro</i> fertilisation (IVF)	The uniting of egg and sperm outside the body (in the laboratory).
Iwi	Tribe.
Mana	Prestige, authority, control, power, influence, status, spiritual power, charisma. A supernatural force in a person, place or object.
Manaakitanga	Hospitality, kindness, generosity, support — the process of showing respect, generosity and care for others.
Stem cells	Cells that can be reprogrammed to become different types of cells in the body. Embryonic stem cells have the greatest potential to do this; in scientific terms, they have the greatest 'pluripotency'.
Te Ao Māori	A Māori worldview or the Māori dimension of understanding.

Tikanga Māori	The customary system of Māori values and practices that have developed over time.
Training	In the context of this paper, training is the process by which relevant staff or researchers learn about the techniques and equipment, and theories relevant to those techniques and equipment, used in a fertility clinic or a laboratory.
Whakapapa	Genealogy, ancestral history, descent.
Whānau	Family group. In the modern context, the term is sometimes used to include friends who may not have any kinship ties to other members.
Whanaungatanga	A relationship, kinship, sense of family connection, through shared experiences of working or being together, which provides a sense of belonging.

Feedback form

Please provide your contact details below.

Name	
If this feedback is on behalf of an organisation, please name the organisation	
Please provide a brief description of the organisation (if applicable)	
Address/email	
Interest in this topic (eg, consumer, health professional, researcher, member of public)	

Feedback as an individual. Are you:

☐ Male ☐ Female ☐ Another gender

Would you like to make an oral submission (either in person or using electronic communications)?

☐ Yes ☐ No

Which age group do you belong to?

☐ 13 to 24 years ☐ 25 to 44 years ☐ 45 to 64 years ☐ 65+ years

What is your ethnicity? (Tick all you identify with.)

☐ NZ European ☐ Māori ☐ Pacific peoples
☐ Asian ☐ Other _____

Privacy

We may publish all submissions, or a summary of submissions on the Ministry of Health's website. If you are submitting as an individual, we will automatically remove your personal details and any identifiable information. You can also choose to have your personal details withheld if your submission is requested under the Official Information Act 1982.

If you do not want your submission published on the Ministry's website, please tick this box:

☐ Do not publish this submission.

Your submission will be subject to requests made under the Official Information Act. If you want your personal details removed from your submission, please tick this box:

☐ Remove my personal details from responses to Official Information Act requests.

If your submission contains commercially sensitive information that you do not wish to be released, please tick this box:

☐ This submission contains commercially sensitive information.

Questions

See separate document.



Appendix 1: Schedule 1 of the HART Act

Prohibited actions

1. Artificially form, for reproductive purposes, a cloned embryo. For the purposes of this item, a cloned embryo is not formed by splitting, on 1 or more occasions, an embryo that has been formed by the fusion of gametes.
2. Artificially form, for reproductive purposes, a hybrid embryo.
3. Implant into a human being a cloned embryo.
4. Implant into a human being an animal gamete or embryo.
5. Implant into a human being a hybrid embryo.
6. Implant into an animal a human gamete or human embryo.
7. Implant into an animal a hybrid embryo.
8. Implant into a human being a genetically modified gamete, human embryo, or hybrid embryo.
9. Implant into a human being gametes derived from a fetus, or an embryo that has been formed from a gamete or gametes derived from a fetus.