Health Canada Santé Canada

Assisted Human Reproduction Implementation Office

Consulation Background Paper
Licensing Under the *Assisted Human Reproduction Act*

Designation of Controlled Activities and
Qualifications to Undertake Controlled Activities

Fall 2006 Consultations

November 17, 2006

Canada

Table of Contents

Seeking Input Concerning Licensing
Under the *Assisted Human Reproduction Act*

Designation of Controlled Activities and
Qualifications to Undertake Controlled Activities

1. Introduction

The *Assisted Human Reproduction Act* (AHR Act) became law on March 29, 2004. The AHR Act governs the area of assisted human reproduction (AHR) in Canada. The AHR Act has three primary objectives: first, to prohibit unacceptable practices such as human cloning; second, to address the health and safety of Canadians who use AHR procedures to help them build their families; and third, to require that research involving the *in vitro* human embryo, which may help find treatments for infertility and certain diseases, takes place within a controlled environment.

The AHR Act prohibits certain activities, such as human cloning. As well, it prohibits other activities - called controlled activities - unless they are carried out with a licence and in accordance with the regulations. Controlled activities include AHR procedures like *in vitro* fertilization and artificial insemination. Assisted Human Reproduction Canada[1] (the Agency), established by Order in Council on January 12, 2006, will be responsible for licensing administration under the AHR Act.

The majority of procedures performed by AHR centres[2] today fall under the category of controlled activities under the AHR Act and will be allowed only with a licence obtained from the Agency.[3] As the Agency becomes operational and licences are issued,

---

[1]Assisted Human Reproduction Canada (AHRC) has been registered by the Treasury Board of Canada as the official name of the Assisted Human Reproduction Agency of Canada.

[2]For the purposes of this paper, an AHR centre refers to a facility that specializes in the area of infertility medical treatment and often includes two components: a "clinic" where patients undergo examination and treatment undertaken by a medical practitioner and an "AHR laboratory" where specialized procedures such as *in vitro* fertilization take place. Another kind of AHR facility is a "cryopreservation bank" which may be a stand-alone unit or incorporated as part of an AHR centre where tissue, gametes and *in vitro* embryos may be stored.

[3] To allow for the uninterrupted provision of fertility services while the regulatory framework is developed and the Agency is established, section 71 of the AHR Act (the "grandfathering clause") provides an exception to this requirement. It provides that any person who undertakes a controlled activity under the Act in the year prior to sections 10 to 13 coming into force, may continue to perform

inspections of AHR Centres will be conducted to verify that their activities are in compliance with the legislation and regulations.

The purpose of this paper is to provide background information to support consultations on policy proposals being developed for regulations that will designate controlled activities which may be authorized by a licence and the qualifications necessary for persons to be licensed to undertake such activities. This paper will focus on proposals related to the designation and licensing of clinical and laboratory AHR procedures. Controlled activities that are not clinical and laboratory AHR procedures, such as reimbursement of expenditures or research involving an *in vitro* embryo, and the licensing of those activities will be the subject of separate consultations. This paper builds upon the results of the *Workshop on Licensing and Information to be Made Available by the Agency*, held on February 24-25, 2006. The expert advice obtained during that workshop helped Health Canada to develop the proposals set out in this paper for the designation of controlled activities and qualifications.

Following these consultations, a summary report will be prepared and posted on the Health Canada Web site. Information from these consultations, and any future consultation activities, will inform the development of policy options and draft regulations. Once draft regulations are developed they will be pre-published in Part I of the *Canada Gazette* for public review. Subsequently, or in parallel with pre-publication, the draft regulations will be subject to parliamentary review as required by the AHR Act. Following parliamentary review and approval by the Governor in Council, the final regulations will be published in Part II of the *Canada Gazette.*

2. Licensing Provisions under the *Assisted Human Reproduction Act*

Licensing Systems

Licensing systems are widely used in Canada to support federal, provincial, territorial and municipal regulatory requirements. For instance, individuals are required to have a licence to do a variety of activities such as hunting, fishing, driving a motor vehicle or flying an aircraft. The Canadian health sector also uses licensing for many activities such as practicing medicine, dentistry, and dispensing prescription medicines.

---

that activity without a licence until a date set by regulation.

Licensing systems can be employed to reduce health and safety risks by ensuring that licensed activities are performed by qualified persons in appropriate conditions. In addition, licensing systems often include oversight mechanisms to respond to identified and potential problems.

Licensing systems can be useful tools for:

- controlling inherently risky activities;
- ensuring that persons performing the licensed activity are qualified;
- improving compliance with regulations;
- enhancing the capacity for information sharing; and
- improving communication between the licence authorities and the regulated community to achieve a common understanding of related issues.

Licensing Under the AHR Act

The AHR Act provides a framework for a licensing system that will be administered by the Agency. The system aims to ensure that controlled activities (sections 10-12) are undertaken by qualified persons (subsection 40(1)), in appropriate premises (subsection 40(5)) and in accordance with applicable regulations.

Under the AHR Act, the Agency may issue two kinds of licences: a licence to undertake a controlled activity, and a licence to permit the use of premises for a controlled activity. While it is likely that a number of the licence requirements will be set out in regulations, situations may arise that are specific to individual licence applications. As such, the AHR Act allows the Agency to attach terms and conditions to a licence at the time of issue or any time after that (subsection 40(6)).

The Agency is responsible for issuing, amending, renewing, suspending, and revoking licences as set out in sections 40 to 44 of the Act. The Agency may amend a licence or renew an expiring licence with or without an amendment (section 41). The Agency may amend, suspend or revoke a licence for cause (section 42) where there is:

- contravention of the Act or regulations;
- contravention of the terms and conditions of a licence; or
- failure to comply with any measure ordered to be taken under the AHR Act.

The administrative processes for licensing (applying, reviewing, issuing etc.) will be dealt with in a separate consultation paper.

Controlled Activity Licences

Controlled activity licences may be issued under subsection 40(1) and will permit the licensee to undertake one or more of the controlled activities set out in sections 10 to 12. Controlled activity licences may be issued to persons who meet the minimum qualification requirements (to be stated in regulations) for the controlled activity or class of controlled activities they wish to be licenced to undertake.[4] Specific requirements related to the conduct of various controlled activities referred to in sections 10 to 12 will be the subject of separate consultation documents.

Premises Licences

Premises licenses will be issued under subsection 40(5) of the AHR Act to owners or operators of any premises permitting the use of those premises for a controlled activity. A separate consultation paper will be developed to identify issues and options and to solicit comments on premises licences.

3. Issues

Health Canada has identified two key issues related to controlled activity licences for AHR procedures.

1. The designation of controlled activities for the purpose of licensing AHR procedures.

2. The specification of qualifications required of an applicant to be licenced by the Agency to undertake a controlled activity.

3.1 Designation of Controlled Activities

A controlled activity is generically defined in section 3 of the Act as "an activity that may not be undertaken except in accordance with sections 10 to 12." Sections 10 to 12 provide the activities that will be controlled (refer to Box 1) and impose two general

[4]Licensed persons must also comply with the Act and regulations in undertaking controlled activities.

requirements on persons wishing to undertake a controlled activity - they must have a licence and they must conduct the activity in accordance with any regulations made under the Act.

BOX 1: Controlled Activities

Use of human reproductive material
10. (1) No person shall, except in accordance with the regulations and a licence, alter, manipulate or treat any human reproductive material for the purpose of creating an embryo.

Use of *in vitro* embryos
10. (2) No person shall, except in accordance with the regulations and a licence, alter, manipulate, treat or make any use of an in vitro embryo.

Keeping and handling gametes and embryos
10. (3) No person shall, except in accordance with the regulations and a licence, obtain, store, transfer, destroy, import or export

(a) a sperm or ovum, or any part of one, for the purpose of creating an embryo; or
(b) an in vitro embryo, for any purpose.

Transgenics
11. (1) No person shall, except in accordance with the regulations and a licence, combine any part or any proportion of the human genome specified in the regulations with any part of the genome of a species specified in the regulations.

Reimbursement of expenditures
12. (1) No person shall, except in accordance with the regulations and a licence,

(a) reimburse a donor for an expenditure incurred in the course of donating sperm or an ovum;
(b) reimburse any person for an expenditure incurred in the maintenance or transport of an in vitro embryo; or
(c) reimburse a surrogate mother for an expenditure incurred by her in relation to her surrogacy.

Reimbursement for loss of work-related income - Surrogate mother
12. (3) No person shall reimburse a surrogate mother for a loss of work-related income incurred during her pregnancy, unless

(a) a qualified medical practitioner certifies, in writing, that continuing to work may pose a risk to her health or that of the embryo or foetus; and
(b) the reimbursement is made in accordance with the regulations and a licence.

Given the rapid pace of change in the field of AHR and related research, section 10 is necessarily broad. In order to implement a licensing system, controlled activities, which may be authorized by a licence, must first be designated.

Authority to do this is found in paragraph 65(1)(c) of the AHR Act which states:

> *65.(1) The Governor in Council may make regulations ....*
>
> *(c) for the purposes of sections 10 and 11, designating controlled activities or classes of controlled activities that may be authorized by a licence;*

Following a consultation with representatives from various AHR centres[5], Health Canada has identified various clinical and laboratory AHR procedures within the scope of section 10 (refer to Box 2) that are performed at AHR centres and could be designated as controlled activities requiring a licence.[6] Please refer to Appendix B for a description of the AHR procedures listed in Box 2.

Through designation, the controlled activities that may be authorized by a licence (either individually or as part of a class) are specified. Persons who wish to perform a designated controlled activity apply for a licence to undertake that controlled activity or class of controlled activities. The designation of controlled activities may also be used to:

- mitigate risks through the alignment of qualifications to undertake a controlled activity;
- mitigate risks through the alignment of requirements for licensing of premises; and
- facilitate the administration of the licensing as well as the monitoring of compliance within the licensing system.

---

[5]Health Canada (2006) *Meeting Report: Workshop on Licensing and on Information Available from the Agency*. Available at: http://healthcanada.gc.ca/reproduction

[6]This list represents the core procedures in the provision of AHR services to prospective patients/consumers, rather than an exhaustive list of all controlled activities under section 10. Those controlled activities within the scope of section 10 which are not directly related to the provision of AHR services, such as the creation of an *in vitro* embryo for the purpose of improving or providing instruction in assisted reproduction procedures or the use of an *in vitro* embryo for the purpose of research, will be the subject of future consultations.

Box 2: AHR Procedures

Semen/Sperm Handling - Group 1
- semen/sperm obtaining
- semen/sperm processing
- semen/sperm cryopreservation
- sperm storage
- sperm thawing
- sperm transport
- sperm import
- sperm export
- sperm destruction/disposal

Testicular Tissue Handling - Group 2
- testicular tissue obtaining
- testicular tissue processing
- testicular tissue cryopreservation
- testicular tissue storage
- testicular tissue thawing
- testicular tissue transport
- testicular tissue import
- testicular tissue export
- testicular tissue destruction/disposal

Oocyte[7] Handling - Group 3
- oocyte obtaining
- oocyte processing
- oocyte *in vitro* maturation
- oocyte polar body biopsy
- oocyte cryopreservation
- oocyte storage
- oocyte thawing
- oocyte transport
- oocyte import
- oocyte export
- oocyte destruction/disposal

Ovarian Tissue Handling - Group 4
- ovarian tissue obtaining
- ovarian tissue processing
- ovarian tissue cryopreservation

Ovarian Tissue Handling - Group 4 cont.
- ovarian tissue storage
- ovarian tissue thawing
- ovarian tissue transport
- ovarian tissue import
- ovarian tissue export
- ovarian tissue destruction/disposal

***In-vitro* Fertilization (IVF) and *In vitro* Embryo Handling - Group 5**
- IVF with insemination
- IVF with intracytoplasmic sperm injection (ICSI)
- *in vitro* embryo obtaining
- *in vitro* embryo culture and assessment
- *in vitro* embryo biopsy
- assisted hatching
- *in vitro* embryo cryopreservation
- *in vitro* embryo storage
- *in vitro* embryo thawing
- *in vitro* embryo transport
- *in vitro* embryo import
- *in vitro* embryo export
- *in vitro* embryo destruction/disposal
- preimplantation genetic diagnosis

Clinical Retrieval and Transfer Procedures - Group 6
- controlled ovarian hyperstimulation
- artificial insemination
- oocyte retrieval
- ovarian tissue retrieval
- gamete intrafallopian transfer (GIFT)
- *in vitro* embryo transfer
- zygote intrafallopian transfer (ZIFT)/tubal embryo transfer (TET)
- ovarian tissue transplantation
- clinically retrieving sperm and/or testicular tissue

[7]To ensure consistency with the scientific literature, the term oocyte has been used in this consultation paper and related documents rather than the term ovum which is used in the AHR Act. Oocyte, as used throughout this document, has the same meaning as the term ovum as defined in the AHR Act to mean "a human ovum, whether mature or not".

Designation Proposal

For discussion and consideration, it is proposed that each of the bulleted activities listed in Box 2 be individually designated as controlled activities. Once designated, these activities may be authorized by a licence and undertaken in accordance with the regulations.[8] Activities or applications of activities on this list that may be experimental at this time (e.g., oocyte cryopreservation, ICSI using spermatids) may be subject to additional licensing limitations or subject to a limited number of licenses allowing for clinical trials, which will be the subject of future consultations.

Persons who wish to be licensed to undertake a controlled activity would apply for a licence identifying that specific activity in their application. Persons who wish to be licensed to undertake a number of different controlled activities, would apply for a licence by identifying each of the activities in their application. In this way, individual applicants are able to apply for a licence for only those activities they wish to undertake. As there are no pre-defined classes of activities, applicants would be required to apply and be licensed for all of activities they may undertake in the conduct of their AHR procedures in order to be authorized to undertake those activities. In practical terms, an applicant would select the activities they wish to be authorized to undertake from the list of designated activities on an application form and submit the required documentation and proof of qualifications to the Agency to apply for a licence to undertake those activities.

The qualifications for each individually designated controlled activity would be specified in the regulations (to be discussed in greater detail in the following section).

By individually designating the activities, the qualifications are directly linked to the activity. Individual designation provides maximum flexibility for applicants by allowing the selection of the unique bundle of activities that the applicant wishes to be licensed to undertake. In this way, the system accommodates a range of different scenarios related to the services an individual practitioner or corporation may undertake in the field of AHR. This flexibility may also introduce some durability to the licensing of controlled activities in the face of changes in the AHR field and sector.

[8]In some very limited cases, a designated activity (in whole, part or under certain circumstances) may, alternatively, be exempted from requirements of the AHR Act. One possible example would be an exemption for home insemination.

3.2 Qualifications Required to Undertake Controlled Activities

As previously stated, controlled activity licences would be issued under subsection 40(1) to persons having the qualifications stated in the regulations, and would permit the licensee to undertake one or more of the controlled activities set out in sections 10 to 12. A key term in subsection 40(1) is "to undertake". This term may have somewhat different applications in different contexts.

With respect to individuals, to undertake a controlled activity can include the performance of the activity or taking responsibility for or supervising the performance of the activity where the individual is also involved to some degree in the performance of the activity. The Act also allows the licensing of corporations. Corporations can, of course, be responsible for the controlled activities undertaken by their employees, who must actually perform the controlled activities in question and themselves be licensed. This paper addresses the qualifications of individuals to undertake controlled activities, whether within a corporation or an unincorporated practice.

In order to implement a licensing system, the qualifications for licences for controlled activities or classes of controlled activities which may be authorized by a licence must be specified.

Authority to do this is found in paragraph 65(1)(j) of the AHR Act which states:

> *65.(1) The Governor in Council may make regulations ....*
>
> *(j) respecting the qualifications for licences for controlled activities or any class of controlled activities;*

Qualifications of an applicant can be assessed in three key areas:

- education;
- technical/scientific skills and competencies; and
- relevant work experience.

The Agency may consider a number of different ways to verify qualifications including:

- certified copies of academic credentials;
- proof applicant is a member in good standing in a recognized professional association;
- detailed description of work history;

- copies of training logs;
- letters of reference;
- list of publications authored or co-authored; and
- certified results of written examinations by recognized bodies.

The proposed qualifications for each activity are included in Appendix A.

Mitigating Risk Through Qualifications

A key goal of licensing controlled activities is to mitigate the risks of controlled activities (primarily health and safety risks). One way to mitigate the risk is to ensure that the activities are performed by appropriately qualified persons. As such, the qualifications which are specified should be aligned with the skills, competencies and experience required to safely and effectively undertake the activities. Internationally there are a range of training and certification programs relevant to AHR; however, in Canada there are very few formal education, training or certification programs related to the practice of AHR, particularly with respect to AHR laboratory procedures. In previous consultations, representatives of AHR centres have said that their employees have a wide range of credentials and emphasized the importance of on-the-job training in AHR laboratories.[9] In the Canadian context, the knowledge and skills necessary to safely perform AHR procedures must be obtained through a combination of education, formal on-the-job training and experience in the AHR sector.

Some studies have shown that the skills and technique of the individual performing a procedure can have a significant impact on the outcome of the procedure[10] both in terms of the particular technique employed and on the results obtained through analysis of reproductive material. In addition, the presence of a learning curve in the performance of AHR techniques has been documented[11]. As such, formal training and documented

[9]Health Canada, 2006.

[10] See for instance: Dumoulin, J.C.M., Coonen, E., Bras, M. *et al* (2001) Embryo development and chromosomal anomalies after ICSI: effect of the injection procedure. *Human Reproduction*, Vol 16, No.2, 306-312; Eustache, F., Auger, J. (2003) Inter-individual variability in the morphological assessment of human sperm: effect of the level of experience and use of standard methods. *Human Reproduction*, Vol 18, No.5, 1018-1022; Hearns-Stokes, R.M., Miller, B.T., Scott, L. *et al*. (2000) Pregnancy rates after embryo transfer depend on the provider at embryo transfer. Fertility and Sterility, Vol. 74, No. 1, 80-86.

[11] See for instance: Katz, E., Watts, L.D., Wright, K.E. *et al*. (1996) Effect of incremental time experience on the results of *in vitro* fertilization with intracytoplasmic sperm injection (ICSI). *Journal of Assisted Reproduction and Genetics*., Vol 13, No.6, 345-350; Papageorgiou, T.C., Hearns-Stokes, R.M.,

experience performing the procedure under supervision are recommended to minimize inter-individual variability and mitigate operator-specific risks[12]. Internationally, guidelines and standards have been developed specifying the kinds of training and experience an individual who performs AHR procedures should have in order to mitigate the risks related to inexperience, and the variability in outcomes between different providers and technicians. Regulators and professional organizations are recommending or requiring that individuals who perform AHR procedures have a combination of formal training and on-the-job-training[13].

Looking at the key risks for each controlled activity, one of our key objectives in specifying qualifications required to be licensed, is to specify qualifications that should be helpful in mitigating the risks of those procedures. In addition to the health and safety risks of the procedures themselves, the risks to be mitigated include risks linked to the way the procedure is performed such as: contamination or infection; mislabeling reproductive material or embryos; mishandling reproductive material or embryos; and using equipment or reagents which have not been properly maintained or prepared.

Based on expert advice, our knowledge of AHR practices and a search of relevant literature we have identified the key risks for each type of activities and the way in which the qualifications (presented in Appendix A) are thought to be useful qualifications for mitigating those risks. These are discussed in greater detail below.

Levi, A.J. *et al.* (2000) Training providers in embryo transfer: the identification of a learning curve among reproductive endocrinology fellows. *Fertility and Sterility*, Vol 74, No.3, Supp. 1, S205.

[12]See for instance: Björndahl, L., Barratt, C.L.R., Fraser, L.R. *et al.* (2002) ESHRE basic semen analysis courses 1995-1999: immediate beneficial effects of standardized training. *Human Reproduction*, Vol 17, No. 5, 1299-1305; Ginsburg, E.S., Jackson, K.V. and Racowsky, K. (2002) Defining the optimum number and frequency of embryo transfers in fellowship training. *Fertility and Sterility*, Vol.78, Supp. 1, S7-S8.

[13]See for instance: *Human Fertilisation and Embryology Authority (2003) Code of Practice, 6th Edition*; Practice Committee of the American Society for Reproductive Medicine, Society for Assisted Reproductive Technology (2003) *Revised Minimum Standards for practices offering assisted reproductive technologies.*

Semen /Sperm Handling (Group 1) and Testicular Tissue Handling (Group 2)

Key Risks

The following key risks for these procedures have been identified:

- loss of identity of the sample due to poor or improper documentation;[14]
- loss of reproductive capacity through the loss of gametes due to sample contamination, exposure to extreme or toxic conditions or equipment failure -could require repeat of cycle;[15]
- potential for the transmission of infection (through use of infected material or through contamination) to the woman or the child;[16]
- potential for defect or abnormal development in an embryo due to contamination or mishandling of the gametes or embryo and where the embryo is transferred and successfully implants, risk of harm to the woman (e.g., miscarriage) or to the child;[17]
- reduction in reproductive capacity, fertilization rates or implantation rates; and abnormal embryo development, chromosomal anomalies or congenital malformations, due to less than optimal gametes or embryos being selected or damage to gametes or embryos due to improper analysis or processing methods (technique related risks) - could require additional cycles (and incur the associated health risks) to achieve desired results;[18] and
- unauthorized disclosure of information, violation of personal privacy.

---

[14] See for instance: Mortimer, S.T., Mortimer, D. (2004) Quality and Risk Management in IVF the Laboratory. Cambridge University Press, Cambridge, U.K.; van Kooij, R.J., Peeters, M.F., te Velde, E.R. (1997) Twins of mixed races: consequences for Dutch IVF laboratories. *Human Reproduction*, Vol. 12 No. 12, 2585-2587.

[15]See for instance: Steyaert,S.R., Leroux-Roels, G.G., Dhont, M. (2000) Infections in IVF: review and guidelines. *Human Reproduction Update*, Vol. 6 No. 5, 432-441; Tomlinson, M. (2005) Managing risk associated with cryopreservation. *Human Reproduction*, Vol. 20 No. 7, 1751-1756.

[16]Steyaert *et. al.*, 2000.

[17]See for instance: Steyaert *et. al.*, 2000; Dumoulin, J.C.M., Coonen, E., Bras, M. *et al* (2001) Embryo development and chromosomal anomalies after ICSI: effect of the injection procedure. *Human Reproduction*, Vol. 16, No.2, 306-312.

[18]See for instance: Dumoulin *et. al.*, 2001; Eustache, F., Auger, J. (2003) Inter-individual variability in the morphological assessment of human sperm: effect of the level of experience and use of standard methods. *Human Reproduction*, Vol 18, No.5, 1018-1022; Mortimer, D. (2000) Sperm preparation methods. *Journal of Andrology*, Vol. 21, No. 3, 357-366.

Qualifications

Our analysis suggests that the proposed qualifications outlined in Appendix A would be helpful in mitigating the risks associated with these procedures. The proposed requirement for a Bachelor of Science degree or certification as a Medical Technologist combined with relevant on-the-job training is thought to be necessary to ensure that a licensee who undertakes these procedures has a sound theoretical and practical background concerning the management of relevant physical and biological hazards (e.g., pH, temperature, radiation, viral and bacterial agents) and has gained sufficient practical experience in the procedures in order to carry them out safely and successfully. Proposed requirements for a letter from the training supervisor attesting that the applicant is sufficiently trained and competent to perform the procedure is thought to be helpful in ensuring a licensee is qualified to: prepare documents related to sample identification and tracking; interpret and follow legislative requirements and standard operating procedures (SOPs); ensure that equipment and reagents are appropriately maintained and used; and safely transport, import or export gametes.

Oocyte Handling (Group 3), Ovarian Tissue Handling (Group 4), *In vitro* Fertilization and *In vitro* Embryo Handling (Group 5)

Key Risks

The following key risks for these procedures have been identified:

- loss of identity of the sample due to poor or improper documentation;[19]
- loss of reproductive capacity through the loss of gametes due to sample contamination, exposure to extreme or toxic conditions or equipment failure -could require repeat of cycle;[20]
- potential for the transmission of infection (through use of infected material or through contamination) to the woman or the child;[21]

[19]See for instance: Mortimer *et al*, 2004; van Kooij et al 1997.

[20]See for instance: Wang, W.H., Meng, L., Hackett, R. J., *et. al.* (2001) Limited recovery of meiotic spindles in living human oocytes after cooling-rewarming observed using polarized light microscopy. Human Reproduction, Vol. 16, No.11, 2374-2378; Tomlinson, 2005.

[21]Steyaert *et. al.*, 2000.

- potential for defect or abnormal development in an embryo due to contamination or mishandling of the gametes or embryo and where the embryo is transferred and successfully implants, risk of harm to the woman (e.g., miscarriage) or to the child;[22]
- reduction in reproductive capacity, fertilization rates or implantation rates; and abnormal embryo development, chromosomal anomalies or congenital malformations, due to less than optimal gametes or embryos being selected or damage to gametes or embryos due to improper analysis or processing methods (technique related risks) - could require additional cycles (and incur the associated health risks) to achieve desired results;[23] and
- unauthorized disclosure of information, violation of personal privacy.

Qualifications

Our analysis suggests that the proposed qualifications outlined in Appendix A would be helpful in mitigating the risks associated with these procedures. The proposed requirement for a Bachelor of Science degree or certification as a Medical Technologist combined with relevant on-the-job training is thought to be necessary to ensure that a licensee who undertakes these procedures has a sound theoretical and practical background concerning the management of relevant physical and biological hazards (e.g., pH, temperature, radiation, viral and bacterial agents) and has gained sufficient practical experience in the procedures in order to carry them out safely and successfully. Proposed requirements for a letter from the training supervisor attesting that the applicant is sufficiently trained and competent to perform the procedure is thought to be helpful in ensuring a licensee is qualified to: prepare documents related to sample identification and tracking; interpret and follow legislative requirements and standard operating procedures (SOPs); ensure that equipment and reagents are appropriately maintained and used; and safely transport, import or export gametes.

The proposed training for these procedures is different than for semen /sperm handling and testicular tissue handling procedures as it is thought that training in andrology would not provide sufficient knowledge and training for the identification, selection and maturation requirements of oocytes and embryos. Furthermore, in most cases, oocytes are more limited in number than spermatozoa and therefore the impact of mishandling oocytes (and embryos) is greater on (the potential loss of) reproductive capacity.

---

[22]See for instance: Steyaert *et. al*., 2000; Wang W.H., *et. al*., 2001; Dumoulin *et. al*., 2001.

[23]See for instance: Dumoulin *et. al*., 2001., Wang W.H., *et. al*., Mortimer *et. al*..

Clinical Retrieval and Transfer Procedures (Group 6)

Key Risks

The following key risks for these procedures have been identified:

- controlled ovarian hyperstimulation associated risks (e.g., ovarian hyperstimulation syndrome);[24]
- surgical risks associated with gamete retrieval or transplantation (e.g., infection, damage to organs);[25]
- loss of identity of gametes/embryo/tissue due to poor or improper documentation - could result in the transfer of incorrect gametes, embryos, or tissue;[26]
- poor transfer techniques could result in injury to the woman, reduced implantation rates[27];
- potential for the transmission of infection (through use of infected material or through contamination) to the woman or the child;[28]
- multiple pregnancies - numerous adverse health conditions to both mother and child e.g., premature labour, haemorrhage, high blood pressure, increase in perinatal death;[29]

[24]Rizk, B., Nawar, M.G., (2004) Ovarian hyperstimulation syndrome. In: *Good clinical practice in assisted reproduction.* Eds: Serhal P, Overton C. Cambridge University Press, 146-166.

[25]Ludwig, A.K., Glawatz, M., Griesinger, G. *et. al.* (2006) Perioperative and post-operative complications of transvaginal ultrasound-guided oocyte retrieval: prospective study of >1000 oocyte retrievals. Human Reproduction Advance Access published on July 27, 2006, DOI 10.1093/humrep/del278.

[26]See for instance: Mortimer *et. al.*, 2004; van Kooij *et. al.* 1997.

[27]See for instance: Hearns-Stokes *et. al.* 2000; Quintans, C., Pasqualini, S. (2001) Clinical Practice of Embryo Transfer. *Reproductive BioMedicine Online*, Vol 4 No. 1, 83-92.

[28]Steyaert *et. al.*, 2000.

[29]Reynolds, M.A., Schieve L.A., Martin, J.A.. (2003) Trends in multiple births conceived using assisted reproductive technology, United States, 1997-2000. *Pediatrics*, Vol 111, 1159-1162.; Pinborg, A., Loft, A. Rasmussen, S. *et al* (2004) Neonatal outcomes in a Danish National cohort of 3438 IVF/ICSI and 10362 non-IVF/ICSI twins born between 1995 and 2000. Human Reproduction, Vol. 19, 435-41.

- loss of reproductive capacity through the loss of gametes/embryos due to infection, exposure to extreme conditions without proper pre-treatment, failure to obtain gametes/gonadal tissue or other mishandling at any stage;[30] and
- unauthorized disclosure of information, violation of personal privacy.

Qualifications

Our analysis suggests that the proposed qualifications outlined in Appendix A would be helpful in mitigating the risks associated with these procedures. The proposed qualification are considered to be necessary to ensure that the licensee who undertakes these procedures has a sound theoretical and practical background in the relevant medical disciplines and this is considered important in reducing risks to health and safety of patients and offspring. The academic qualifications for these procedures are different for the other groups of procedures as the procedures in this group are medical procedures which are only allowed to be performed by licenced physicians with specialized training in relevant fields of family medicine, obstetrics and gynaecology, or urology/andrology.

[30]See for instance: Bustillo, M. (2003) Unsuccessful oocyte retrieval: technical artefact or genuine 'empty follicle syndrome'? *Reproductive BioMedicine Online*, Vol. 8, No. 1, 59-67; Dumoulin *et. al.*, 2001., Wang W.H., *et. al*., Mortimer *et. al.*.

APPENDIX A: Proposed Qualifications

The qualifications presented below are for discussion and consideration. Tables 1 to 6 show the various AHR procedures grouped for ease of reference by human reproductive material and procedure type. Proposed academic and training qualifications required for individuals who wish to be licenced to undertake a controlled activity are indicated below each table.

When reviewing this proposal, please consider the following questions:

- In addition to the presented qualifications, should the regulations require that individuals in a supervisory capacity have additional qualifications such as two years work experience as a licensee in the relevant controlled activities?
- Are the proposed qualifications sufficient to mitigate the health and safety risks related to the competencies of the individual performing a given controlled activity?
- Should alternative or additional credentials, certifications, training requirements or other qualifications be considered for any of the designated activities (e.g., completion of a different degree or diploma program, alternate measures of technical competency such as degeneration or damage rates, alternate number of procedures performed under direct supervision)?
- With respect to AHR laboratory procedures, to what extent is experience performing AHR procedures in non-human systems relevant?

Table 1 - Group 1. Semen /Sperm Handling

No.	AHR Procedures
1.1	semen/sperm obtaining
1.2	semen/sperm processing
1.3	semen/sperm cryopreservation
1.4	sperm storage
1.5	sperm thawing
1.6	sperm transport
1.7	sperm import
1.8	sperm export
1.9	sperm destruction/disposal

Group 1. Qualifications

AHR Procedures	Qualifications[31]
1.1 - 1.5	Education: • Bachelor's degree in chemistry, biology, medical technology or other health or medical science from an accredited institution; or • Certification as a medical technologist from an accredited institution. Training: • Documented training in andrology lab protocols, relevant guidelines and legislation, and AHR laboratory safety. • Documented training in each procedure which includes performing each procedure successfully under supervision at least 30 times[32]. • Submission of a letter from training supervisor, to be verified by the Agency, attesting that the applicant is sufficiently trained and competent to perform the procedure.
1.6 - 1.9	• Qualified for 1.2, 1.3, 1.4 or 1.5 and successful completion of appropriate[33] training. • Submission of a letter from training supervisor, to be verified by the Agency, attesting that the applicant is sufficiently trained and competent to perform the procedure.

[31]Qualifications throughout this appendix have been adapted from the *Revised guidelines for human embryology and andrology laboratories* by The Practice Committee of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology. Fertility and Sterility, Vol., 82, No. 6, December 2004.

[32] Ibid.

[33]Appropriate training means training as set out in the regulations and tailored to the activity in question (transport, import or export) for the biological material being handled (sperm/semen, ova, embryo or tissues) and includes training in the packaging, labelling and documentation requirements set out by the relevant provincial or federal authority.

Table 2 - Group 2. Testicular Tissue Handling

No.	AHR Procedures
2.1	testicular tissue obtaining
2.2	testicular tissue processing
2.3	testicular tissue cryopreservation
2.4	testicular tissue storage
2.5	testicular tissue thawing
2.6	testicular tissue transport
2.7	testicular tissue import
2.8	testicular tissue export
2.9	testicular tissue destruction/disposal

Group 2. Qualifications

AHR Procedures	Qualifications
2.2 - 2.5	Education: • Bachelor's degree in chemistry, biology, medical technology or other health or medical science from an accredited institution; or • Certification as a medical technologist from an accredited institution. Training: • Documented training in andrology lab protocols, relevant guidelines and legislation, and AHR laboratory safety. • Documented training in each procedure which includes performing each procedure successfully under supervision at least 30 times. • Submission of a letter from training supervisor, to be verified by the Agency, attesting that the applicant is sufficiently trained and competent to perform the procedure.
2.1, 2.6 - 2.9	• Qualified for 2.2, 2.3, 2.4 or 2.5 and successful completion of appropriate training. • Submission of a letter from training supervisor, to be verified by the Agency, attesting that the applicant is sufficiently trained and competent to perform the procedure.

Table 3 - Group 3. Oocyte Handling

No.	AHR Procedures
3.1	oocyte obtaining
3.2	oocyte processing
3.3	oocyte in vitro maturation
3.4	oocyte polar body biopsy
3.5	oocyte cryopreservation
3.6	oocyte storage
3.7	oocyte thawing
3.8	oocyte transport
3.9	oocyte import
3.10	oocyte export
3.11	oocyte destruction/disposal

Group 3. Qualifications

AHR Procedures	Qualifications
3.2 - 3.7	Education: • Bachelor's degree in chemistry, biology, medical technology or other health or medical science from an accredited institution; or • Certification as a medical technologist from an accredited institution. Training: • Documented training in embryology lab protocols, relevant guidelines and legislation, and AHR laboratory safety. • Documented training in each procedure which includes performing each procedure successfully under supervision at least 30 times. • Submission of a letter from training supervisor, to be verified by the Agency, attesting that the applicant is sufficiently trained and competent to perform the procedure.
3.1, 3.8 - 3.11	• Qualified for 3.2, 3.5 or 3.6 and successful completion of appropriate training. • Submission of a letter from training supervisor, to be verified by the Agency, attesting that the applicant is sufficiently trained and competent to perform the procedure.

Table 4 - Group 4. Ovarian Tissue Handling

No.	AHR Procedures
4.1	ovarian tissue obtaining
4.2	ovarian tissue processing
4.3	ovarian tissue cryopreservation
4.4	ovarian tissue storage
4.5	ovarian tissue thawing
4.6	ovarian tissue transport
4.7	ovarian tissue import
4.8	ovarian tissue export
4.9	ovarian tissue destruction/disposal

Group 4. Qualifications

AHR Procedures	Qualifications
4.2 - 4.5	Education: • Bachelor's degree in chemistry, biology, medical technology or other health or medical science from an accredited institution; or • Certification as a medical technologist from an accredited institution. Training: • Documented training in embryology lab protocols, relevant guidelines and legislation, and AHR laboratory safety. • Documented training in each procedure which includes performing each procedure successfully under supervision at least 30 times. • Submission of a letter from training supervisor, to be verified by the Agency, attesting that the applicant is sufficiently trained and competent to perform the procedure.
4,1, 4.6 - 4.9	• Qualified for 4.2, 4.3, or 4.4 and successful completion of appropriate training. • Submission of a letter from training supervisor, to be verified by the Agency, attesting that the applicant is sufficiently trained and competent to perform the procedure.

Table 5 - Group 5. *In vitro* Fertilization and *In vitro* Embryo Handling

No.	AHR Procedures
5.1	*in vitro* fertilization (IVF) with insemination
5.2	IVF with intracytoplasmic sperm injection (ICSI)
5.3	*in vitro* embryo obtaining
5.4	*in vitro* embryo culture and assessment
5.5	*in vitro* embryo biopsy
5.6	assisted hatching
5.7	*in vitro* embryo cryopreservation
5.8	*in vitro* embryo storage
5.9	*in vitro* embryo thawing
5.10	*in vitro* embryo transport
5.11	*in vitro* embryo import
5.12	*in vitro* embryo export
5.13	*in vitro* embryo destruction/disposal
5.14	preimplantation genetic diagnosis

Group 5. Qualifications

AHR Procedures	Qualifications
5.1, 5.2, 5.4 - 5.9	Education: • Bachelor's degree in chemistry, biology, medical technology or other health or medical science from an accredited institution; or • Certification as a medical technologist from an accredited institution. Training: • Documented training in embryology lab protocols, relevant guidelines and legislation, and AHR laboratory safety. • Documented training in each procedure which includes performing each procedure successfully under supervision at least 30 times. • Submission of a letter from training supervisor, to be verified by the Agency, attesting that the applicant is sufficiently trained and competent to perform the procedure.
5.3, 5.10 - 5.13	• Qualified for 5.4, 5.7 or 5.8 and successful completion of appropriate training. • Submission of a letter from training supervisor, to be verified by the Agency, attesting that the applicant is sufficiently trained and competent to perform the procedure.
5.14	A duly qualified medical or clinical geneticist who has been granted certification by the Canadian College of Medical Geneticists.

Table 6 - Group 6. - Clinical Retrieval and Transfer Procedures

No.	AHR Procedures
6.1	controlled ovarian hyperstimulation
6.2	artificial insemination
6.3	oocyte retrieval
6.4	ovarian tissue retrieval
6.5	gamete intrafallopian transfer (GIFT)
6.6	*in vitro* embryo transfer
6.8	zygote intrafallopian transfer (ZIFT)/tubal embryo transfer (TET)
6.9	ovarian tissue transplantation
6.10	clinically retrieving sperm and/or testicular tissue

Group 6. Qualifications

AHR Procedures	Qualifications
6.1 -6.2	A duly qualified medical practitioner who has been granted certification by the Royal College of Family Physicians of Canada or the Royal College of Physicians and Surgeons of Canada in obstetrics and gynaecology and who has received specialized training acceptable to the responsible provincial authority where such a requirement exists.
6.3 - 6.9	A duly qualified medical practitioner who has been granted certification by the Royal College of Physicians and Surgeons of Canada in obstetrics and gynaecology.
6.10	A duly qualified medical practitioner who has been granted certification by the Royal College of Physicians and Surgeons of Canada in urology.

APPENDIX B

Description of AHR Procedures

Artificial Insemination

Artificial insemination refers to procedures which place sperm (or semen) into the female reproductive tract by artificial means. It includes intrauterine insemination (IUI), intracervical insemination (ICI), and intravaginal insemination (IVI).

Intrauterine insemination (IUI)

IUI is the most commonly used artificial insemination method. The objective of IUI is to bypass the filtering effect of the cervical mucus by placing thousands of motile spermatozoa directly into the uterine cavity by means of a catheter. This method of artificial insemination may be performed only after adequate *in vitro* sperm processing. To maximize the chances of conceiving, IUI is often combined with controlled ovarian hyperstimulation (COH).

Intracervical insemination (ICI)

ICI is relatively simple, inexpensive and non-invasive technique and does not require *in vitro* sperm preparation. The semen sample is placed into the cervix using a catheter.

Intravaginal insemination (IVI)

IVI is a type of artificial insemination where sperm is placed directly inside the vagina using a needle-less syringe in order to increase the chances of fertilization.

Assisted hatching

Assisted hatching is a micromanipulation procedure in which the zona pellucida of an *in vitro* embryo (usually at the 8-cell stage or blastocyst stage) is artificially thinned or perforated by chemical, mechanical or laser-assisted methods to assist separation of the blastocyst from the zona pellucida. Different terms such as: partial zona dissection, zona drilling, zona cracking, and zona thinning are commonly used to describe laboratory procedures that manipulate a portion of zona pellucida.

Cleavage-stage blastomere biopsy - See: *In vitro* embryo biopsy

Clinically retrieving sperm and/or testicular tissue

Clinically retrieving sperm and/or testicular tissue involves any medically-assisted collection or retrieval of semen, sperm or testicular tissue including surgical sperm retrieval, vibratory stimulation and electrostimulation.

Sperm or testicular tissue can be surgically retrieved from different parts of the male reproductive tract such as the epididymis, testis, vas deferens or seminal vesicles in cases of uncorrectable obstructive or non-obstructive azoospermia (no sperm in ejaculate). Surgically retrieved sperm is always used in conjunction with intracytoplasmic sperm injection. The most common methods of surgical sperm retrieval are:

- microsurgical epididymal sperm aspiration (MESA) and percutaneous epididymal sperm aspiration (PESA) which are procedures where the spermatozoa are obtained from the epididymis, either by surgical or needle-aspiration methods;
- testicular sperm aspiration (TESA) which is a procedure where spermatozoa are obtained from the testes by needle aspiration technique; and
- testicular sperm extraction (TESE) which is a procedure for recovering spermatozoa from the testes by open exicisional testicular biopsy.

Less frequently used sperm retrieval methods include:

- vasal sperm aspiration which is a procedure for recovering spermatozoa from the vas deferens by needle-aspiration technique; and
- seminal vesicle sperm aspiration aided by transrectal ultrasonography, which is a procedure for recovering spermatozoa from seminal vesicles by needle-aspiration technique under ultrasound guidance.

Semen/sperm may also be obtained through mechanical or electrical procedures to induce ejaculation. In men who have a physical inability to ejaculate (e.g., due to spinal cord injury, neurological disorders or diabetes) vibratory stimulation of the penis may induce an artificially induced ejaculation. Alternatively, electroejaculation, or semen procurement by rectal probe electrostimulation, may be used when vibratory stimulation fails, or if autonomic dysreflexia intervenes.

Controlled Ovarian Hyperstimulation (COH)

Controlled ovarian hyperstimulation (COH) entails the administration of fertility

medications and subsequent monitoring in order to enhance ovarian follicles' growth and the production of (multiple) oocytes. It may be performed in the context of *in vivo* fertilization, i.e. before timed intercourse or intrauterine insemination, as well as in the context of *in vitro* fertilization (IVF), before retrieving the oocytes. There are large numbers of regimens for COH involving different drugs combinations (clomiphene citrate, gonadotropins preparations, gonadotropin releasing hormone (GnRH) analogues: agonists or antagonists) with different doses, routes and duration of administration. When used in conjunction with IVF, mature oocyte retrieval is performed 35 to 36 hours following human chorionic gonadotropin (hCG) administration which triggers final oocyte maturation.

Gamete intrafallopian transfer (GIFT)

GIFT is an alternative to IVF and involves the transfer of both gametes (oocytes and sperm) into a fallopian tube, which is where natural fertilization of an ovulated mature oocyte by a spermatozoon occurs. GIFT is an invasive procedure, as it requires laparoscopy. Considering the increased risk of side-effects from laparoscopic transfer in GIFT and the lack of any evidence that results are superior to the standard IVF technique, this alternative technique is not used as a primary treatment option.

***In vitro* embryo biopsy**

In vitro embryo biopsy includes cleavage-stage blastomere biopsy and trophectoderm/blastocyst-stage biopsy.

Cleavage-stage blastomere biopsy

Blastomere biopsy refers to the removal of one or two cells of an 8-cell stage *in vitro* embryo (the individual cells of the embryo are called blastomeres). Embryo biopsy can be performed using three techniques: zona drilling with acidified Tyrode solution, zona slicing and laser drilling. Generally, a small hole is made in the zona pellucida of an *in vitro* embryo and the blastomere can be displaced either by liquid or by exerting pressure using a micropipette or by suction.

Trophectoderm/blastocyst-stage biopsy

Trophectoderm/blastocyst-stage biopsy involves the extraction of cells (5-10 cells)

from the trophectoderm layer of a blastocyst. The trophectoderm is the outer layer of cells of a blastocyst which gives rise to the placenta, but not the developing fetus. Similar to cleavage stage biopsy, trophectoderm biopsy can also be performed using mechanical or laser methods.

In vitro embryo culture and assessment

In vitro embryo culture refers to the process of *in vitro* (extracorporeal) embryo development. Embryos are typically cultured in an incubator, at 37°C and a gas atmosphere containing 6% CO_2. The development of stage-specific sequential culture media systems which support embryo development to the blastocyst stage (extended culture) has made it possible to delay embryo transfer and cryopreservation of surplus embryos until day 5 or 6.

In order to optimize the embryo selection process, numerous criteria have been suggested in determining which embryos have the greatest developmental potential. Morphological assessment is the most widely used. Morphological assessment encompasses examination of pronuclei, cleavage-stage embryo development and blastocyst-stage embryo development.

In vitro embryo cryopreservation

After the creation of *in vitro* embryos, embryos at the zygote, cleavage and blastocyst stages can be frozen by cryopreservation. Conventional cryopreservation of *in vitro* embryos occurs by a slow cooling or, less frequently, by rapid freezing vitrification protocols. In both cases, cryoprotective agents are used to reduce the formation of ice crystals during freezing which can damage cells and lead to cell death.

In vitro embryo destruction/disposal

In vitro embryos are disposed of in biohazard container for solid or liquid waste. The biohazard material is destroyed by autoclaving (high temperature and pressure) or by hydroclaving (high temperature and steam). The biohazard material is then removed from the clinic or hospital and disposed of in accordance with provincial and local laws.

In vitro embryo export

In vitro embryo export involves the exportation of an *in vitro* embryo that is created or stored in Canada to a country other than Canada, for any purpose.

In vitro embryo import

In vitro embryo import involves the importation of an *in vitro* embryo that is created or stored in a country other than Canada and transported to Canada, for any purpose.

In vitro embryo obtaining

In vitro embryo obtaining refers to the acceptance of an *in vitro* embryo for any purpose which has been created or stored in another AHR centre, or related facility, in Canada (e.g., receiving an embryo donated for third-party reproductive use that is shipped from a different AHR centre).

In vitro embryo storage

In vitro embryo storage involves the maintenance and storage of cryopreserved embryos in appropriately labelled storage containers, which are secured in cryopreservation units.

In vitro embryo thawing

Thawing of *in vitro* embryos involves the rapid warming of cryopreserved *in vitro* embryos at 37°C with appropriate dilution steps to remove the cryoprotective agents from the sample. Once thawed, the *in vitro* embryo may be incubated at 37°C for culture.

In vitro embryo transfer

Embryo transfer is a procedure in which embryos created *in vitro* are placed in the uterus. The majority of embryo transfers are currently carried out by non-surgically cannulating the uterine cavity via the cervix (transcervical transfers). Transcervical embryo transfer does not require analgesics or anaesthetics and most often is performed under ultrasound guidance. Embryo transfer is usually conducted at day 2 or day 3 post-oocyte

insemination (i.e., at early-cleavage embryo stage); however, the development of stage-specific (i.e., sequential culture) media systems which support embryo development to the blastocyst stage has made it possible to delay embryo transfer until day 5 or 6.

In vitro embryo transport

In vitro embryo transport involves the sending of an *in vitro* embryo (including appropriate packaging, labelling and shipping) to another licensed person for any purpose.

In vitro fertilization (IVF) with insemination

Conventional IVF, also known as IVF with insemination, involves the mixing and incubation of oocytes with motile sperm in a dish. Fertilization is assessed 16–18 hours after insemination. The presence of two pronuclei indicates normal fertilization.

In vitro fertilization (IVF) with intracytoplasmic sperm injection (ICSI)

ICSI is a micromanipulation technique whereby a single immobilized spermatozoon is injected directly into the cytoplasm (ooplasm) of a mature (metaphase II) oocyte. Using either ejaculated or surgically retrieved sperm, ICSI is most commonly performed for the treatment of severe male infertility with very low sperm count (oligozoospermia), poor motility (asthenozoospermia) or abnormal sperm morphology (teratozoospermia), and in males with total absence of sperm cells in the ejaculate (obstructive or non-obstructive azoospermia).

Intracervical insemination (ICI) - See: Artificial Insemination

Intrauterine insemination (IUI) - See: Artificial Insemination

Intravaginal insemination (IVI) - See: Artificial Insemination

Oocyte cryopreservation

Oocytes can be cryopreserved and stored in liquid nitrogen by standard slow cooling or rapid freezing (vitrification) protocols, both of which use cryoprotective agents that reduce the formation of ice crystals during freezing thereby preventing cell death. Oocytes can be slowly frozen at early stages of gamete development such as the germinal vesicle stage or at mature stages such as during metaphase II.

Oocyte destruction/disposal

Oocytes are disposed of in biohazard containers for solid or liquid waste. The biohazard material is destroyed by autoclaving (high temperature and pressure) or by hydroclaving (high temperature and steam). The biohazard material is then removed from the clinic or hospital and disposed of in accordance with provincial and local laws.

Oocyte export

Oocyte export involves the exportation of an oocyte that is retrieved, or stored in Canada to a country other than Canada for the purposes of creating an embryo.

Oocyte import

Oocyte import involves the importation of an oocyte that is retrieved or stored in a country other than Canada and transported to Canada, for the purpose of creating an embryo.

Oocyte *in vitro* maturation

Oocyte *in vitro* maturation, also called *in vitro* oocyte maturation (IVM), involves culture of immature oocytes following retrieval generally from unstimulated ovaries. Immature oocytes are left to incubate for 24 to 36 hours and are constantly assessed for progression of maturation and only mature oocytes are selected for fertilization procedures.

Oocyte obtaining

Oocyte obtaining refers to the acceptance of an oocyte for the purpose of creating an embryo which has been retrieved or stored in another AHR centre, or related facility, in Canada (e.g., receiving an oocyte donated for third-party reproductive use that is shipped from a different AHR centre).

Oocyte polar body biopsy

Ooctye polar body biopsy refers to the removal of the first or second polar body of an oocyte for preimplantation genetic diagnosis (PGD). A polar body is a cell structure that is extruded from an oocyte during meiosis and contains genetic material from the mother.

Oocyte processing

Oocyte processing involves the identification, handling, assessment and manipulation of oocytes for use in fertilization or transfer procedures (e.g., IVF, ICSI, GIFT). The oocyte is surrounded by the zona pellucida, the corona radiata and the cumulus oophorus (i.e. oocyte-cumulus-corona complex). After oocyte retrieval, aspirated follicular fluid is placed in a Petri dish and carefully inspected for the presence of a cumulus mass under a stereo dissecting microscope. The stage of oocyte maturity is assessed by noting the volume, density and condition of the surrounding cumulus-corona complex.

Oocytes that are to be fertilized by ICSI are denuded from the surrounding cumulus-corona cells both enzymatically and mechanically (using an enzymatic procedure with hyaluronidase followed by mechanical denudation using a pipette).

Oocyte retrieval

Oocyte retrieval is a procedure for recovering oocytes from a woman's ovarian follicles in order to be used for AHR procedures. Most often, oocyte retrieval is performed in a stimulated cycle with the aid of transvaginal ultrasonography, under intravenous sedation. On very rare occasions, when the ovaries are not accessible from the vagina, laparoscopic oocyte retrieval which includes the need for general anesthesia, may be conducted.

Oocyte storage

Oocyte storage involves the maintenance and storage of cryopreserved oocytes in appropriately labelled storage containers, which are secured in cryopreservation units.

Oocyte thawing

Thawing of cryopreserved oocytes occurs by placing cryovials in a 30°C water bath which are then transferred into solutions with gradual dilutions of the cryoprotective agent and are eventually placed in medium lacking cryoprotective agents and incubated at 37.5°C for culture.

Oocyte transport

Oocyte transport involves the sending of an oocyte (including appropriate packaging, labelling and shipping) to another licensed person for the purpose of creating an embryo.

Ovarian tissue cryopreservation

Ovarian tissue is most frequently cryopreserved to preserve fertility in patients undergoing cancer treatment which may result in infertility. Following ovarian tissue retrieval, the tissue is diced into small pieces, placed in cryovials and cryopreserved using a slow-cooling method.

Ovarian tissue destruction/disposal

Ovarian tissue is disposed of in biohazard containers for solid or liquid waste. The biohazard material is destroyed by autoclaving (high temperature and pressure) or by hydroclaving (high temperature and steam). The biohazard material is then removed from the clinic or hospital and disposed of in accordance with provincial and local laws.

Ovarian tissue export

Ovarian tissue export involves the exportation of an oocyte that is retrieved or stored in Canada to a country other than Canada, for the purposes of creating an embryo.

Ovarian tissue import

Ovarian tissue import involves the importation of ovarian tissue that is retrieved or stored in a country other than Canada and transported to Canada, for the purpose of creating an embryo.

Ovarian tissue obtaining

Ovarian tissue obtaining refers to the acceptance of ovarian tissue for the purpose of creating an embryo which has been retrieved or stored in another AHR centre, or related facility, in Canada (e.g., receiving cryopreserved ovarian tissue retrieved from a female patient and stored in a hospital prior to cancer treatment which at some future point is shipped to an AHR centre for transplantation back into the woman for reproductive use).

Ovarian tissue processing

Ovarian tissue processing refers to the preparation of tissue for cryopreservation or transplantation. If an entire ovary is removed, the ovarian cortex (where the primordial follicles reside) is carefully separated from the medulla, then sliced into smaller pieces and subjected to cryopreservation. After thawing a cryopreserved ovarian tissue sample, ovarian tissue may be processed and assessed for potential transplantation.

Ovarian tissue retrieval

Ovarian tissue retrieval, in conjunction with cryopreservation and transplantation, is an approach to preserve female fertility after cancer treatment which may result in reproductive sterility. Ovarian tissue (i.e., ovarian cortical tissue which contains the primordial follicles) is collected through a laparoscopic procedure. An entire ovary may be removed because it provides a large amount of tissue and minimizes trauma to the cortex. However, in pediatric patients, ovarian cortical biopsy may be sufficient because the ovarian reserve is much larger in younger females.

Ovarian tissue storage

Ovarian tissue storage involves the maintenance and storage of cryopreserved ovarian tissue in appropriately labelled storage containers, which are secured in cryopreservation units.

Ovarian tissue thawing

Cryopreserved ovarian tissue is thawed by placing cryovials in a 30°C water bath which are then transferred into solutions with gradual dilutions of the cryoprotective agent until the tissue is placed in a medium lacking cryoprotective agents and incubated at 37.5°C for culture.

Ovarian tissue transplantation

Autologous transplantation of ovarian tissue can be performed orthotopically or heterotopically subcutaneously in the forearm. Heterotopic transplantation avoids the use of general anaesthesia for surgery and because ovarian tissue is transplanted in the forearm, close monitoring can be performed, and subsequent oocyte retrieval will require less invasive surgery.

Ovarian tissue transport

Ovarian tissue transport involves the sending of ovarian tissue (including appropriate packaging, labelling and shipping) to another licensed person for the purpose of creating an embryo.

Preimplantation Genetic Diagnosis (PGD)

Preimplantation genetic diagnosis is the analysis of genetic material from an oocyte or *in vitro* human embryo before the embryo is transferred to the body of a woman. PGD is used primarily for screening for aneuploidy (an abnormal chromosome number) by fluorescent *in situ* hybridization (FISH) and screening for single gene disorders by polymerase chain reaction (PCR).

Semen/Sperm cryopreservation

Semen/sperm can be cryopreserved in liquid nitrogen, which stops sperm from undergoing cell death. After collection, semen/sperm are mixed in a solution of nutrients and cryoprotective chemicals that during freezing will reduce the formation of ice crystals which affect the viability of sperm cells. Cryopreservation of sperm is generally performed using slow freezing methods

although fast vitrification can also be performed. The ratio of cryoprotectants to semen also vary and depend on sperm concentration and motility.

Semen/Sperm obtaining

Semen/sperm obtaining encompasses those activities where semen/sperm are collected by the donor or patient through non-clinical methods and provided to a AHR practitioner or AHR centre for the purposes of creating an embryo. The male donor may collect the sample directly through masturbation (with, or without pharmaceutical or mechanical aides), during intercourse with an appropriate seminal pouch or collection condom, or it may be retrieved from urine collected by the donor under special circumstances. Where semen/sperm obtaining is directly from a donor or patient, it encompasses the activities related to obtaining the semen or urine sample from a donor such as providing appropriate directions, conditions for acceptance of the sample, as well as labelling and record keeping requirements.

Semen/sperm obtaining also refers to the acceptance of semen/sperm for the purpose of creating an embryo which has been obtained, retrieved or stored in another AHR centre, or related facility, in Canada (e.g., receiving sperm donated for third-party reproductive use that is shipped from a sperm bank).

Semen/Sperm processing

Semen/sperm processing involves both the analysis of semen and the separation of sperm from seminal plasma. Basic semen analysis aims to evaluate descriptive parameters of an ejaculate. The qualities that are routinely assessed by initial macroscopic and microscopic examination are visual appearance, liquefaction, viscosity, volume, pH, sperm concentration and the total number of sperm, sperm motility and sperm vitality. In addition, differential count with respect to sperm morphology, assessment of sperm agglutination/aggregation, assessment of the presence of debris and other cell types in semen such as leukocytes or immature germ cells, and testing for antibody-coating of spermatozoa are performed.

Sperm preparation/processing involves the separation of sperm from seminal plasma and aims to achieve a final sperm preparation with a high percentage of morphologically normal and motile spermatozoa which are free from debris, dead spermatozoa and contaminants. There are four basic techniques: 1) dilution and washing, 2) sperm migration, i.e., "swim-up" technique 3) ‘‘selective" washing procedures using density

gradient centrifugation, and 4) adherence methods to eliminate debris and dead spermatozoa (e.g., glass wool, glass beads, and SephadexTM columns).

Sperm destruction/disposal

Sperm are disposed of in biohazard containers for solid or liquid waste. The biohazard material is destroyed by autoclaving (high temperature and pressure) or by hydroclaving (high temperature and steam). The biohazard material is then removed from the clinic or hospital and disposed of in accordance with provincial and local laws.

Sperm export

Sperm export involves the exportation of sperm that is obtained or stored in Canada to a country other than Canada, for the purposes of creating an embryo.

Sperm import

Sperm import involves the importation of sperm that is obtained or stored in a country other than Canada and transported to Canada, for the purpose of creating an embryo.

Sperm storage

Sperm storage involves the maintenance and storage of cryopreserved sperm in appropriately labelled storage containers, which are secured in cryopreservation units.

Sperm thawing

Thawing of cryopreserved sperm may occur at room temperature or by placing cryovials or straws in a water bath. Media is slowly added to the thawed sperm to gradually dilute the cryoprotective agent. The thawed and diluted sperm is then centrifuged to allow removal of the cryoprotective agent and resuspension of the thawed sperm in an appropriate media.

Sperm transport

Sperm transport involves the sending of an sperm (including appropriate packaging, labelling and shipping) to another licensed person for the purpose of creating an embryo.

Testicular tissue cryopreservation

Male patients who undergo chemotherapy or radiation therapy for cancer treatment may decide to surgically remove testicular tissue prior to treatment in order to preserve their fertility. Testicular tissue can be isolated from sexually immature males and adult patients and cryopreserved using a slow cooling method in liquid nitrogen. Testicular tissue may be cryopreserved either as a cell suspension or as pieces of tissue generally using glycerol as a cryoprotective agent.

Testicular tissue destruction/disposal

Testicular tissue is disposed of in biohazard containers for solid or liquid waste. The biohazard material is destroyed by autoclaving (high temperature and pressure) or by hydroclaving (high temperature and steam). The biohazard material is then removed from the clinic or hospital and disposed of in accordance with provincial and local laws.

Testicular tissue export

Testicular tissue export involves the exportation of testicular tissue that is retrieved or stored in Canada to a country other than Canada, for the purposes of creating an embryo.

Testicular tissue import

Testicular tissue import involves the importation of testicular tissue that is retrieved or stored in a country other than Canada and transported to Canada, for the purpose of creating an embryo.

Testicular tissue obtaining

Testicular tissue obtaining refers to the acceptance of testicular tissue for the purpose of creating an embryo which has been retrieved or stored in another AHR centre, or related facility, in Canada (e.g., receiving testicular tissue which has been retrieved by an off-site urologist and shipped to an AHR centre for processing and use in ICSI).

Testicular tissue processing

Testicular tissue processing refers to the preparation of tissue for cryopreservation or the isolation of spermatozoa for use in IVF with ICSI. The isolation of spermatozoa is performed either by mechanical shredding or enzymatic digestion of fresh or cryopreserved-thawed testicular tissue.

Testicular tissue storage

Testicular tissue storage involves the maintenance and storage of cryopreserved testicular tissue in appropriately labelled storage containers, which are secured in cryopreservation units.

Testicular tissue thawing

Cryopreserved testicular tissue may be thawed at room temperature or by placing the frozen specimen in a water bath. Subsequent dilution and centrifuge steps are then performed to dilute and remove the cryoprotective agents before further processing the tissue sample to isolate sperm.

Testicular tissue transport

Testicular tissue transport involves the sending of testicular tissue (including appropriate packaging, labelling and shipping) to another licensed person for the purpose of creating an embryo.

Trophectoderm biopsy - See: *In vitro* embryo biopsy

Zygote intrafallopian transfer/Tubal embryo transfer

Zygote intrafallopian transfer (ZIFT) is the transfer of a zygote into a fallopian tube whereas tubal embryo transfer (TET) is a procedure in which early cleavage *in vitro* embryos are placed in a fallopian tube. ZIFT and TET can only be used when a fallopian tube is patent. Fewer patients are currently undergoing ZIFT or TET because of the invasive nature of laparoscopy and the potential adverse effects of general anesthesia.