

The Risk Acceptability Framework used by the Advisory Committee on Assisted Reproductive Technology

ACART welcomes your feedback on this framework. Comments can be sent to acart@moh.govt.nz or to the ACART Secretariat, PO Box 5013, Wellington.

Introduction

When the Advisory Committee on Assisted Reproductive Technology (ACART) recommends that an assisted reproductive procedure become an 'established procedure', it must provide the Minister of Health with a report that includes advice on whether, in its expert opinion, the known risks to health of the procedure or treatment fall within a level of risk that is acceptable in New Zealand.¹

ACART has developed a risk acceptability framework to help it to assess those risks. The framework is not a simple mechanical procedure for reaching decisions. Rather, it sets out a process and considerations for ACART to take into account in its analysis. Some of these considerations may not be relevant to all assisted reproductive procedures that ACART provides advice on. And although the framework might indicate the acceptability or otherwise of a particular technology, it is a guide only – ACART is ultimately responsible for advising whether a risk is acceptable.

Note that a risk acceptability decision fits into a broader process of determining the regulatory category for an assisted reproductive procedure. This process involves:

- defining the problem and ensuring the procedure falls within the scope of the Human Assisted Reproductive Technology Act 2004 and ACART's jurisdiction
- gathering information about the procedure (see the Appendix for ACART's technical paper template)
- analysing and reviewing the information gathered
- consulting with interested parties
- making the recommendation.

The risk acceptability framework

Risk

'Risk' is a combination of two concepts:

- the likelihood of an effect occurring
- the consequences of an effect if it occurs.

Likelihood and consequences can be described qualitatively or quantitatively.

Likelihood

To consider the likelihood of risks associated with the use of any new assisted reproductive technology, ACART uses the following categories.

¹ See section 6(2)(c) of the Human Assisted Reproductive Technology Act 2004.

	Category	Description
A	Frequent	Is expected to occur again either immediately or within a short period of time (likely to occur most weeks or months)
B	Likely	Will probably occur in most circumstances (several times a year)
C	Possible	Possibly will recur – might occur at some time (may happen every one to two years)
D	Unlikely	Possibly will recur – could occur at some time in two to five years
E	Rare	Unlikely to recur – may occur only in exceptional circumstances (may happen every five to 30 years)

Consequences

To assess the consequences of the risks associated with the use of any new assisted reproductive technology, ACART uses the following categories of consequences.

Category	Description (risks and costs)
Serious	Patients whose death is unrelated to the natural course of the illness and differs from the immediate expected outcome of patient management
Major	Patients suffering a major permanent loss of function (sensory, motor, physiological or psychological) unrelated to the natural course of the illness and differing from the expected outcome of patient management
Moderate	Patients with permanent reduction in bodily function (sensory, motor, physiological or psychological) unrelated to the natural course of the illness and differing from the expected outcome of patient management or any of the following: <ul style="list-style-type: none"> • increased length of stay as a result of the incident • surgical intervention required as a result of the incident
Minor	Patients requiring an increased level of care, including review and evaluation, additional investigations, or referral to another clinician
Minimum	Patients with no injury or increased level of care or length of stay

Comparing the risks

ACART uses the following table to quantify and compare each aspect of the risk associated with a particular assisted reproductive technology.

Likelihood	Consequences				
	Serious	Major	Moderate	Minor	Minimum
A (frequent)	E	E	H	M	M
B (likely)	E	E	H	M	L
C (possible)	E	H	H	M	L
D (unlikely)	E	H	M	L	L
E (rare)	H	M	M	L	L

Notes: E = extreme risk; H = high risk; M = moderate risk; L = low risk

Analysis and decision-making

Using the consequences table

To begin its analysis, ACART places each of the known risks associated with a procedure in the consequences table shown above. Presenting the information in this way helps ACART to compare the relative risks of one procedure (eg, an established procedure) against another (eg, the proposed procedure). However, use of the consequences table has its limitations. For one thing, it is difficult to calculate and assess the cumulative risks associated with a procedure. It should also be noted that the consequences table is simply a tool for presenting and comparing information – ACART does not use it to make decisions.

ACART's analysis will then take into account the various issues outlined below.

Relevant principles of the HART Act 2004

ACART is guided in its decision-making by the principles of the HART Act 2004. All of these principles are relevant to a risk acceptability analysis. The principles can be divided between health and ethics.

Health principles

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

Ethical principles

- 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.
- Donor offspring should be made aware of their genetic origins and be able to access information about those origins.
- The needs, values and beliefs of Māori should be considered and treated with respect.
- The different ethical, spiritual and cultural perspectives in society should be considered and treated with respect.

Questions to address

Effect of data uncertainty

Are there aspects of the data that are uncertain? ACART will identify areas of uncertainty and will attempt to elucidate the effect of this uncertainty in its analysis.

Effect of cumulative risk

What is the effect of all of the risks combined?

Revealed preferences

How do the risks associated with this technology compare with the risks associated with other assisted reproductive technologies? If the risks are similar, this might indicate that people could feel that the risks associated with the technology are acceptable.

Although precedence will be given to the views of New Zealanders, ACART may take into account the technology's uptake in comparable overseas jurisdictions. If the technology is used relatively widely in other countries, this might indicate that some people feel that the risks associated with the technology are acceptable.

What is the demand for the technology? It may be difficult for ACART to assess the potential demand for a technology without undertaking consultation. However, demand may also be an indicator of a technology's acceptability. Consultation with fertility clinics and other interest groups may provide some indication of demand.

What are the risks of comparable health procedures:

- to the individual/s (eg, heart surgery, minor surgery, other elective procedures)?
- to the unborn child (eg, amniocentesis, ultrasound)?

Risk reduction/management

Can the risks be mitigated/managed in any way? For example, could clinical indicators be used to reduce risk?

Monitoring the pregnancies of women who conceive using new assisted reproductive procedures may also reduce the risks to the unborn child and the mother. It will also be important for ACART to consider the extent to which any outcomes of births from established procedures will be monitored in New Zealand, particularly where there is some uncertainty in the evidence.²

Risk–benefit analysis

What are the benefits of the procedure? Section 6(c) of the HART Act 2004 only requires ACART to assess the risks of the procedure, but consideration of the benefits of the procedure may go some way towards assessing the acceptability of those risks. If the benefits are significant, these benefits may make the risks associated with the technology more acceptable.

Decision-maker

Who is best placed to make the decisions associated with the procedure?
What is the nature of the ethical issues associated with the procedure?

A technology that is not common, is used for personal or clinical reasons and has very few ethical issues associated with it may not easily lend itself to oversight by the Ethics Committee on Assisted Reproductive Technology (ECART)³. If the majority of risks are better dealt with in discussions between the clinician and the patient/s, this might indicate that the risks are 'acceptable' for the purposes of making that procedure an established procedure. ACART might ask: Are the risks so great that reasonable individuals (in their position) could not weigh up and decide on the risks themselves?

If there appear to be a number of difficult ethical issues associated with the use of a procedure, ACART may consider regulating that procedure through guidelines and having ECART examine the use of that procedure on a case-by-case basis. Other options for regulating a procedure include a moratorium (under section 24 of the HART Act 2004), regulation (section 76 of the Act) or prohibition (through amendment to the Act).

Formal analysis and professional judgement

Formal analysis and professional judgement are two approaches often used in risk acceptability decisions. ACART will consider formal analysis and professional judgement as separate strands in its decision-making and, where appropriate, will compare the conclusions from each strand.

Formal analysis assumes that intellectual technologies (eg, cost–benefit analysis and decision analysis) can help us manage the problems created by physical technologies. Formal analysis might involve:

² Under section 35(2)(a) of the HART Act 2004, ACART is responsible for monitoring the application and health outcomes of assisted reproductive procedures and established procedures.

³ The Ethics Committee on Assisted Reproductive Technology, which was established under the HART Act, considers and determines case-by-case applications to undertake assisted reproductive procedures or conduct human reproductive research.

- conceptualising acceptable-risk problems as decision problems (ie, requiring a choice between alternative courses of action)
- developing a methodology, which usually involves breaking down a problem into more manageable components that can be analysed individually and then combined to provide an overall assessment
- developing a strongly prescriptive rule that combines the components according to a formalised procedure: 'if one accepts the assumptions underlying the analysis and its implementation, then one should follow its recommendations' (Fischhoff et al 1981)
- explicitly using a common metric (ie, reducing aspects of a problem to dollar or other values to assist comparison)
- following a line of official neutrality when defining the problem.

Professional judgement relies on the judgement of the technical experts most knowledgeable in a field. Professionals are sometimes better placed to make particular acceptable-risk decisions and may be better able to mitigate the risks that may arise. One aspect of professional judgement – determining who is best placed to make decisions associated with the procedure – is taken into account in the above analysis in relation to the appropriate decision-maker.

Presenting the analysis

ACART will provide as full an account as possible of how the decision was made, incorporating the above considerations (where appropriate) and including (where appropriate):

- a definition of the problem
- the hazards and consequences of the procedure
- reference to the literature review or reports used
- the sources of uncertainty and how they affected ACART's decision-making
- any gaps, and how such gaps affected ACART's decision-making
- any potential bias in the information and how that affected ACART's decision-making
- all options considered
- the values considered and, when societal consensus on a value was absent, what weight was given to which values and why
- an explanation of the chosen option.

References

Fischhoff B, Lichtenstein S, Slovic P, et al. 1981. *Acceptable Risk*. Cambridge: Cambridge University Press.

Standards and Codes Used

Guidelines for Managing Risk in Healthcare HB 228:2001. Standards Australia International Ltd, Sydney.

Risk Management AS/NZS 4360:2004. Standards Australia International Ltd, Sydney.

Severity Assessment Code (SAC), November 2005, SHRN (OSB) 050138 (Form). NSW Health.

Appendix: Technical Paper Requirements

Background

When advising the Minister of Health that a procedure or treatment should be declared an established procedure, ACART must⁴ provide the Minister of Health with a report that sets out the following:

- (a) information about the procedure or treatment
- (b) an assessment, drawn from the published and peer-reviewed research, of the known risks and benefits to health of the procedure or treatment
- (c) advice as to whether, in its expert opinion, the known risks to health fall within a level of risk that is acceptable in New Zealand
- (d) an ethical analysis of the procedure or treatment
- (e) advice as to whether, in its expert opinion, the Minister should recommend that the procedure or treatment be declared an established procedure.

The first step in preparing such a report to the Minister will be to review recent evidence. This is likely to involve commissioning a technical paper on the benefits and risks to health of the procedure under investigation.

Such a paper must:

- (a) be based on published and peer-reviewed research (if there is no published literature in a specific area some unpublished material may be referred to)
- (b) include references to all published and peer-reviewed research used
- (c) identify any areas where there is deficient information.

It must also include an evaluation of the information requested under sections A–D below, to facilitate a thorough assessment of the procedure. If a clause is not relevant, this must be clearly stated and explained.

⁴ Under section 6(2) of the HART Act.

Example template for a technical paper on a procedure

ACART has, to date, commissioned papers on the use of frozen eggs in fertility treatment and the use of in vitro maturation in fertility treatment. The template below is based on one used in commissioning the paper on the use of frozen eggs in fertility treatment. It would need to be adapted for any subsequent papers according to the particular procedure under investigation.

A. Current status of procedure/treatment

1. Indicate if the procedure has been 'approved' for human use in other countries. Alternatively, indicate if the procedure has not been banned and is being used for reproductive purposes in other countries.
2. If it has been approved (or is in use), specify:
 - (a) which countries
 - (b) when approval was given/use began
 - (c) the extent or conditions of the approval/use.
3. If it has been banned (or has proven to be controversial), specify:
 - (a) which countries
 - (b) why it was banned/proved controversial.
4. Indicate the number of individuals who have used the procedure and/or the number of individuals studied who have used the procedure.
5. Describe the information that is available on the outcomes of using the procedure.
6. Describe the information that is available on the risks of using the procedure.
7. Describe the information that is available on the benefits of using the procedure, including whether there are potential recipients of the technology who would otherwise have no available option.
8. Describe any areas where there is deficient information about the procedure (eg, potential risks, benefits and outcomes).

B. Information from human studies

9. Outline the efficacy of the procedure, including:
 - (a) fertilisation rates
 - (b) survival rate of the oocyte following the procedure (please compare with fresh mature eggs)
 - (c) embryo development rates

- (d) pregnancy rates (please compare to the use of fresh mature eggs in IVF⁵)
 - (e) live birth rates (please compare to the use of fresh mature eggs in IVF)
 - (f) diagnostic accuracy of the procedure (if applicable).
10. Detail any risks to health through the use of the procedure, including:
- (a) any potential side effects (please compare to the use of fresh mature eggs in IVF)
 - (b) health outcomes for female patients (if applicable) – this includes both short term and long term (eg, the treatment could increase the risk of cancer many years later)
 - (c) any suggested exclusions of potential patients based on clinical indicators (eg, cancer, diabetes, previous ovarian hyper-stimulation syndrome)
 - (d) health outcomes for male patients (if applicable)
 - (e) observed damage to the oocyte.
11. Detail the obstetric outcomes (risks and/or benefits to health), including:
- (a) observed damage to the oocyte
 - (b) neonatal/infant complications
 - (c) chromosomal abnormality
 - (d) congenital malformations (birth defects)
 - (e) child development (physical, psychomotor and cognitive)
 - (f) psychological outcomes for child and family
 - (g) epigenetic disorders (ie, imprinting)
 - (h) maternal outcomes (including complications).
12. Indicate if the use of the procedure introduces any medicines to be used in a new way. If it involves a new medicine it will have to go to the Health Research Council's Standing Committee on Therapeutic Trials. If yes, please address the following:
- (a) toxicity
 - (b) interactions
 - (c) long-term effects of medications.
13. Indicate if other treatment (eg, for cancer) might be delayed as a result of the procedure.
14. Indicate the potential age range of people undergoing this procedure.
15. Indicate if the procedure can increase the risk of other disease (eg, cancer).

⁵ IVF: in vitro fertilisation.

C. Information from animal studies

16. Indicate if the procedure has been used in animals. If so, please specify which species and address clauses 17–20 for each species.
17. Specify the number of animals studied that have undergone the procedure.
18. Outline the efficacy of using the procedure in terms of:
 - (a) fertilisation rates
 - (b) survival rate of the oocyte following the procedure
 - (c) embryo development rates
 - (d) pregnancy rates (please compare to the use of fresh mature eggs)
 - (e) live birth rates (please compare to the use of fresh mature eggs)
 - (f) diagnostic accuracy of the procedure (if applicable).
19. Detail any risks to health of using the procedure, including (but not limited to):
 - (a) any potential side effects
 - (b) health outcomes for the male subject (if applicable)
 - (c) ongoing development of offspring born as a result of the procedure.
20. Detail the obstetric outcomes (risks and/or benefits to health), including:
 - (a) neonatal/infant complications
 - (b) chromosomal abnormality
 - (c) congenital malformations (birth defects)
 - (d) offspring development (physical, psychomotor and cognitive)
 - (f) epigenetic disorders (ie, imprinting).

D. General

21. Specify any alternative procedures or treatments that could be used to gain the same result (ie, preserve fertility). If so please:
 - (a) discuss how the benefits to health of the alternative procedures/treatments compare to the benefits of the procedure
 - (b) discuss how the risks to health of the alternative procedures/treatments compare to the risks of the procedure.
22. Specify and detail any additional information related to the risks or benefits to health of the procedure, and not canvassed in the above clauses, that should be considered when making an assessment of the risks and benefits to health of the procedure.
23. Outline any long-term follow-up studies presented to date and any planned for the future.
24. Comment on the quality of the published research.

25. List references to all published and peer-reviewed research used in the report.