POLICY ON APPROVAL OF DIAGNOSTIC PROCEDURES INVOLVING EMBRYOS

REPRODUCTIVE TECHNOLOGY COUNCIL

Based on recommendations from
The PGD Committee

November 2017

REPRODUCTIVE TECHNOLOGY COUNCIL
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1. BACKGROUND.

At its meeting of 9 November 2004 the Reproductive Technology Council (Council) endorsed the *Report to the Reproductive Technology Council from the PGD (Implementation) Technical Advisory Committee* (PGD Committee) and agreed that the Council's policy on approval of applications to carry out embryo diagnostic procedures should be based on recommendations in the Report. Council approved the Policy on Approval of Diagnostic Procedures involving Embryos (the Policy) on the 14 December 2004.

In mid 2005, the PGD Committee commenced a review of the Policy to incorporate changes based on the experience of the committee during the initial operation of the approval processes. In December 2006 the PGD Committee presented a revised version of the Policy for ratification by the Council. The Council considered these changes and approved the revised Policy on 11 December 2007.

The amendments to the *Human Reproductive Technology Act 1991* (HRT Act) proclaimed on 1 December 2004 permit the diagnostic testing of embryos (including pre-implantation genetic diagnosis (PGD)) to be undertaken in Western Australia.

All diagnostic procedures carried out, on or with a fertilising egg or an embryo must have the prior approval of the Council. General approval may be provided in the Code of Practice (or Directions) or specific approval given in a particular case (sections 7(1)(b), 14(2b) 53(W)(2)(d) and 53(W)(4) of the HRT Act).

This Policy sets out approaches and processes for the approval of all diagnostic testing involving embryos, as recommended by the PGD Committee. It does not deal with diagnostic procedures that may be carried out on unfertilised eggs or eggs undergoing fertilisation, such as the testing of polar bodies removed prior to the formation of two pronuclei. Although such testing is regulated under the HRT Act and requires Council approval, there are no specific provisions about criteria that the Council is to consider in granting approval.

The HRT Act places different requirements on approval of each of the two broad categories of diagnostic testing that may be undertaken on embryos, depending on whether the diagnostic procedures are to be carried out prior to implantation or on embryos that are not to be implanted.

(a) Pre-implantation procedures
Where the embryo is to be implanted, the Council must be satisfied, based on scientific and medical knowledge, that the procedure is 'unlikely to leave the embryo unfit for implantation' and there is 'a significant risk of a serious genetic abnormality or disease being present in the embryo'.

Diagnostic testing carried out prior to implantation is generally intended to allow selection of embryos that do not have an abnormality or disease for implantation.

A distinction may be made between-
Pre-implantation genetic diagnosis (which may be known as PGD-familial or simply, PGD), where pre-existing diagnosis indicates that an embryo is at a significant risk of being affected by a serious genetic condition; and
Pre-implantation genetic screening (which may be known as PGD-aneuploidy screening, aneuploidy screening, or PGS), carried out in categories of patients thought to be at higher than average risk of conceiving abnormal embryos.

(b) Diagnosis in excess ART embryos
Most uses of excess ART embryos are subject to a licensing requirement that is to be administered by the National Health and Medical Research Council.

One exception to this requirement is in relation to excess ART embryos that are being tested as 'part of diagnostic investigations conducted in connection with the assisted reproductive technology treatment of the woman for whom the excess ART embryo was created'. The Council can approve diagnostic testing of an embryo in this circumstance if the embryo is not suitable for implantation (solely on the basis of its biological fitness).

The Framework set out in Attachment 1 summarises the approach to be taken.

An Application Form for Approval under the *Human Reproductive Technology Act 1991* (HRT Act) for a diagnostic procedure to be carried out upon or with an embryo is included as Attachment 2.

2. POLICY

2.1 Approach to applying the legislation

The starting point for this approach is found in the terms of the HRT Act, in particular the criteria that are set out in section 14(2b). The legislative provisions are to be applied according to their ordinary meaning conveyed by the text. Extrinsic material such as the Explanatory Memorandum and the Parliamentary debate on the Bill can be used to confirm the ordinary meaning or to assist in determining the meaning if the text is unclear.

Section 14(2b) states:

> The Council must not grant approval to any diagnostic procedure to be carried out upon or with a human embryo unless —
>
> (a) the embryo is intended for use in the reproductive technology treatment of a woman and the Council is satisfied, on the basis of existing scientific and medical knowledge, that —
>
> (i) the diagnostic procedure is unlikely to leave the embryo unfit to be implanted in the body of a woman; and
>
> (ii) where the diagnostic procedure is for the genetic testing of the embryo, there is a significant risk of a serious genetic abnormality or disease being present in the embryo;
>
> or
>
> (b) the diagnostic procedure consists of a use referred to in section 53W(2)(d) or (f).

The following approach should be taken in the application of the terminology in section 14(2b) of the HRT Act:

"the Council is satisfied, on the basis of existing scientific and medical knowledge"

This phrase sets the parameters of the matters that are relevant to the Council's considerations.

1. The Council should rely on the guidance of experts in the medical and scientific field to provide it with opinions and conclusions about the existing scientific and medical knowledge that is relevant to the matters which the Council is required to consider.

2. It is not appropriate to specify a degree of probability for the Council to be satisfied about the matters in section 14(2b). Rather, the Council should look at whether it has been provided with information or evidence to give it confidence in the decision that it is required to make.

"Unlikely to leave the embryo unfit to be implanted in the body of a woman"

3. The decision making on “fitness to implant” is largely a question of clinical criteria. In the context of diagnostic testing for embryos that are intended for ART treatment the testing should not damage the embryo in a way that means a viable pregnancy could not be achieved using the embryo.

4. Whether a diagnostic test is unlikely to leave an embryo unfit for implantation is a matter for evidence of the risks associated with the procedure, and it is not appropriate to specify a degree of mathematical probability.

"significant risk of a serious genetic abnormality or disease”

5. It is not appropriate to specify a statistical probability as the sole criterion for the risk of a genetic abnormality or disease being present in the embryo to be “significant”.

6. The level of risk should be measured against the risk of the disease or disability occurring in the general population. The Council should be satisfied that there is a higher risk of the embryo in question being affected by the abnormality or disease being tested for than for embryos in the general population.

7. The significance of the risk for the persons seeking the testing may also be relevant, in that the persons seeking treatment may have varying perceptions of the significance of risk that need to be taken into account.

"significant risk of a serious genetic abnormality or disease”

8. In assessing whether a genetic abnormality or disease is serious it is appropriate to look at environmental and personal factors as well as the impairment to body functions and structures that may arise from the condition. The assessment should consider the limits that these factors impose on the extent to which a person can engage in activities or participate in life situations.

9. The *International Classification of Functioning Disability and Health* (ICF) developed by the World Health Organisation provides a broad overview for assessment of seriousness, which covers many different aspects of disease, however, does not consider an individuals perspective of seriousness. The infrastructure of the ICF may be adapted to the assessment of the seriousness of a genetic abnormality or disease.

2.2 Factors to be considered in deciding whether to approve an embryo diagnostic procedure

10. In deciding whether to approve an embryo diagnostic procedure the Council needs to consider:

- the risk and severity of the condition that is to be tested for, and
- the safety and reliability of the procedure.

It is noted that genetic testing of embryos will only be available for participants who are eligible to receive IVF treatment in accordance with the requirements in section 23 of the HRT Act.

2.2.1 Conditions that may be tested for

11. In considering conditions that may be tested for, a distinction is made between Pre-implantation Genetic Screening (also known as PGD-aneuploidy screening, aneuploidy screening or PGS), and Pre-implantation Genetic Diagnosis testing for known single gene defects and translocations (also known as PGD-familial or PGD).

Aneuploidy

Aneuploidy is the scientific term that refers to the occurrence of one or more extra or missing chromosomes. This can have serious consequences for a single cell or an entire organism. Chromosomal aneuploidy may lead to infertility, pregnancy loss – such as miscarriage or stillbirth – the death of a child, as well as a number of birth defects, genetic syndromes and/or mental retardation.

12. Aneuploidy is considered to be a serious genetic abnormality.

13. Aneuploidy screening should be available to the following categories of people who are eligible for the IVF program and who are considered to be at risk of producing an embryo that is chromosomally abnormal:

- women over 35 years of age providing eggs; or
- women with 2 or more miscarriages; or
- women with more than 2 failed IVF attempts where embryos have been transferred; or
- women referred by a clinical geneticist with a family history of aneuploidy not caused by translocations or other chromosomal rearrangements.

14. There may be additional circumstances in which aneuploidy testing may be appropriate and this should be subject to case by case approval by the Council.

Single gene defects and translocations

15. It is not appropriate to specify a list of conditions that could be tested for by PGD. Each application needs to be considered on its own merits, as the Council needs to be satisfied that the condition will be serious in the embryo (potential offspring).

16. The Council should evaluate PGD for individual cases, based on support of a clinical geneticist or genetic counsellor (accredited by the Human Genetics Society of Australasia) as per s 2.4.1 paragraph 43, who has assessed the risk and seriousness of the condition to be tested for and discussed relevant issues with the participants requesting the testing.

17. In making its determination the Council should also take into account that the genetic abnormality or disease in the embryo is not simply a defect in the genetic material, but is one associated with a known clinical deficit.

18. Where approval for embryo diagnostic testing is being sought for a condition where there may be carrier embryos but no affected embryos (e.g. a male participant with an X linked recessive condition), Council must consider whether the condition will have a serious effect on the carrier embryo.

2.2.2 Applications for conditions requiring case by case approval

19. An application to the Council for approval should be made by the clinic using the Application Form for Approval for a Diagnostic Procedure to be Carried Out Upon or With an Embryo (Attachment 2). The application should contain only de-identified information about any participant. Care must also be taken not to disclose any non-relevant personal, private or confidential matters.

20. An application for approval of testing should include a report from the clinical geneticist or genetic counsellor if directed as per s 2.4.1 paragraph 43 addressing the following questions as relevant:

Areas to be addressed	Criteria
Is there a significant risk of a serious genetic abnormality or disease in the context of the family that is requesting the testing?	E
What is the genetic abnormality or disease that is to be tested for?	E
What experience with, and attitude to, the abnormality or disease does the family requesting the testing have?	E
What factors indicate that there is a risk that the embryo will be affected by the genetic abnormality or disease?	E
What is the level of impairment to body functions and structures that is usually associated with the abnormality or disease?	E
What difficulties would a person with the abnormality or disease be expected to have in participating in activities such as learning and applying knowledge, communication, mobility, self care, employment and community, social and civic life?	E
What is the level of support that would be required by a person who has the abnormality or disease?	D
What are the prospects for new and longer-term treatments and interventions for the condition?	D
What is the capacity of the family who are requesting the testing to provide the level of support required by a child with the abnormality or disease?	D
What clinical genetic and diagnostic data are to be used in the testing procedure?	D

What other testing options are available?	D
What level of information will be possible from the test, in terms of interpretation, sensitivity and specificity (includes error)?	D
Has the person requesting the testing been provided with counselling about the potential impact of testing and contact information for other persons or organisations that have experience with the condition?	D

Criteria: E = essential D = desirable

21. For conditions where the genetic abnormality or disease results predominantly in a psychological impact, a report from a psychologist addressing the potential psychological impact upon the embryo (as a potential future person) should be included in the application.

22. There should also be an opportunity, but not a requirement, for the person(s) requesting the testing to provide a statement to the Council about the impact of the abnormality or disease on them.

2.2.3 Feasibility Testing and the Application Process

23 The Council may grant approval for a PGD procedure where positive feasibility study results are available.

In cases where the feasibility results are pending (e.g. prior to the ordering of the feasibility study) the Council may grant conditional approval, with the below outlined conditions:

- *Where the feasibility results are positive (i.e. the diagnostic procedure as outlined in the application and approved by Council could be undertaken) –*

a) Council be provided with documentation to confirm that the approved diagnostic test was feasible; and
b) at the time the diagnostic procedure is carried out, there have been no unapproved changes to relevant procedures, staffing, test etc;

- *Where the feasibility results are negative (i.e. the diagnostic procedure as outlined in the application and approved by Council could <u>not</u> be undertaken) –*

a) Council be provided with documentation to confirm that the approved diagnostic test was **not** feasible; and
b) where an alternate embryo diagnostic procedure is offered the participants be offered an appointment with a clinical geneticist to discuss the alternative options for genetic testing of embryos; and
c) an amended application be provided for Council approval providing details of the alternate diagnostic procedure to be undertaken.

24. In regard to organising feasibility studies-

a) ART clinics should inform Genetics Services when organising feasibility studies, so that the clinical geneticists can communicate with the testing laboratories; and
b) The clinical geneticist should encourage patients to keep them informed of the progress of their cases, especially in the event of a negative feasibility, when the couple would be offered a follow-up appointment.

25. In considering an amended application for an alternative diagnostic procedure subsequent to a negative feasibility study (such as approval for the use of FISH for sex selection to avoid transmission), one factor to be considered by Council will be that options have been fully canvassed with a clinical geneticist.

2.2.4 Additional considerations in embryos diagnostic testing

Sex selection

The HRT Act makes it clear that the use of an embryo diagnostic procedure for sex selection alone would not be permitted. The 2004 National Health and Medical Research Council's *Ethical guidelines on the use of assisted reproductive technology in clinical practice and research* also prohibit this use of sex selection.

26. Although genetic testing for other purposes may provide information about the sex of an embryo, information conveyed to participants by clinicians or scientists should not include information about the sex of the embryo, unless this is relevant to the genetic abnormality or disease.

27. Applications for sex selection to avoid transmission of a genetic disease should be applied for using the "Testing for a specific condition" part of the application.

Carrier embryos

For some single gene defects a person may be a "carrier" of the condition. People who are carriers may be at risk of passing the gene on to their offspring. For further information on types of gene defects refer to:
http://www.genetics.edu.au/factsheet/index.html

28. Where approval is granted by Council for genetic testing for a specific condition, the participant may consent to implant unaffected non-carrier embryos or to preferentially implant non-carrier embryos.

- Implanting unaffected non-carrier embryos means selecting only those embryos with no copy of the mutated gene (ie not selecting either affected or carrier embryos).
- Preferentially implanting non-carrier embryos means selecting unaffected non-carrier embryos as a first preference and carrier embryos as a second preference).

29. Where participants are considering either implanting only unaffected non-carrier embryos or preferentially implanting unaffected non-carrier embryos and the condition being tested is passed on through autosomal recessive inheritance participants should be informed of the low risk of inheritance of the condition to the second and future generation.

30. Where parents consent to preferential selection of unaffected non-carrier embryos for autosomal recessive conditions, they should not routinely be informed of the carrier status of the embryo or embryos implanted.

So as to ensure that individuals can give informed consent for their own testing at an appropriate time, clinical geneticists do not recommend carrier testing in minors. This will be discussed with parents undertaking PGD at their clinical genetics consultation. Experience has shown that most couples choose not to be informed of the carrier status of the embryo implanted.

2.3 Safety and Reliability of testing – Standards for facilities, staffing and technical procedures

31. In deciding whether a diagnostic test is likely to leave an embryo fit for implantation it is necessary to consider the safety and reliability of diagnostic procedures to be undertaken. The Council provides guidelines (below) on the appropriate standards for facilities, staffing and technical procedures, and clinics should seek approval to undertake the testing based on their demonstrated capacity to meet the guidelines.

32. At the time an approved procedure is carried out approvals granted must be current.

2.3.1 Guidelines for embryology laboratories

33. Prior approval by the Council for the embryo biopsy procedures and any other new or amended embryology procedures (such as the use of extended culture to enable the transfer of fresh embryos following biopsy and diagnosis) should be required. The normal processes of specific approval should apply, including a requirement for prior approval from a Human Research Ethics Committee.

34. The standards for approval of embryology laboratories and procedures set out in Attachment 3 should be applied.

35. Where appropriate intra-cytoplasmic sperm injection (ICSI) may be used to develop embryos that will be genetically tested prior to implantation (in accordance with the Minimum Standards for ICSI use).

2.3.2 Guidelines for genetic testing laboratories

36. The standards for approval of genetics laboratories and procedures set out in Attachment 4 should be applied.

37. Where a local ART laboratory is carrying out aneuploidy screening, such as using FISH based tests, the clinic must have oversight /supervision for the first 50 patients from a WA-based cytogeneticist experienced in carrying out FISH (such as for pre-natal diagnosis) on a regular (i.e. weekly) basis.

38. At the completion of the 50 cases the clinic should arrange for the cytogeneticist who carried out the supervision to report to the PGD Committee on progress and

competency with FISH within the ART laboratory. Any concerns may result in the PGD Committee advising the Council that the supervision should be continued.

39. Where genetic testing is to be performed by a laboratory external to the ART clinic, relevant information from the Service Level Agreement must be provided to the Council to enable adequate consideration of the application.

40. Clinics should be permitted to export samples derived from embryo biopsy from Western Australia for genetic testing elsewhere, if that testing has been approved by the Council. These samples should not be exported for testing elsewhere if that testing has not been approved by the Council.

2.3.3 Record keeping

41. To allow comprehensive follow-up of outcomes after diagnostic procedures are carried out, the following data items that are not already being reported for inclusion in the Registers should be collected:

- # embryos biopsied;
- # embryos damaged;
- reason for genetic testing (aneuploidy screening or PGD);
- # embryos successfully screened;
- and list of gene defects tested for.

2.4 PGD Clinical Process

Attachment 5 provides Flow Charts for the Coordination of Pre-implantation Genetic Diagnostic Services in WA in the two differing scenarios of aneuploidy screening and PGD.

42. Clinics offering embryo diagnostic procedures should be required to put in place a named staff member whose role it is to act as 'PGD coordinator' and coordinate the information relating to each person undergoing the procedures and respond to patient queries about progress with their testing. This person may be the clinic counsellor, a nurse or other person.

2.4.1 Counselling

43. It is necessary that participants in IVF have access to accurate information and counselling about any proposed genetic testing of embryos. In the case of single gene defects and translocations, this consultation will usually be provided by a clinical geneticist. Although, Genetic Services of Western Australia may direct a genetic counsellor to provide the consultation when considered appropriate.

Some genetics expertise should be available in the IVF clinic for those undergoing aneuploidy screening.

44. Approved counsellors providing counselling in a clinic that offers aneuploidy screening should have some understanding of genetics, as ideally also should

embryologists and nurses, so that they can adequately assist couples undergoing PGD or aneuploidy screening. This would not replace the role of the clinical geneticist or trained genetic counsellor as being the main source of complex genetic information where this is requested, required or recommended.

45. In the case of single gene defects and translocations there should be a mandatory genetic consultation with a clinical geneticist (or genetic counsellor if directed as per s 2.4.1 paragraph 43), who provides a report to the Council as required in the application for approval.

46. In the case of aneuploidy screening it should be mandatory for participants to see the clinic counsellor (an 'approved counsellor' under the HRT Act), to assist in understanding the ramifications of genetic testing in the IVF setting.

47. The Council should liaise with WA Genetics Services and the Genomics Directorate of the Department of Health in the development and facilitation of training in genetics for approved counsellors and other interested staff at licensed ART clinics.

2.5 Diagnostic testing of excess ART embryos

48. The scope of testing permitted under the HRT Act is very narrow. The diagnostic testing must be part of clinical practice and approval to undertake assessment should be on the same basis as approval for an innovative procedure; that is, on a clinic by clinic basis.

49. Conditions on the approval should address issues such as counselling, information giving and reporting and record keeping. Part B of the Framework (Attachment 1) sets out the guidelines that should be addressed.

2.6 Ongoing Council process of consideration of issues in embryo diagnostic testing

50. The constitution and terms of reference of the PGD Committee are appropriate to allow it to provide advice to the Council about individual applications that are made for approval to undertake diagnostic testing of embryos.

In addition to the expertise of members on the Committee it is noted that the Committee can seek additional input from relevant experts if required. As a smaller group, with specialist knowledge, the Committee is well equipped to provide an efficient assessment of applications.

51. The Council should request the PGD Committee to provide it with advice on applications for approval of embryo diagnostic procedures as these are received.

52. The Council should request the PGD Committee to liaise with an appropriate body on ethical issues specific to genetics and regularly update the Council on ethical issues and matters of interest from the Committee.

ATTACHMENT 1: FRAMEWORK FOR APPROVAL OF AN EMBRYO DIAGNOSTIC PROCEDURE

A. Pre-implantation genetic diagnostic procedures
PGD/ PGS

May only be offered where participants are eligible for IVF under the HRT Act:
Either they are unable to conceive a child due to medical reasons OR their child would otherwise be likely to be affected by a genetic abnormality or disease.

Clinics seeking authorisation should obtain a copy of the
Application for Approval to Carry Out Embryo Diagnostic Procedures.

A.1 Diagnostic procedures to be carried out in categories of patients thought to be at higher than average risk of conceiving abnormal embryos.

(PGD-aneuploidy screening/aneuploidy screening/PGS)

1. Generally authorised under the Act, under certain conditions

a) Initially general authorisation will be clinic by clinic, but all to the same standards.

b) Criteria for eligibility:

- women over 35 years of age providing eggs; or
- women with 2 or more miscarriages; or
- women with more than 2 failed IVF attempts where embryos have been transferred; or
- women referred by a clinical geneticist with a family history of aneuploidy not caused by translocations or other chromosomal rearrangements; or
- otherwise as approved on a case by case basis by the Council.'
-

A.2 Diagnostic procedures to be carried out where pre-existing diagnosis indicates that an embryo is at a significant risk of being affected by a serious genetic condition.
(PGD-familial/PGD)

1. Case by case approval

(a) Applications for approval must be made on the proforma provided.

(b) Support from a clinical geneticist accredited by the Human Genetics Society of Australasia (or genetic counsellor if directed as per s 2.4.1 paragraph 43)

(c) A report from the clinical geneticist(or genetic counsellor if directed as per s 2.4.1 paragraph 43) addressing the following questions as relevant:

- Is there a significant risk of a serious genetic abnormality or disease in the context of the family that is requesting the testing? (E)
- What is the genetic abnormality or disease that is to be tested for? (E)
- What experience with, and attitude to, the abnormality or disease does the family requesting the testing have? (E)
- What factors indicate that there is a risk that the embryo will be affected by the genetic abnormality or disease? (E)
- What is the level of impairment to body functions and structures that is usually associated with the abnormality or disease? (E)
- What difficulties would a person with the abnormality or disease be expected to have in participating in the activities such as learning and applying knowledge, communication, mobility, self care, employment and community, social and civic life? (E)
- What is the level of support that would be required by a person who has the abnormality of disease? (D)
- What are the prospects for new and longer term treatments and interventions for the condition? D)
- What is the capacity of the family who are requesting the testing to provide the level of support required by a child with the abnormality or disease? ? D)
- What clinical genetic and diagnostic data is to be used in the testing procedure? ? D)

- What other testing options are available? ? D)
- What level of information will be possible from the test, in terms of interpretation, sensitivity and specificity (includes error)? ? D)
- Has the person requesting the testing been provided with counselling about the potential impact of testing and contact information for other persons or organisations that have experience with the condition? ? D)

E=essential D=desirable

Conditions:

(a) Any participant whose embryos are to be tested must meet criteria for eligibility for the testing that are set by the Council.

(b) Any licensee proposing to carry out such tests must have prior approval from the Council for all stages of the procedures involved in the biopsy and ongoing culture of the embryos (innovative practices), to ensure that the procedures are 'unlikely to leave the embryo unfit for implantation';

(c) The types of genetic tests to be carried out and the laboratories where they are to be performed must be approved by the Council to ensure that the tests are feasible and likely to be safe and effective; and

(d) Reporting and record keeping requirements must be complied with.

(e) Counselling, information giving and consent requirements must be complied with.

2. Extensions to the criteria for eligibility:

Clinics may apply to the Council for any extension to the criteria for eligibility for this testing.

This request should detail why the extension is needed and provide documented evidence that the requirements of the Act that there be a 'significant risk of a serious genetic abnormality or disease being present in the embryo' would still be met..

Conditions:

2.1 Where approval is sought on the basis of applicable positive feasibility study results -

(a) Any licensee proposing to carry out such tests must have prior approval from the Council for all stages of the procedures involved in the biopsy and ongoing culture of the embryos (innovative practices), to ensure that the procedures are 'unlikely to leave the embryo unfit for implantation';

(b) The types of genetic tests to be carried out and the laboratories where they are to be performed must be approved by the Council to ensure that the tests are feasible and likely to be safe and effective; and

(c) Reporting and record keeping requirements must be complied with.

(d) Counselling, information giving and consent requirements must be complied with.

2.2 Where approval is sought and feasibility study results are not yet available, any approval granted by the Council will have the following additional conditions-

(a) Any relevant Council approvals are to be still current at the time the procedure is carried out; and

(b) If the feasibility study is negative, the participants are offered an appointment with a clinical geneticist to discuss their available options in full.

Any subsequent application for an alternative diagnostic procedure for these participants will take into account the provision of this counselling.

B. Excess ART embryos

Note: To be eligible for Council approval Clinics must comply with s 53W(2)(d)(ii) , ie the diagnostic procedure to be carried out must be in connection with the ART treatment of the woman.

If the diagnostic procedure is to be carried out as part of a Quality Assurance program, approval MUST be sought from the National Health and Medical Research Council.

A diagnostic procedure involving an excess ART embryo may be generally authorised under the Act, under certain conditions.

General authorisation is to be granted clinic by clinic.

Clinics seeking authorisation should obtain a copy of the *Application for Approval to Carry Out Embryo Diagnostic Procedures.*

Conditions:

1. That the embryo to be tested is unfit for implantation on the basis of its biological fitness for implantation (as required by s.53W(2)(d)(i)); and

2. That the procedure also complies with s 53W(2)(d)(ii), ie is in connection with the ART treatment of the woman.

3. That reporting and record keeping requirements set out on approval must be complied with.

4. That counselling, information giving and consent protocols on approval must be complied with.

APPLICATION FORM FOR APPROVAL UNDER THE *HUMAN REPRODUCTIVE TECHNOLOGY ACT 1991* (HRT ACT) FOR A DIAGNOSTIC PROCEDURE TO BE CARRIED OUT UPON OR WITH AN EMBRYO

Name of Licensee: _____

Licence Supervisor: _____
(Full name)

PGD Coordinator: _____
(Full name)

Address: _____

Tel: _____

Fax: _____

Is approval being sought to undertake **aneuploidy screening** prior to implantation?

☐ yes* ☐ no

*If yes please complete Part A & Part B.

Is approval being sought to undertake **genetic testing for a specified condition** prior to implantation?

☐ yes* ☐ no

*If yes please complete Part A & Part C.

Is approval being sought to undertake **diagnostic testing on an excess ART** embryo?

☐ yes* ☐ no

*If yes please complete Part D.

For office use only

Reference No:

Issued: (Date):

Signed:
(Chairman, Reproductive Technology Council)

INSTRUCTIONS:

- This form is available electronically on the Reproductive Technology Council website at http://www.rtc.org.au/ under Information for Clinics>Forms.

- The information requested may be printed or typed in the shaded boxes or provided as attachments.

- Please do not include patient identifying information in the application.

- The application may be submitted:

  - by e-mail to the Executive Officer at rtc@health.wa.gov.au or

  - by post to:

The Executive Officer
The WA Reproductive Technology Council
PO Box 8172
Perth Business Centre WA 6849
Telephone: (08) 9222 4490
Facsimile: (08) 9222 4183

PART A: APPROVAL OF TECHNICAL PROCEDURES.

Item 1: BIOPSY PROCEDURES

Do you have specific approval from the Reproductive Technology Council to undertake the relevant embryo biopsy procedures?

☐ yes ☐ no*

*If no please provide details of the procedures intended to be used by reference to the following standards.

- Laboratories must be licensed under the HRT Act and maintain accreditation by the Reproductive Technology Accreditation Committee (RTAC).
- Laboratories must participate in a QA program recognised by RTAC/NATA.
- The biopsy procedure to include setting up of microtools on an inverted microscope, placing oocyte/embryo in microdroplets for the procedure, removal of cell/polar body, placing cell into appropriate transport container.
- HREC approval for the procedure(s) to be used.
- The biopsy techniques to be used may be acid Tyrode's or laser as approved by the Council.
- Biopsy may be in the form of polar body biopsy, embryo biopsy (at day 3) or blastocyst as approved by the Council.
- Staff performing the biopsy must have demonstrated competency in:
  - ➢ the proposed biopsy technique;
  - ➢ placing the cell(s) in transport vessel, in the case of single gene defects; and
  - ➢ fixing of cell(s) on a slide in the case of chromosome analysis.

Please provide attachments if necessary and note the attachment numbers in this box.

Item 2: EXTENDED BLASTOCYST CULTURE

Are you intending to use extended blastocyst culture?

☐ yes* ☐ no

*If yes do you have specific approval from the Reproductive Technology Council to undertake extended blastocyst culture?

☐ yes ☐ no*

*If no please provide details of the procedure intended to be used as required for a standard application for specific approval.

Please provide attachments if necessary and note the attachment numbers in this box.

----------end of Part A----------

PART B: APPROVAL TO UNDERTAKE ANEUPLOIDY SCREENING

Item 1: Criteria to be applied to undertake aneuploidy screening.

Are you seeking approval for screening against the following standard criteria?

- The woman or couple is eligible for IVF under the HRT Act; and
  - women over 35 years of age providing eggs; or
  - women with 2 or more miscarriages; or
  - women with more than 2 failed IVF attempts where embryos have been transferred; or
  - women referred by a clinical geneticist with a family history of aneuploidy not caused by translocations or other chromosomal rearrangements.

☐ yes ☐ no*

*If no please provide details of the criteria to be applied and the scientific or medical justification for the criteria.

Please provide attachments if necessary and note the attachment numbers in this box.

Item 2: GENETIC TESTING

Please provide details of the proposed testing and the testing facility to be used by reference to the following standards.

- Laboratories must be accredited by the National Association of Testing Authorities (NATA), (or working towards accreditation within the NATA 3 year cycle) to carry out the type of testing being undertaken.
- Laboratories must meet all relevant NATA and National Pathology Accreditation Advisory Council (NPAAC) requirements for testing.
- Laboratories must participate in an accredited quality assurance program (QAP) for FISH, preferably with a PGD component, which may be offshore.
- Laboratories should adhere to the standards set by the European Society for Reproduction and Embryology (ESHRE) (see. ESHRE website) unless otherwise approved by the Council.
- All PGD testing should confirm with the Australian standard for PGD-AS (if any).

Please provide attachments if necessary and note the attachment numbers in this box.

Item 3: Details of information and counselling to be provided in respect of screening.

Please provide attachments if necessary and note the attachment numbers in this box.

----------**end of Part B**----------

PART C: APPROVAL TO UNDERTAKE TESTING FOR A SPECIFIC CONDITION

Item 1: Details of condition to be tested for.

Does the application have the support of a clinical geneticist (or genetic counsellor if directed as per s 2.4.1 paragraph 43) who has assessed the risk and seriousness of the condition to be tested for?

☐ yes ☐ no

Please attach a report from a clinical geneticist (or genetic counsellor if directed as per s 2.4.1 paragraph 43) addressing the following questions as relevant:

Areas to be addressed	Criteria
Is there a significant risk of a serious genetic abnormality or disease in the context of the family that is requesting the testing?	E
What is the genetic abnormality or disease that is to be tested for?	E
What experience with, and attitude to, the abnormality or disease does the family requesting the testing have?	E
What factors indicate that there is a risk that the embryo will be affected by the genetic abnormality or disease?	E
What is the level of impairment to body functions and structures that is usually associated with the abnormality or disease?	E
What difficulties would a person with the abnormality or disease be expected to have in participating in activities such as learning and applying knowledge, communication, mobility, self care, employment and community, social and civic life?	E
What is the level of support that would be required by a person who has the abnormality or disease?	D
What are the prospects for new and longer term treatments and interventions for the condition?	D
What is the capacity of the family who are requesting the testing to provide the level of support required by a child with the abnormality or disease?	D
What clinical genetic and diagnostic data are to be used in the testing procedure?	D
What other testing options are available?	D
What level of information will be possible from the test, in terms of interpretation, sensitivity and specificity (includes error)?	D
Has the person requesting the testing been provided with counselling about the potential impact of testing and contact information for other persons or organisations that have experience with the condition?	D

Criteria: E = Essential D = Desirable

Item 2: GENETIC TESTING

Please provide details of the proposed testing and the testing facility to be used by reference to the following standards.

- Laboratories must be NATA accredited (or working towards accreditation within the NATA 3 year cycle) to carry out the type of testing being undertaken.
- Laboratories must meet all relevant NATA and NPAAC requirements for testing.
- Laboratories must participate in an accredited QAP for molecular genetics, preferably with a PGD component, which may be offshore
- .
- Laboratories should adhere to the standards set by the European Society for Reproduction and Embryology (ESHRE) (see .ESHRE website) unless otherwise approved by the Council.
- All PGD testing should conform with the Australian standard for PGD-by molecular techniques (if any).
- Laboratories must demonstrate competency in transfer of cell(s)/polar body(s) to a testing laboratory in a state capable of being analysed and free from contaminants.
- Where the cell(s) are to be couriered interstate/overseas for PGD analysis, laboratories must demonstrate that the proposed courier system is safe, accurate and efficient (including quick 'turn-around').

Please provide attachments if necessary and note the attachment numbers in this box.

Item 3: Additional statement from the person requesting testing (optional)

Please provide attachments if necessary and note the attachment numbers in this box.

----------**end of Part C**----------

PART D: APPROVAL FOR DIAGNOSTIC PROCEDURE ON EXCESS ART EMBRYOS

Item 1: Detail of procedure to be carried out.

Please provide attachments if necessary and note the attachment numbers in this box.

Item 2: Criteria by which an embryo will be identified as unfit for implantation.

Please provide attachments if necessary and note the attachment numbers in this box.

Item 3: Details of how the procedure will benefit the woman for whom it is undertaken.

Please provide attachments if necessary and note the attachment numbers in this box.

Item 4: Is approval being sought for the procedure to be part of general clinical practice?

☐ yes* ☐ no

*If yes please provide a copy of the relevant sections of the clinical protocol.

Please provide attachments if necessary and note the attachment numbers in this box.

----------**end of application**----------

Standards for Laboratories performing embryo biopsy

- Laboratories must be licensed under the HRT Act and maintain accreditation by the Reproductive Technology Accreditation Committee (RTAC)

- Laboratories must participate in a QA program recognised by RTAC or NATA

- The biopsy procedure to include setting up of microtools on an inverted microscope, placing oocyte/embryo in microdroplets for the procedure, removal of cell/polar body, placing cell into appropriate transport container

- The biopsy techniques to be used may be acid tryode's or laser as approved by the Council

- Biopsy may be in the form of polar body biopsy, embryo biopsy (at day 3) or blastocyst biopsy as approved by the Council

- Staff performing the biopsy must have demonstrated competency in:

    - the proposed biopsy technique
    - placing the cell(s) in transport vessel, in the case of single gene defects; and,
    - fixing of cell(s) on a slide in the case of chromosome analysis

  through documented evidence of training and use in an animal model or under a licence issued by the NHMRC Licensing Committee.

- Laboratories must demonstrate competency in transfer of cell(s)/polar body(s) to a testing laboratory in a state capable of being analysed and free from contaminants

- Where the cell(s) are to be couriered interstate/overseas for PGD analysis, laboratories must demonstrate that the proposed courier system is safe, accurate and efficient (including quick 'turn-around')

- Where cell(s) from a day 3 embryo are to be couriered interstate/overseas for PGD analysis with the intention of the embryo(s) being transferred in the same cycle, the laboratory/centre must have approval to undertake blastocyst culture as part of clinical procedures

- Embryo(s) from which biopsies have been taken may not be transferred with any other (non-biopsied) embryos in the same treatment cycle

ATTACHMENT 4

Standards for Labs performing Pre-implantation genetic diagnosis- aneuploidy screening (PGD-AS) or other Fluorescence in situ Hybridisation (FISH) based tests

- Laboratories must be accredited by the National Association of Testing Authorities (NATA), (or working towards accreditation within the NATA 3 year cycle) to carry out the type of testing being undertaken.
- Laboratories must meet all relevant NATA and National Pathology Accreditation Advisory Council (NPAAC) requirements for testing.
- Laboratories must participate in an accredited quality assurance program (QAP) for FISH, preferably with a PGD component, that may be offshore.
- Laboratories should adhere to the standards set by the European Society for Reproduction and Embryology (ESHRE) (see .ESHRE website) unless otherwise approved by the Council.
- All PGD testing should conform with the Australian standard for PGD-AS (if any).
- Where a local ART laboratory is carrying out aneuploidy screening, such as using FISH based tests, the clinic must have oversight /supervision for the first 50 patients from a WA-based cytogeneticist experienced in carrying out FISH (such as for pre-natal diagnosis) on a regular (ie weekly) basis.

Following consideration of a report from the cytogeneticist at completion of the 50 cases, the Council may require this oversight to be continued.

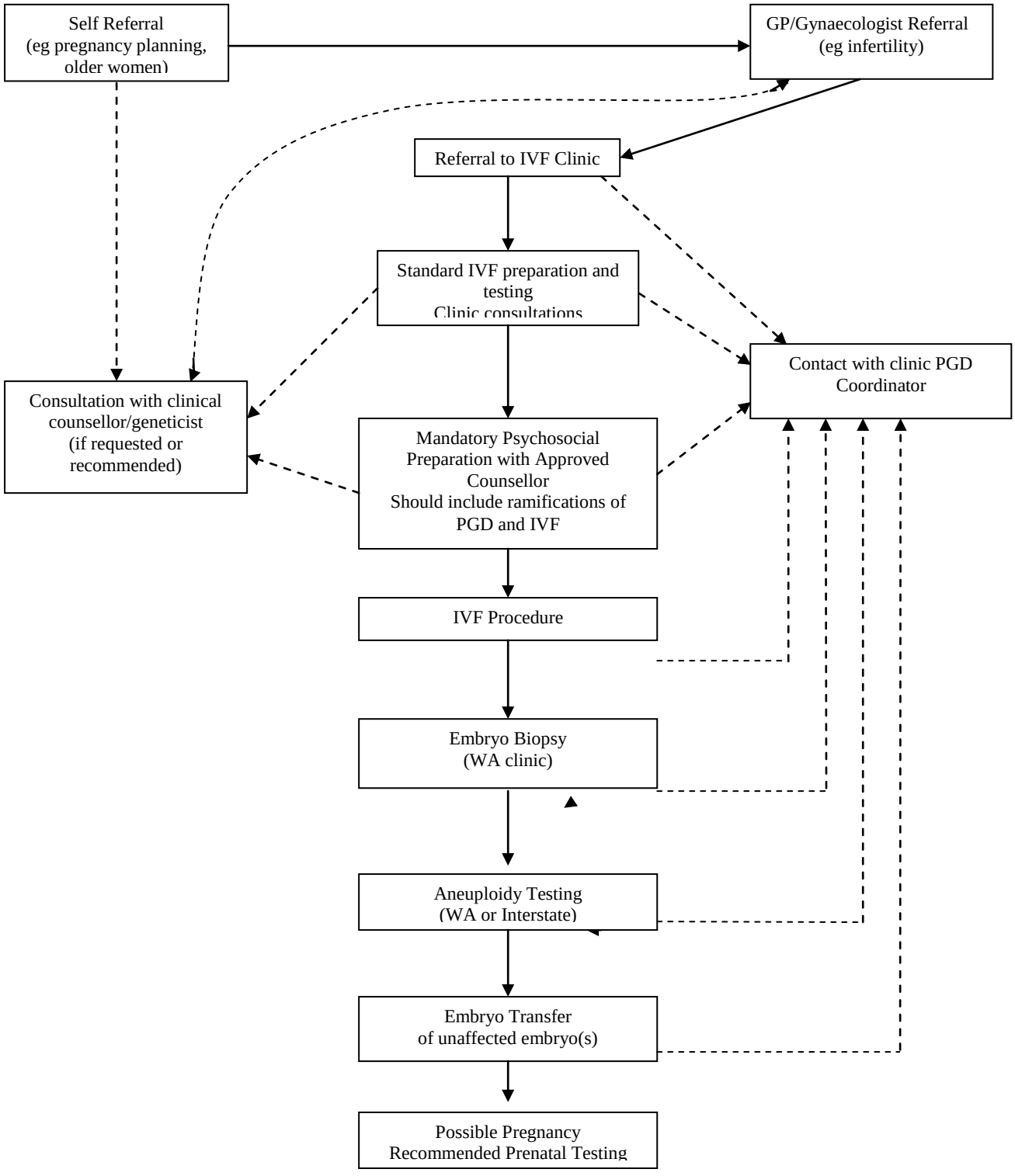
Standards for Labs performing PGD by molecular genetic methods

- Laboratories must be NATA accredited (or working towards accreditation within the NATA 3 year cycle) to carry out the type of testing being undertaken.
- Laboratories must meet all relevant NATA and NPAAC requirements for testing.
- Laboratories must participate in an accredited QAP for molecular genetics, preferably with a PGD component, that may be offshore.
- Laboratories should adhere to the standards set by the European Society for Reproduction and Embryology (ESHRE) (see .ESHRE website) unless otherwise approved by the Council.
- All PGD testing should conform with the Australian standard for PGD-by molecular techniques (if any).

Where testing is to be performed outside a WA-licensed ART clinic, sufficient information must be provided about the Service Level Agreement with the genetic testing laboratory to enable the Council to adequately consider any application.

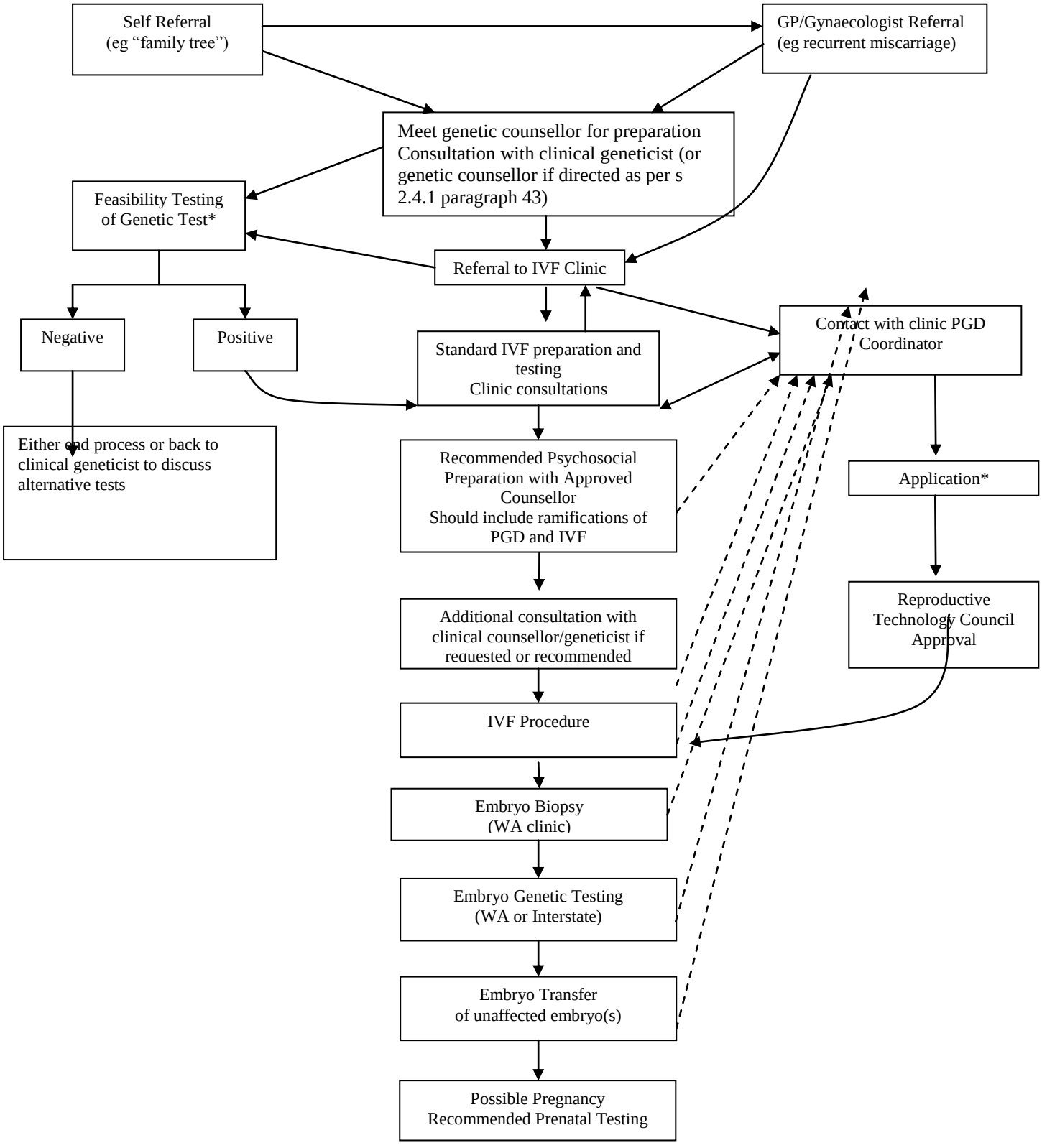
ATTACHMENT 5: FLOW CHARTS FOR COORDINATION OF PRE-IMPLANTATION EMBRYO DIAGNOSTIC PROCEDURES IN WA: TWO SCENARIOS

A. PROCEDURES TO BE CARRIED OUT IN CATEGORIES OF PATIENTS AT HIGHER THAN AVERAGE RISK OF CONCEIVING ABNORMAL EMBRYOS (ANEUPLOIDY SCREENING)



* conditional RTC approval may be obtained prior to availability of results of feasibility testing

B. PGD WHERE PRE-EXISTING DIAGNOSIS INDICATES SIGNIFICANT RISK OF A SERIOUS GENETIC CONDITION IN THE EMBRYO



* conditional RTC approval may be obtained prior to availability of results of feasibility testing