



# Guidelines for Third Party Reproduction

**Jon Havelock, MD, FRCSC**

**Kimberly Liu, MD, FRCSC**

**Sherry Levitan, B.Sc, LL.B.**

**Angel Petropanagos, PhD**

**Lawrence Kahn, QC**

***CFAS Clinical Practice Guideline Committee***

**William Buckett, MD**

**Jon Havelock, MD**

**Hananel Holzer, MD**

**Neal Mahutte, MD**

**Jason Min, MD (Chair)**

**Jeff Roberts, MD**

**Sony Sierra, MD**

**Camille Sylvestre, MD**

**Beth Taylor, MD**

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**Notice to Reader**

**Terminology in this guideline is specific and terms used may not have the meaning ascribed to them in other contexts. Please refer to the glossary for definitions.**

**GLOSSARY**

**ART-** Assisted reproductive technologies including intrauterine insemination and in vitro fertilization

**Embryo donor(s)-** a person or persons who choose(s) to donate their embryo(s) to a known or anonymous recipient for the purpose of achieving pregnancy for the recipient and their partner (if applicable)

**Embryo donor recipient-** an intended parent who will undergo an embryo transfer of a donated embryo for the purpose of achieving a pregnancy for themselves and their partner (if applicable)

**Embryo donor (oocyte donor)-** a person who provides the oocyte for an embryo, which will be donated to a recipient for the purpose of achieving a pregnancy for the recipient and their partner (if applicable)

**Embryo donor (sperm donor)-** a person who provides sperm for an embryo, which will be donated to a recipient for the purpose of achieving a pregnancy for the recipient and their partner (if applicable)

**Gamete donor-** a person who donates oocytes or sperm to a known or anonymous recipient for the purpose of achieving a pregnancy for the recipient and their partner (if applicable)

**Gamete donor recipient-** an intended parent who will undergo ART procedures using either donor sperm or donor oocytes for the purpose of achieving a pregnancy for themselves and their partner (if applicable)

**Gamete provider-** a person who provides either the oocyte or sperm for an embryo which will be transferred to a surrogate for the purpose of achieving a pregnancy for themselves and their partner (if applicable)

**Gestational Surrogate-** a person who undergoes an embryo transfer in order to achieve and carry a pregnancy for another person/couple, who will be the intended parent(s) of the child. The gestational surrogate is not genetically linked to the embryo.

**Intended Parent(s)-** a person or couple who intend to parent a child who is conceived through third party reproduction. And intended parent may provide their gamete for the creation of an embryo

**Oocyte donor-** a person who donates oocytes to a known or anonymous recipient for the purposes of achieving a pregnancy for the intended parent(s)

**Oocyte donation recipient-** an intended parent who will undergo ART procedures using donor oocytes for the purpose of achieving a pregnancy for themselves and their partner (if applicable)



**Oocyte provider-** a person who provides the oocyte for an embryo which will be transferred to a surrogate for the purpose of achieving a pregnancy for themselves and their partner (if applicable)

**Partner-** a person who is in an intimate relationship with a person who is involved in third party reproduction.

**Sperm donor-** a person who donates sperm to a known or anonymous recipient for the purposes of achieving a pregnancy for intended parent(s)

**Sperm donation recipient-** an intended parent who will undergo ART procedures to carry a pregnancy using donor sperm for the purpose of achieving a pregnancy for themselves and their partner (if applicable)

**Sperm provider-** a person who provides sperm for the purpose of achieving a pregnancy for themselves and their partner (if applicable)

**Surrogate-** a person who undergoes an embryo transfer or donor sperm insemination in order to achieve and carry a pregnancy for another person/couple, who will be the intended parent(s) of the child. The intended parent(s) may or may not be genetically linked to the pregnancy. The term “surrogate” includes gestational and traditional surrogates.

**Traditional surrogate-** a person who undergoes an insemination from a sperm donor or sperm provider in order to achieve and carry a pregnancy for another person/couple, who will be the intended parent(s) of the child. The intended parent(s) may or may not be genetically linked to the embryo. A traditional surrogate is therefore both an egg donor and the carrier for the pregnancy.

## **Introduction**

Third party reproduction refers to all cases of human reproduction that involve the use of gametes (sperm, oocytes), embryos, or gestation from a third party for the purposes of reproduction by the intended parent(s). Third party gestation, commonly referred to as surrogacy, is where a gestational surrogate or a traditional surrogate carries a pregnancy for intended parent(s). In gestational surrogacy, an embryo is transferred to the surrogate who is not the oocyte donor. In such cases, either the intended parents or a third party provide the oocyte and sperm. In traditional surrogacy, the surrogate is also the oocyte donor and undergoes insemination with semen from the intended parent or a sperm donor. Third party reproduction allows individuals and/or couples to attain a pregnancy that they may not have otherwise been able to achieve through spontaneous conception or assisted reproductive technologies (ART) treatments using their own gametes or uterus.

Third party reproduction is governed by federal legislation in Canada, the Assisted Human Reproduction Act (AHR Act), which was proclaimed, in part, on March 29, 2004. While some sections of the AHR Act have been determined to exceed, in whole or in part, the legislative authority of the Parliament of Canada under the *Constitution Act, 1867*, and other sections are not yet in force, there are specific provisions in the AHR Act that are in force and specifically apply to third party reproduction. The most current form of the AHR Act can be found at the following website: <http://laws-lois.justice.gc.ca/PDF/A-13.4.pdf>. The



Agency, Assisted Human Reproduction Canada (AHRC), was initially responsible for administering and enforcing the AHR Act. As of March 31, 2013, AHRC ceased operations and the AHR Act is now under the purview of Health Canada. Sections of the AHR Act specifically relevant to third party reproduction are as follows:

#### Section 6

- (1) No person shall pay consideration to a female person to be a surrogate mother, offer to pay such consideration or advertise that it will be paid.
- (2) No person shall accept consideration for arranging for the services of a surrogate mother, offer to make such an arrangement for consideration or advertise the arranging of such services.
- (3) No person shall pay consideration to another person to arrange for the services of a surrogate mother, offer to pay such consideration or advertise the payment of it.
- (4) No person shall counsel or induce a female person to become a surrogate mother, or perform any medical procedure to assist a female person to become a surrogate mother, knowing or having reason to believe that the female person is under 21 years of age.

#### Section 7

- (1) No person shall purchase, offer to purchase or advertise for the purchase of sperm or ova from a donor or a person acting on behalf of a donor.
- (2) No person shall
  - (a) purchase, offer to purchase or advertise for the purchase of an *in vitro* embryo; or
  - (b) sell, offer for sale or advertise for sale an *in vitro* embryo.
- (3) No person shall purchase, offer to purchase or advertise for the purchase of a human cell or gene from a donor or a person acting on behalf of a donor, with the intention of using the gene or cell to create a human being or of making it available for that purpose.
- (4) In this section, “purchase” or “sell” includes to acquire or dispose of in exchange for property or services.

#### Section 9

No person shall obtain any sperm or ovum from a donor under 18 years of age, or use any sperm or ovum so obtained, except for the purpose of preserving the sperm or ovum or for the purpose of creating a human being that the person reasonably believes will be raised by the donor.

Section 12 of the AHR Act, which prohibits reimbursement of expenditures to donors and surrogates except in accordance with regulations, has not yet been proclaimed, as it refers to regulations which, as of the date of this Guideline, do not exist. Currently the use of donor semen for assisted reproduction falls under the Food and Drugs Act. The regulations governing the use of donor semen have been in force since 1996 and fall under the Processing and Distribution of Semen for Assisted Conception Regulations (Semen



Regulations). These regulations can be found at: <http://laws-lois.justice.gc.ca/PDF/SOR-96-254.pdf>. Specific requirements are outlined in the Health Canada Directive: Technical Requirements for Therapeutic Donor Insemination (available at [http://www.hc-sc.gc.ca/dhp-mps/brgtherap/applic-demande/guides/semen-sperme-acces/semen-sperme\\_directive-eng.php](http://www.hc-sc.gc.ca/dhp-mps/brgtherap/applic-demande/guides/semen-sperme-acces/semen-sperme_directive-eng.php)). In June 2012, Bill C-38, which contained amendments to the Assisted Human Reproduction Act, passed the House of Commons (available at: [http://www.parl.gc.ca/content/hoc/Bills/411/Government/C-38/C-38\\_4/C-38\\_4.PDF](http://www.parl.gc.ca/content/hoc/Bills/411/Government/C-38/C-38_4/C-38_4.PDF)). The amendments included the non-application of the Food and Drug Act for sperm and oocytes for assisted human reproduction and the development of regulations for the importation, distribution and use of sperm and oocytes. These regulations to the AHR Act have yet to be developed, and until they are in force, the Food and Drugs Act and the Semen Regulations will remain in force for the use of donor sperm. The above Acts and regulations lay the framework for certain mandatory requirements for the treatment of patients in the context of third party reproduction, and discuss the potential penalties for infractions.

In the United States, the American Society for Reproductive Medicine (ASRM) has developed detailed guidelines respecting the oversight of their Food and Drug Administration (FDA) regulations with respect to gametes.<sup>1</sup> More recently, the ASRM has developed guidelines pertaining to the treatment of surrogates as well.<sup>2</sup> The European Society for Human Reproduction and Endocrinology (ESHRE) does not have specific guidelines pertaining to third party reproduction, quality management of gametes/ embryos, and mandatory infectious disease testing for blood borne viruses and infectious diseases. However, the European Union Tissues and Cells Directive (EUTCD) offers some guidelines for screening of potential gamete or embryo donors and recipients/ surrogates.<sup>3</sup> Additional recommendations for the European Union were developed in a consensus document for gamete donation,<sup>4</sup> and most of their recommendations have been supplanted by the EUTCD.

In Canada, guidance with respect to indications, contraindications, psychological counselling, screening and selection of gamete or embryo donors or surrogates has not been standardized. The Canadian Standards Association (CSA) group has developed a standard “Tissues for assisted reproduction” for the safe use of donor sperm, oocytes, and embryos in assisted reproduction, which includes requirements for facilities, quarantine, handling of tissue as well as eligibility and screening of donors.<sup>5</sup> These CSA standards have been developed with input from CFAS and Health Canada; however, they have not been universally applied for all third-party tissue use in ART clinics in Canada. These CSA standards are not legally binding and compliance is voluntary.

In some instances, there may be separate provincial regulations pertaining to assisted reproduction and the treatment of patients in the context of third party reproduction. It is the responsibility of ART practitioners to be familiar with the provincial rules and regulations governing their practice, and understand the requirement to comply with any existing provincial rules and regulations supersedes the recommendations within the CSA standards and this guideline. The following recommendations are made to provide guidelines for ART clinics providing treatment of patients in the context of third party reproduction. Evidence is graded as outlined in the report of the Canadian Task Force on Preventative Health Care (Table 1).



### **Medical records in Third Party Reproduction**

Provinces have different minimum standards for the length of time that medical records must be maintained. For donor semen, medical records must be kept indefinitely (as per the Semen Regulations). Given potential health implications for children conceived through third party reproduction, clinics should also keep medical records indefinitely for other gamete donors and recipients, embryo donors and recipients, and surrogates. The creation of a national information registry for third-party procreation would facilitate the collection and storage of this information.

### **Recommendations**

1. Semen regulations dictate that medical records must be kept indefinitely for sperm donors and recipients.
2. Medical records should be kept indefinitely for other gamete donors and recipients, embryo donors and recipients, and surrogates. (Level III-A)

### **Consent**

The AHR Act provides that the principle of free and informed consent must be applied as a fundamental condition of the use of reproductive technology. Section 8 of the AHR Act provides:

#### Section 8

- (1) No person shall make use of human reproductive material for the purpose of creating an embryo unless the donor of the material has given written consent, in accordance with the regulations, to its use for that purpose.
- (2) No person shall remove human reproductive material from a donor's body after the donor's death for the purpose of creating an embryo unless the donor of the material has given written consent, in accordance with the regulations, to its removal for that purpose.
- (3) No person shall make use of an *in vitro* embryo for any purpose unless the donor has given written consent, in accordance with the regulations, to its use for that purpose.

Regulations under Section 8 of the AHR Act (Section 8 Consent Regulations), came into force on December 1, 2007, and can be found at: <http://laws-lois.justice.gc.ca/PDF/SOR-2007-137.pdf>. As per the regulations, there are three controlled activities: using gametes to create an embryo, posthumously removing gametes for the purpose of creating an embryo, and using an embryo for any purpose. Consent to those three controlled activities must be in writing, and must contain the information specified by the Regulation. The consent must be signed by the donor of the material (as such term is defined in the Regulation), and such signature must be witnessed. The withdrawal of consent must also be in writing. With respect to third party reproduction, the Section 8 Consent Regulations provide, in part, as follows:

- 1) If the human reproductive material is used to create *in vitro* embryos for a third party's reproductive use and there are *in vitro* embryos in excess of the third party's reproductive needs, the excess *in vitro* embryos will be used in accordance with the third party's consent and, if the use is providing instruction in assisted reproduction procedures, improving assisted reproduction procedures or other research, the consent of the donor in accordance with section 4.



- 2) If the human reproductive material is used to create *in vitro* embryos for the reproductive use of a third party who is a couple, along with human reproductive material from an individual who is a spouse or common law partner in the couple, the use of the *in vitro* embryos will be subject to the consent of that individual alone if, prior to the use of the *in vitro* embryos, the individual is no longer a spouse or common-law partner in the couple, and
- 3) if the donor consents to the human reproductive material being used to create an *in vitro* embryo for the purpose of providing instruction in assisted reproduction procedures or improving assisted reproduction procedures, no additional consent from the donor is required to permit the use of the embryo for that purpose.<sup>6</sup>

### **Recommendation**

3. In addition to the elements of consent required by law, gamete donor(s), gamete donor recipients, and surrogates must sign consent forms outlining the process, risks and benefits of treatment(s). They must be informed of and acknowledge their right to withdrawal from treatment at any time prior to gamete donation or embryo transfer for surrogates. (Level III-A)

### **Medical History Evaluation and Genetic Screening of Gamete Donors, Gamete Providers, Embryo Donors and Surrogates**

There must be a balance between mitigating risks to donors, recipients and surrogates, while ensuring accessibility to treatment for intended parent(s). In order to reduce the risk of a conflict of interest and to protect the best interest of the third party, consideration should be given for gamete donors and surrogates to have a different physician from the intended parent(s). In the event that the third party does not have a different physician from the intended parent(s), physicians must ensure that the third party is treated as a patient in their own right, so as to protect the safety and interests of the third party.

It is recommended that surrogates, gamete donors that do not fall under the Semen Regulations, embryo donors, and gamete providers using a surrogate undertake a thorough medical history. This may include the same screening questions found in the Exclusion Criteria in Section 2 of the Health Canada Directive – Technical Requirements for Therapeutic Donor Insemination ([http://www.hc-sc.gc.ca/dhp-mps/alt\\_formats/hpfb-dgpsa/pdf/prodpharma/semen-sperme\\_directive-eng.pdf](http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/prodpharma/semen-sperme_directive-eng.pdf)) (Table 2). Documentation of such screening should be in the medical record of the gamete donor, gamete provider, embryo donor or surrogate. However, the answers to the screening questions in Table 2 should not be considered absolute exclusionary criteria for gamete donors, gamete providers, embryo donors or surrogates.

All gamete donors should undergo genetic screening according to the SOGC guidelines for preconception screening as outlined in Table 3.<sup>7</sup> Further genetic testing of the gamete donor(s) and genetic counseling for the gamete donor(s) and intended parent(s) can be undertaken as deemed appropriate with consent from all parties. When this information is not available for a gamete donor, the intended parent(s) must be informed.



## Recommendation

4. Gamete donors and surrogates must be treated as patients in their own right.
5. After obtaining informed consent and confirming the intention to pursue treatment from the gamete donor, intended parent gamete provider, embryo donor and/or surrogate, full disclosure of the results of the medical screening and genetic screening must be made to gamete donor recipients, intended parent(s) and/or surrogates as applicable. In cases of anonymous relationships, care must be taken to protect the anonymity of all parties. Where consent to disclose the relevant medical history is refused, treatment must not proceed. (Level III-A).

## Infectious Disease Screening

It is important that gamete donors, intended parent(s) gamete providers, embryo donors, and their respective recipients or surrogates undergo specific serological testing for infectious disease screening. Since the use of donor semen for assisted conception is regulated by federal law, the appropriate infectious disease screening requirements can be found in the Health Canada Directive – Technical Requirements for Therapeutic Donor Insemination. Donor semen requires quarantine of semen and re-testing of donors prior to clearance for use. Leukocyte-rich semen donation may pose additional risks that oocyte and embryo donation do not, hence the reason for specific regulations and legislation. Until Bill C-38 and the associated regulations come into force, there are no specific legislation or guidelines in Canada for testing of oocyte or embryo donors, or their recipients/ surrogates. However, the CSA Group Standard “Tissues for assisted reproduction” provides specific screening requirements for all gamete donors, gamete providers and embryo donors to which ART clinics in Canada should adhere.

Regulations for the testing of gamete donors exists in the USA (Food and Drug Administration (FDA) Regulations), as well as in Europe (European Union Tissues and cells Directive (EUTCD)). Interestingly, the USA FDA requirements for screening and testing of donors of human cells, tissues, and cellular and tissue based products (HCT/Ps), does not address testing of gamete recipients/ surrogates. The USA FDA requirements only concern the safety of the gamete recipient/ surrogate and not the potential vertical transmission risk to the offspring created in the process of gamete donation. However, ASRM does recommend, appropriately, that gamete recipients/ surrogates are screened for infectious diseases that may potentially result in vertical transmission.<sup>8</sup>

The frequency and timing of serological testing for infectious diseases in assisted reproduction is based largely on empirical recommendations and relevant local regulations or guidelines. The European Union (EU) Directives 2004/23/EC, 2006/17/EC and 2006/86/EC pertain to screening of donors of gametes that are to be used for a partner use. The directive states that screening must occur at the time of donation of tissues and cells. This has been interpreted differently in the various EU countries. The time of donation in Ireland has been defined as “within 30 days of donation.” This testing is repeated within 30 days of all in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) cycles and every 6 months for couples undergoing intrauterine insemination (IUI). Between 2007-2009, this has resulted in more than 33000 HIV and Hepatitis B and C serological tests on more than 13000 patients. There were 0 cases of HIV, 18 cases of Hepatitis B surface antigen positivity, and 16 cases of Hepatitis C antibody positive testing. There were



no cases of seroconversion in the subsequent 20000 repeat tests.<sup>9</sup> While repeat serological screening has been suggested to be important for detecting new infections, detecting early seroconversion, and reducing of cross-contamination of cryopreserved gametes or embryos in common storage tanks, it appears the risk is extremely low. Additionally, new evidence suggests that the risks for cross-contamination of cryopreserved oocytes or embryos is negligible.<sup>10,11</sup> A recent study demonstrated no detection of virus by polymerase chain reaction, in 23 women infected with either HIV, Hepatitis B (HBV) or Hepatitis C (HCV), in the follicular fluid, spent culture media, or within the liquid nitrogen used for vitrification, or within the tank of the Hepatitis C patient with a high viral load.<sup>12</sup> However, this is in contrast to an earlier study detecting HCV RNA in the majority of follicular fluid samples of women infected with HCV.<sup>13</sup> It is important to note that HCV RNA was undetectable in the culture media of all 44 media samples on the day of embryo transfer. It is also worth noting that there has never been a reported case of cross contamination of any communicable disease to oocytes or embryos from cryostorage. In addition, there has never been a reported case worldwide of transmission of HIV, Hepatitis B or Hepatitis C from oocyte donation, use of fresh donated sperm during IVF, embryo donation, or to a gestational surrogate.

The quarantining of oocytes and embryos in order to repeat serological infectious disease testing at least 180 days after donation would increase financial costs to the patient and delay treatment. Also, if initial treatment fails, subsequent treatments will be delayed an additional 180 days. Such quarantining can be offered to all gestational surrogates, recipients of donor embryos or oocytes, and their response should be documented. However, the risk of seroconversion is extremely low.

Infectious disease testing should be carried out prior to gamete donation, gamete provision from an intended parent, or embryo donation in third party reproduction. The use of sperm in gestational surrogacy has been interpreted to fall outside the Donor Semen Regulations in Canada, as the semen is not being used for assisted conception, but rather an embryo is being transferred for the purposes of assisted conception. It is strongly recommended that initial screening take place within the 6 months **prior to** the donation, to determine suitability of surrogates, gamete donors and gamete providers, and to allow sufficient time for selection of alternate gamete donors, gamete providers or surrogates prior to treatment. Testing of partners to donors or surrogates will help determine whether additional risks for infectious diseases exists to the donor or surrogate prior to the time of donation, and allow for mitigating these risks, or selecting alternate donors/surrogates. In addition, gamete and embryo recipients and surrogates should undergo infectious disease testing to reduce the risks of vertical transmission. Testing of the partners of recipients and surrogates should be performed to address medico-legal concerns in cases of seroconversion.

### Recommendations

6. Donor semen for use in artificial insemination must comply with the Semen Regulations.
7. Transmission of HIV, Hepatitis B and Hepatitis C and other viruses is a theoretical risk with oocyte donation, sperm donation in conjunction with in vitro fertilization (IVF), embryo donation or gestational surrogacy treatments. Quarantine for 180 days and repeat serological testing can be offered to patients. (Level II-3C)



8. For oocyte or embryo donations in Canada, testing of a donor for the infectious agents discussed in the tables 4-7 below should be performed with test kits that are approved by Health Canada. (Level III-B)
9. When gametes are obtained from donors outside of Canada and testing of infectious agents was not performed by Health Canada approved testing kits, this information should be disclosed to the intended parent(s) and/or surrogate. (Level III-B).
10. In cases where nucleic acid amplification testing (NAT) is readily available for HIV-1 and Hepatitis C testing, it can be offered in addition to antibody testing when testing in the 30 day period prior to donation. (Level III-B)
11. Infectious disease screening and appropriate timing of testing in the relevant third party reproduction patients should be completed as described in Tables 4-7. (Level III-A)
12. After obtaining consent in accordance with Section 8 of the AHR Act, and confirming the intention to continue treatment from the gamete donor, gamete provider, embryo donor and/or surrogate, full disclosure of the infectious diseases test results must be made to recipients, intended parent(s) and/or the surrogate as applicable. In cases of anonymous relationships, care must be taken to protect the anonymity of all parties. Where consent to disclose the medical history is refused, treatment must not proceed. (Level III-A)

### **Management of Positive Infectious Disease Test Results**

Positive results should be confirmed by retesting. Positive results should be referred for appropriate management after notification of the individual. Recommendations for the management of positive infectious disease test results are as follows:

- a. Positive HIV testing of a gamete donor, gamete provider, embryo donor or a surrogate would exclude them from being a gamete donor, gamete provider, embryo donor or surrogate.
- b. Recipients of donated gametes or embryos, intended parent(s), and gestational surrogates should be informed that there is a remote chance of active HIV infection in the donor even in the presence of negative antibody HIV testing, due to a 4 week window between HIV infection and antibody positivity (and sometimes up to 6 months before detectable HIV antibody).
- c. Positive Hepatitis B surface antigen testing of a surrogate would exclude the individual from becoming a surrogate.
- d. Positive Hepatitis B surface antigen testing of a gamete donor, gamete provider, or embryo donor, would not necessarily exclude donation. After informing the donor of the positive result, and appropriate management and counselling, the donor may proceed with donation, after informed consent and **confirmed Hepatitis B immunity of the recipient/surrogate**.



- e. Positive Hepatitis C antibody testing of a gamete donor, gamete provider, embryo donor or surrogate would not necessarily exclude donation or surrogacy. After informing the donor/surrogate of the positive result, and appropriate management and counselling, and **confirmation of absence of active Hepatitis C virus infection**, the donor/surrogate can proceed with donation/surrogacy, after informed consent of the recipient/surrogate.
- f. Positive test results for Chlamydia trachomatis or Neisseria Gonorrhoeae requires treatment for the patient, as well as the screening and treatment of their partner, if applicable. Prior to participating in embryo donation or a surrogacy IVF cycle, the third party must be rescreened and a negative test for Chlamydia trachomatis or Neisseria Gonorrhoeae must be confirmed.
- g. Positive nontreponemal syphilis testing requires confirmatory treponemal specific testing. If treponemal specific testing is positive, appropriate referral, reporting and treatment is required. Confirmation of resolution of syphilis infection is required prior to participating in third party reproduction/donation/surrogacy cycle.
- h. Patients who test positive for active CMV infection (IgM) should be excluded until active infection has resolved.

### **Counselling in Third Party Reproduction**

The CFAS Counselling Special Interest Group (SIG) has developed Assisted Human Reproduction Counselling Practice Guidelines that have been endorsed and approved by the CFAS Executive. These guidelines can be found in pdf format on the CFAS website at the following link: [http://www.cfas.ca/images/stories/pdf/csig\\_counselling\\_practiceguidelines\\_december\\_2009 .pdf](http://www.cfas.ca/images/stories/pdf/csig_counselling_practiceguidelines_december_2009.pdf). All individuals involved in third party reproduction (and their partners, if appropriate) should undergo counseling prior to treatment.<sup>14</sup> The requirement to involve a gamete donor's partner or surrogate's partner for counseling can be determined individually based on factors such as the length and status of their relationship. As counseling is specific to the individuals involved, the involvement of new parties or new arrangements for gamete donation and/or surrogates requires additional counseling. In addition, changes in life circumstances such as a new partner, a change in relationship status or death of a partner require additional counseling prior to continuing treatment.

### **Recommendation**

- 13. All individuals involved in third party reproduction (and their partners, if appropriate) should undergo counseling in accordance with the CFAS Counseling Practice Guideline prior to treatment. Donors, recipients/intended parent(s) and surrogates should be counseled in separate sessions (Level II-2B).



### **Legal Counsel in Third Party Reproduction**

Third party reproduction, particularly with surrogates and known donors, can result in parentage and other legal issues, which may arise during pregnancy and antenatal care, in the birth registration process or after delivery. Lawyers providing advice to all parties involved in third party reproduction should be versed in the complexities of this area as well as inter-provincial differences, if applicable. Due to the legal issues related to birth registration and the recognition of the intended parents' parental rights in surrogacy arrangements, all parties involved in third party reproduction should have a legal agreement prior to embarking on treatment, except in Quebec where such agreements are non-enforceable.

With the exception of situations where a surrogate expects to deliver a baby in Quebec (where surrogacy contracts are unenforceable by legislation), intended parent(s) should have a contract in place with the surrogate carrier prior to commencing surrogacy treatment. Both British Columbia and Alberta have legislation relevant for surrogacy; however, the enforceability of surrogacy agreements is not legislated in any province outside of Quebec. The intended parent(s) and the surrogate should obtain separate and independent legal counsel with respect to the surrogacy contract, and the surrogate's partner should be included in the legal counselling. Legal counsel should come from a legal practitioner who is, if possible, licensed in the relevant province or territory, and who has expertise in surrogacy contracts. It is the obligation of the physician engaging in the treatment of a surrogate to confirm that a surrogacy contract is in place and signed by the surrogate and the intended parent(s) prior to commencing treatment. Surrogacy contracts do not supersede federal or provincial law, so contracts should conform to applicable provincial, territorial and federal law, where appropriate. In instances where the surrogate and intended parent(s) live in different provinces or countries, the physician should refer the parties to a lawyer with expertise in the relevant jurisdictions to address potential inter-jurisdictional issues.

Physicians should not review the surrogacy contract nor provide legal advice, either directly or by implication.

### **Recommendation**

14. All gamete donors and gamete donor recipients, and their partners, (if appropriate) should be offered independent legal counsel prior to treatment, particularly known gamete donation. (Level III-A)
15. All embryo donors and embryo donor recipients, and their partners (if appropriate) should be offered independent legal counsel prior to donation or treatment, particularly known embryo donation. (Level III-A)
16. All individuals involved in surrogacy (intended parents and surrogate and their partner), should have legal counsel prior to treatment. (Level III-A)
17. Outside of Quebec, all parties should have a comprehensive surrogacy agreement in place prior to treatment. Clinics should receive clearance letters from both lawyers involved confirming that a surrogacy agreement has been completed before treatment commences. All individuals involved in surrogacy in Quebec should have independent legal advice prior to treatment (Level III-A)



## **Sperm Donation**

### **Sperm Donation Recipients**

Indications for sperm donation include, but are not limited to, individuals without a partner who can provide sperm, or where the sperm provider has azoospermia, severe oligozoospermia, ejaculatory dysfunction not responsive to therapy or therapy declined, an inheritable genetic defect or previously affected offspring with presumptive inheritable genetic defect and screening is either not feasible, not available, or not desired, is Rh positive with a partner with prior severe Rh isoimmunization, has an incurable sexually transmitted infection that may be transmitted to the partner by sexual contact or ART, or demonstrates significant infertility not improved with IVF/ICSI. Initial infectious disease screening should be undertaken on the recipient and their partner as outlined in Table 4. Standard preconception counselling and testing should occur, including confirming immunity to rubella and varicella, and offering appropriate immunization prior to treatment if not immune. Blood type Rh and antibody screening are also recommended preconception. The recipient should be offered genetic screening as appropriate, based on the results of the genetic evaluation of the sperm donor. Uterine cavity and tubal evaluation should be considered to rule out any uterine or tubal abnormalities that may diminish chance of intrauterine pregnancy. Documentation of ovulation should be confirmed by history, or if history is inconclusive, confirmation by other indicators of ovulation.

### **Sperm Donors**

Both known and anonymous sperm donation are available in Canada. The screening and testing for known and anonymous sperm donors are addressed by the Semen Regulations; the regulations pertain to use of semen for therapeutic donor insemination. Sperm donors should undergo medical and genetic screening as outlined in Tables 2 and 3.

All sperm donors must be 18 years of age or older, in accordance with the AHR Act. The age of exclusion for a sperm donor in the Semen Regulations is age greater than 40 years. There are no restrictions surrounding the number of donations in the Semen Regulations. Limitations of the number of families or offspring created by gamete donation vary widely throughout the world.<sup>15</sup> Donors should be asked whether they have donated previously during their screening process.

## **Oocyte Donation**

### **Oocyte Donation Recipients and Partners**

Indications for oocyte donation include, but are not limited to, primary ovarian insufficiency, advanced reproductive age, repeated in vitro fertilization (IVF) failure or individuals with poor oocyte or embryo quality, or prevention of transmission of genetic disease when the intended egg provider parent carries a known genetically inheritable disease (chromosomal translocation, autosomal dominant or X-linked



disorder, autosomal recessive disorder where the sperm provider partner is also a carrier of the disorder). Medical history and physical examination should be performed prior to treatment. Infectious disease screening, standard preconception counselling and testing should occur, including confirming immunity to rubella and varicella, and offering appropriate immunization prior to treatment if not immune (Table 5). Blood type, Rh factor, and antibody screening are also recommended preconception. Uterine cavity evaluation should be performed to rule out any uterine abnormalities that may diminish embryo implantation. If applicable, a partner who is planning on being the sperm provider should have semen analysis testing performed. This partner should be offered genetic screening as appropriate, based on the results of the genetic evaluation of the oocyte donor.

There are no legal upper age limits for oocyte donation recipients. There is some evidence to demonstrate good neonatal outcomes and outcomes in individuals conceiving with oocyte donation between ages 50-60, with the exception in increased incidence of pre-eclampsia and gestational diabetes.<sup>16,17</sup> It is beyond the scope of this guideline to impose upper age limits for treatment. The current ASRM committee opinion discourages the transfer of oocytes or embryos to women greater than 55 years, even with no underlying medical conditions.<sup>18</sup> However, it is recommended individuals age 45 or greater planning to be an oocyte donor recipient undergo appropriate medical testing and a high risk obstetrical consultation prior to undertaking treatment (Level II-2B).

### **Oocyte Donors**

Both known and anonymous oocyte donation are available in Canada. Some Canadian couples access oocyte donation by traveling to fertility clinics outside of Canada or importing oocytes from oocyte banks. Clinics must also ensure that frozen oocytes imported into Canada meet Canadian standards including (but not limited to) ensuring the donor is over the age of 18, has provided appropriate informed consent, screening was performed (as outlined in Table 5) and ensuring the donor is provided with accessible and high-quality follow-up care. As outlined in the AHR Act, oocyte donors must be 18 years of age or greater. If a prospective donor is 35 years of age or greater, the intended parent(s) should be informed of the age related reduction in pregnancy and live birth rates and increase in aneuploidy risks with increasing age of the donor. Genetic counselling for prenatal genetic screening should be offered to the potential oocyte donor as recommended in the Society of Obstetrics and Gynecology of Canada Guidelines<sup>7</sup> (Table 3), and the results shared with the intended parent(s) after proper consent has been obtained.

Oocyte donors must be informed of the side-effects and risks of ovarian stimulation with gonadotropins, and the risks and complications of oocyte retrieval. Oocyte donors must also be informed of the risks of ovarian hyperstimulation. Good evidence exists to support an increase in live birth rates, embryo cryopreservation, and cumulative live birth rates in a single ovarian stimulation, with increasing numbers of oocytes).<sup>19,20</sup> However, the number of developing follicles during ovarian stimulation correlates with the risk of ovarian hyperstimulation syndrome (OHSS)<sup>21</sup>, the predominant OHSS experienced in oocyte donors. There needs to be a balance between these two dichotomous endpoints that must err in the goal of minimizing risks to the oocyte donor. Strategies to minimize OHSS risk (including agonist trigger) are addressed in the CFAS clinical practice guideline – Guidelines on Management of Ovarian Hyperstimulation Syndrome.



Ovarian reserve testing should be undertaken to provide appropriate determination of likelihood of adequate ovarian stimulation for information purposes for the oocyte donation recipient, and to ensure appropriate ovarian stimulation regime to minimize the risk of OHSS. Oocyte donors should be advised of the risk of unintended pregnancy and the need for contraception during ovarian stimulation until post-retrieval. Additionally, post-procedure care, counselling, and follow-up must be available and offered to oocyte donors.

The concern regarding the number of families created similarly exists for egg donors; in addition to the potential cumulative risks of ovarian stimulation and egg retrieval. In the USA, the ASRM recommends limiting the number of stimulated cycles for oocyte donations per donor to 6 or less within their lifetime.<sup>22</sup> However, there currently seems to be little evidence to suggest that repetitive oocyte donation affects ovarian reserve, although long term data is lacking.<sup>23,24</sup> There are procedural risks associated with each ovarian stimulation and oocyte retrieval, regardless of the number of procedures. Physicians and clinics should ask potential oocyte donors the number of times they have donated previously as part of their medical assessment. If applicable, oocyte donors should be counseled on the potential risks of multiple oocyte donation cycles. As the oocyte donor's and recipient's personal health information is confidential, it may not be possible to prevent an oocyte donor from undergoing multiple ovarian stimulations at multiple ART clinics. In spite of this, it seems reasonable to arbitrarily accept a liberal recommendation, of no more than 6 ovarian stimulations for oocyte donation per donor within their lifetime.



## **Surrogacy**

### **Intended Parent(s) and Intended Parent Gamete Providers**

For surrogates, the intended parent(s) are often the gamete providers (the sperm and egg providers) used to create the embryo and their potential offspring. However, in certain cases, the intended parent(s) may require a sperm and/or oocyte donor to achieve a pregnancy. In traditional surrogacy the surrogate is also the oocyte donor. The pregnancy is typically conceived by insemination of the traditional surrogate using sperm from the sperm provider (or donor semen selected by the intended parent(s)). A traditional surrogate should undergo the steps required for an oocyte donor as outlined previously and also for a surrogate as outlined below. Indications for surrogacy include, but are not limited to: absence of uterus or destruction of uterine cavity, a person or couple without a partner who can carry a pregnancy, a medical indication that would cause significant risk to the carrying parent or fetus if the intended parent were to become pregnant, recurrent miscarriage, or an endometrial or uterine factor (multiple recurrent implantation failures in a good prognosis IVF patient). In addition, there may be a role for biological lesbian co-parents, where one partner is the egg provider and the other partner carries the pregnancy in order to share in the reproductive process.<sup>25,26</sup> In instances where pregnancy by the intended parent would entail neonatal or personal risks, consultation with a maternal fetal medicine specialist should be undertaken, in order to review the risks of pregnancy and determine whether it is a medical indication for surrogacy.

The Semen Regulations in Canada have been accepted to fall outside the purview of the transfer of an embryo created for the purpose of a surrogacy cycle. As a result, sperm from the sperm provider partner in a surrogacy treatment cycle should undergo medical history screening and infectious disease screening as outlined in Table 6. In the case of traditional surrogacy, the semen from the sperm provider must be considered donor semen and will need to follow the Semen Regulations. In addition to infectious disease screening, blood type and Rh factor are also recommended preconception. If the surrogate is Rh negative and either of the sperm or oocyte providers are Rh positive, the surrogate and intended parent(s) should be informed of the risks of Rh isoimmunization, hemolytic disease of the fetus and newborn, and possible risks to the surrogate's offspring in subsequent pregnancies. Where applicable, semen analysis testing should be performed.

### **Surrogates**

It is of paramount importance that surrogates are appropriately screened to minimize the risks to the carrier's health, which are inherent in the process of undertaking an altruistic, but potentially health compromising situation. Health Canada has documented in Canada from 1997-2000, the risk of pregnancy-related death was 6.1 per 100,000 live births, and the risk of severe morbidity in Canada from 1991-2001 was 4.6 per 1000 deliveries). The surrogate must be made aware of the risks of pregnancy. The surrogate must be at least 21 years of age, by law. While oocyte donation recipients of advanced age have demonstrated acceptable outcomes for themselves and neonatal outcomes, a lower threshold for acceptable obstetrical risk should be assumed by a surrogate than a pregnant person with their own genetic child, due to increased risks to themselves and neonatal risks with advancing age.<sup>27,28</sup> Optimally, a surrogate should be under age 35 at the time of embryo transfer and it is recommended that surrogates are under the age of 45, due to potential increased perinatal risk.<sup>29</sup> A thorough medical, obstetrical, and social history and physical exam should be undertaken by the treating physician to determine the medical



suitability of the surrogate. Optimally, surrogates should have a body mass index (BMI) between 18.5-24.9 kg/m<sup>2</sup> and preferably under 30 kg/m<sup>2</sup>. Surrogates with a BMI above 35 kg/m<sup>2</sup> should be discouraged from treatment<sup>30</sup>. Surrogates should have had at least one uncomplicated term pregnancy, have a stable social environment, and be a non-smoker. In addition to previously discussed infectious disease screening, prior to treatment, the surrogate should have confirmation of a current and normal Pap smear, Blood type and Rh antibody screen, and uterine cavity screening such as hysterosalpingogram, sonohysterogram or hysteroscopy (Table 6). Rubella and varicella serology should be performed and immunization offered if the surrogate is non-immune. If the surrogate declines immunization, then the intended parent(s) should be informed of the risks of congenital rubella syndrome and congenital varicella syndrome. Urine drug screen of the surrogate may be considered. Clinical judgement should be applied in assessing surrogates for other potential factors for increased obstetrical risk (eg. multiparity, number of previous caesarean sections).

Some of the issues that may be addressed by the physician in anticipation of treatment in a surrogacy cycle include appropriate screening and testing and pregnancy care of the surrogate, the possibility of pregnancy termination or selective fetal reduction if indicated or requested by the intended parent(s), and the management of pregnancy specific complications as they arise. With risk mitigation being of utmost importance to the surrogate, two specific considerations must be addressed with the surrogate, and the intended parent(s). First, given the extremely small risk of seroconversion of the gamete providers for one of the tested infectious diseases between the designated testing interval and embryo transfer, cryopreservation and quarantining of the embryos for 180 days or greater can be offered to all surrogates. Second, the increased pregnancy-related morbidity in multiple pregnancy should warrant strong consideration of single embryo transfer to limit the risk of multiple pregnancy. The transfer of more than one embryo, in accordance with the CFAS guidelines,<sup>31</sup> should involve discussion of the pregnancy-related and neonatal risks and agreement by the surrogate, their partner (if applicable), and the intended parent(s).

### **Embryo Donors**

There is an opportunity for individuals who have created supernumerary (surplus) embryos that they no longer wish to use for their own attempts at human reproduction, to donate these embryos to other intended parent(s) that may require or desire gamete donation, and wish to use such embryos. Individuals should be made aware of this option at the time of embryo disposition. However, the majority of individuals who have supernumerary cryopreserved embryos that they no longer wish to use for their own use, rarely wish to donate these embryos for the use by another individual or couple.<sup>32-34</sup>

Embryos used for embryo donation are previously cryopreserved embryos that individuals or couples are now choosing to donate, and provide unique circumstances that slightly differ from the process for sperm donors or oocyte donors. The recommended testing for the embryo donors is described in Table 7. These tests should be done a minimum of 180 days after embryo cryopreservation (meaning donated embryos should be quarantined for a minimum of 180 days with repeat serological testing prior to use for donation). If the testing in Table 7 is negative, the risk of infectious transmission to the recipient is negligible.



Potential embryo donors should consider delaying the decision to donate until at least 1 year after pregnancy and delivery or completion of their treatment. Counselling and consent requirements for these individuals is described in the relevant sections above. Embryo donors must give consent for use of their reproductive material for use by a third party. Embryo donors must be 18 years of age or greater. If the oocyte donor of the created embryo is 35 years of age or greater at the time of initial donation and cryopreservation of the embryos, the recipient should be informed of the age related reduction in pregnancy and live birth rates and increase in aneuploidy risks with increasing age of the donor. If the sperm donor of the embryo is above 40 years of age when the embryo was created, the recipient should be informed of the relevant provisions of the Semen Regulations with respect to age of semen donors. Genetic counselling for prenatal genetic screening should be offered to embryo donors as recommended in the Society of Obstetrics and Gynecology of Canada Guidelines (Table 3)<sup>4</sup>, and the results shared with the recipients. The intended parent(s) must be informed if genetic screening results are unavailable. Additional genetic screening/testing of the embryo donors can be undertaken as deemed appropriate by the embryo donors and recipients, after informed consent by all parties.

### **Embryo Donor Recipients**

Embryo donor recipients should undergo infectious disease screening and specific third party reproduction treatment recommendations as described in Table 7. Counselling and consent to treatment/use is previously addressed.

### **Recommendations:**

18. Sperm donation recipients should undergo infectious disease and preconception medical and genetic screening. (Level III-A)
19. Sperm donors must undergo screening as required by the Semen Regulations. (Level III-A)
20. Oocyte donation recipients should undergo infectious disease screening and preconception medical screening. (Level III-A)
21. Individuals age 45 or greater planning to be an oocyte donor recipient undergo appropriate medical testing and a high risk obstetrical consultation prior to undertaking treatment (Level II-2B)
22. Oocytes donors should not undergo more than 6 lifetime ovarian stimulations for oocyte donation. (Level III-L)
23. Surrogates and intended parent(s) should have infectious screening and genetic screening, if the intended parent(s) is the gamete provider. (Level III-A)
24. Surrogates should undergo thorough medical, obstetrical, and social screening to determine eligibility as well as counseling regarding the risks associated with pregnancy. (Level II-2B).
25. Embryo donors should undergo infectious screening at least 180 days after embryo cryopreservation. (Level III-A)



### **Conclusion**

Third party reproduction provides individuals with medical and/ or social infertility the opportunity to create and parent a child, which may not otherwise be possible without the use of gamete donation or the assistance of a surrogate. It provides reproductive options for individuals without competent gametes/ a functional uterus or with Mendelian inherited disease, as well as individuals who are single or identify as LGBTQ. It is important that Canadian specific guidelines exist that allow for safe and effective screening, testing and treatment of individuals involved in third party reproduction, and that the recommended practices are consistent with relevant Canadian legislation, ethics and regulations.



Quality of Evidence Assessment*	Classification of Recommendations‡
I: Evidence obtained from at least one properly randomized controlled trial	A. There is good evidence to recommend the clinical preventive action
II-1: Evidence from well-designed controlled trials without randomization	B. There is fair evidence to recommend the clinical preventive action
II-2 Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group	C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making
II-3 Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in the category	D. There is fair evidence to recommend against the clinical preventive action
III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees	E. There is good evidence to recommend against the clinical preventive action
	L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

**Table 1 - Key to evidence statements and grading of recommendations, using the ranking of the Canadian Task Force on Preventative Health Care**

\*The quality of evidence reported in these guidelines has been adapted from the Evaluation of Evidence criteria described in the Canadian Task Force on the Periodic Preventive Health Exam Care.

‡ Recommendations included in these guidelines have been adapted from the Classifications of Recommendations criteria described in the Canadian Task Force on the Periodic Preventive Health Exam Care.



1. Employment by the facility or having a family member employed by the facility
2. Indications of high risk for the Human Immunodeficiency Virus (HIV), Hepatitis B virus (HBV), Hepatitis C virus (HCV), or Human T-cell Lymphotropic Virus (HTLV), including:
  - a. men who have had sex with another man, even once, since 1977
  - b. persons who report intravenous, intramuscular, or subcutaneous injection of drugs that are not prescribed by a licensed physician for medical purposes
  - c. persons who report tattoos or body piercing involving non-sterile skin penetration in the preceding 12 months
  - d. persons with hemophilia or related clotting disorder who have received human derived clotting factor concentrates
  - e. persons who have engaged in sex in exchange for money or drugs at anytime since 1977
  - f. persons who have had sex in the preceding 12 months with any person described in item (2)(a) through (2)(e) above
  - g. persons who have been exposed to known or suspected HIV infected blood or body fluids through percutaneous inoculation or through contact with an open wound, non-intact skin, or mucous membrane
  - h. persons who cannot be tested for infectious disease agents because of refusal, inadequate blood sample, or other reasons
  - i. persons with a history of repeatedly reactive screening for antibody to HIV-1 or HIV-2, Hepatitis B surface antigen (HBsAg), antibody to Hepatitis B core (HBc) antigen, antibody to HCV, or antibody to HTLV-I or HTLV-II, regardless of the results of supplemental assays
  - j. persons whose history, physical examination, medical records, or pathology report reveal other evidence of infection or high-risk behaviours, such as:
    - i. diagnosis with Acquired Immuno-Deficiency Syndrome (AIDS)
    - ii. unexplained weight-loss
    - iii. night sweats
    - iv. blue or purple spots on the skin or mucous membranes typical of Kaposi's Sarcoma
    - v. unexplained lymphadenopathy lasting more than 1 month
    - vi. unexplained temperature greater than 38.6 C (100.5 F) for more than 10 days
    - vii. unexplained persistent diarrhea
    - viii. needle tracks or other signs of parenteral drug use
  - k. persons who have, or have had, sex with a person known to have HIV, HBV, HCV, or HTLV infection, or who is at high risk for such infection;
  - l. persons who are at risk of having acquired HIV from geographic regions which are endemic for HIV strains that are not detectable by current screening tests (these individuals may be reconsidered once tests to detect the variant strains become available);
  - m. persons with active viral hepatitis;
  - n. persons who have received, or whose sexual partners have received blood, blood components, blood products or other human tissues in the preceding 12 months
  - o. persons who have been exposed to blood or body fluids through percutaneous inoculation or through contact with an open wound, non-intact skin, or mucous membrane in the preceding 12 months
  - p. persons who have been excluded permanently from donating blood; persons who have used intranasal cocaine in the preceding 12 months
3. Sexually transmitted disease in the preceding 12 months
4. Sexual encounter in the preceding 12 months with someone whose sexual background the potential donor is unsure of
5. Urethral discharge, genital warts, or genital ulcers at the time of donation
6. History of alcoholism
7. Diagnosis with Creutzfeldt-Jakob Disease (CJD) or a first degree family member with a history of CJD
8. Receipt of human pituitary-derived growth hormone or dura mater
9. Spongiform encephalopathy or prion disease
10. Viral encephalitis or encephalitis of unknown origin
11. Any major systemic diseases, including systemic malignancies.

**Table 2 - Screening Questionnaire for Gamete Donors, Gamete Providers or Gestational Carriers**

(adapted from the Exclusion Criteria in Section 2 of the Health Canada Direction- Technical Requirements for Therapeutic Donor Insemination: [http://www.hc-sc.gc.ca/dhp-mps/bratherap/applic-demande/guides/semen-sperme-accs/semen-sperme\\_directive-eng.php](http://www.hc-sc.gc.ca/dhp-mps/bratherap/applic-demande/guides/semen-sperme-accs/semen-sperme_directive-eng.php))



**GENETIC HISTORY FOR GAMETE DONORS**

A thorough pre-conception history identifies gamete donors who are at increased risk of donating gametes with genetic disease. When gamete donors and potential gamete donor recipients are informed of the risks of having a baby with birth defects or a genetic disorder prior to pregnancy, they are then able to determine their options regarding a pregnancy and the use of gametes from a specific donor.

Family History of Gamete Donor

- Construct three-generation pedigree.
- Include assessment of **genetic diseases**, including muscular dystrophy, hemophilia, cystic fibrosis, fragile X syndrome, congenital heart disease, phenylketonuria, dwarfism, sickle cell anemia, and Tay-Sachs disease.
- Include assessment of **multifactorial congenital malformations**, such as spina bifida, anencephaly, cleft palate and cleft lip, hypospadias, and congenital heart disease.
- Include assessment of **familial diseases with a major genetic component**, such as developmental disability, premature arteriosclerosis, diabetes mellitus, psychosis, epileptic disorders, hypertension, rheumatoid arthritis, deafness, and severe refractive disorders of the eye.

Ethnic History

Establish risk for specific conditions related to ethnic origin, such as sickle cell anemia, Tay-Sachs disease, neural tube defects, beta-thalassemia, and alpha-thalassemia.

Age

Establish risks associated with age

**Table 3 – Genetic history for gamete donors**

**(adapted from SOGC Guidelines, “Genetic considerations for woman’s preconception evaluation”)<sup>4</sup>**



	<b>Infectious Disease Screening</b> HIV-1 & HIV-2 Antibody Hepatitis C Antibody Hepatitis B Surface Ag Hepatitis B Core Ab (IgG & IgM) Syphilis serology CMV IgM & IgG	<b>Table 2 – Screening Questionnaire</b>  <b>Table 3 - Genetic History</b>	<b>Legal counsel</b>	<b>Counseling</b>	<b>Additional testing</b>
<b>Sperm donor</b>	Required As per Semen Regulations	As per Semen Regulations	Recommended	Recommended	
<b>Sperm donor partner</b>	No	No	No	Recommended	
<b>Sperm donation recipient</b>	Within 6 months prior to donation*	No	Recommended	Recommended	ABO, Rh & antibodies Rubella & varicella titres Uterine cavity and tubal assessment Document ovulation
<b>Sperm donation recipient partner</b>	Within 6 months prior to donation*	No	Recommended	Recommended	

**Table 4- Recommended steps for individuals involved in sperm donation PRIOR to donation and treatment.**

\* Initial screening is recommended for the sperm donor recipient and sperm donor recipient partner. As all donor sperm samples undergo quarantine and repeat testing on the donors, the frequency of subsequent testing can be determined by the individual ART clinic.



	<b>Infectious Disease Screening</b> HIV-1 & HIV-2 Antibody* Hepatitis C Antibody* Hepatitis B Surface Ag Hepatitis B Core Ab (IgG & IgM) Syphilis serology	<b>Table 2 – Screening Questionnaire</b>  <b>Table 3 - Genetic History</b>	<b>Legal counsel</b>	<b>Counseling</b>	<b>Additional testing</b>
<b>Oocyte donor</b>	-Within 6 months prior to donation -Recommended within 30 days of donation -Repeat at least 180 days after donation if oocytes cryopreserved and quarantined	Recommended	Recommended	Recommended	ABO & Rh factor N. gonorrhea/C. Trachomatis# Ovarian reserve tests
<b>Oocyte donor partner</b>	Within 6 months prior to donation	No	No	Recommended	
<b>Oocyte donation recipient</b>	Within 6 months prior to donation	No	Recommended	Recommended	ABO, Rh & antibodies Rubella & varicella titres N. gonorrhea/C. Trachomatis# Uterine cavity assessment
<b>Oocyte donation recipient partner</b>	Within 6 months prior to donation	No	Recommended	Recommended	If sperm provider: Semen analysis ABO & Rh factor

**Table 5- Recommended steps for individuals involved in oocyte donation PRIOR to donation and treatment.**

\* HIV-1 and Hepatitis C NAT should be offered if available for testing within 30 days of donation

# Cervical cultures or nucleic acid-based test on urine or swab from cervix or vagina for Neisseria gonorrhoeae and Chlamydia trachomatis



	<b>Infectious Disease Screening</b> HIV-1 & HIV-2 Antibody* Hepatitis C Antibody* Hepatitis B Surface Ag Hepatitis B Core Ab (IgG & IgM) Syphilis serology N. gonorrhoea/C. Trachomatis#	<b>Table 2 – Screening Questionnaire</b>  <b>Table 3 - Genetic History</b>	<b>Legal counsel</b>	<b>Counseling</b>	<b>Additional testing</b>
<b>Gestational surrogate (GS)</b>	-Within 6 months prior to embryo transfer - Recommend within 30 days prior to embryo transfer	Screening Questionnaire recommended	Recommended with surrogacy agreement <sup>‡</sup>	Recommended	ABO, Rh & antibodies Rubella & varicella titres Pap smear Uterine cavity assessment
<b>Gestational surrogate partner</b>	-Within 6 months prior to embryo transfer	No	Recommended with surrogacy agreement <sup>‡</sup>	Recommended	HTLV-1 and HTLV-2 Antibody CMV IgM & IgG
<b>Sperm provider/donor- Gestational surrogate</b>	-Within 6 months prior to donation - Recommend within 30 days prior to donation -Recommended at least 180 days after donation if embryos cryopreserved and quarantined	-Screening Questionnaire recommended -Genetic History recommended if sperm donor	Recommended with surrogacy agreement <sup>‡</sup>	Recommended	ABO & Rh factor Semen analysis
<b>Oocyte provider/donor-gestational surrogate</b>	-Within 6 months prior to treatment -Recommend within 30 days prior to donation -Recommended at least 180 days after donation if embryos cryopreserved and quarantined	-Screening Questionnaire recommended -Genetic History recommended if oocyte donor	Recommended with surrogacy agreement <sup>‡</sup>	Recommended	ABO & Rh factor
<b>Intended parent(s)-gestational surrogate (if not the sperm or oocyte provider)</b>	No	No	Recommended with surrogacy agreement <sup>‡</sup>	Recommended	

**Table 6- Recommended steps for individuals involved in gestational carrier and traditional surrogacy arrangements PRIOR to treatment.**

\* HIV-1 and Hepatitis C NAT should be offered where available for testing within 30 days of donation

# Cervical cultures or nucleic acid-based test on urine or swab from urethral meatus, cervix or vagina for Neisseria gonorrhoeae and Chlamydia trachomatis

‡ Except in Quebec where surrogacy contracts are not enforceable by legislation



	<b>Infectious Disease Screening</b> HIV-1 & HIV-2 Antibody* Hepatitis C Antibody* Hepatitis B Surface Ag Hepatitis B Core Ab (IgG & IgM) Syphilis serology N. gonorrhoea/C. Trachomatis#	<b>Table 2 – Screening Questionnaire</b>  <b>Table 3 - Genetic History</b>	<b>Legal counsel</b>	<b>Counseling</b>	<b>Additional testing</b>
<b>Traditional surrogate</b>	-Within 6 months prior to insemination -Recommended within 30 days prior to insemination	Recommended	Recommended with surrogacy agreement¥	Recommended	ABO, Rh & antibodies Rubella & varicella titres Pap smear Uterine cavity assessment
<b>Traditional surrogate partner</b>	-Within 6 months prior to insemination	No	Recommended with surrogacy agreement¥	Recommended	HTLV-1 and HTLV-2 Antibody CMV IgM & IgG
<b>Sperm provider/donor-traditional surrogate</b>	As per Semen Regulations	-Screening Questionnaire recommended -Genetic History recommended if sperm donor	Recommended with surrogacy agreement¥	Recommended	ABO & Rh factor Semen analysis
<b>Intended parent(s)-traditional surrogate (if not the sperm or oocyte provider)</b>	No	No	Recommended with surrogacy agreement¥	Recommended	

**Table 6 (cont)- Recommended steps for individuals involved in gestational carrier and traditional surrogacy arrangements PRIOR to treatment.**

\* HIV-1 and Hepatitis C NAT should be offered where available for testing within 30 days of donation

# Cervical cultures or nucleic acid-based test on urine or swab from urethral meatus, cervix or vagina for Neisseria gonorrhoeae and Chlamydia trachomatis

¥ Except in Quebec where surrogacy contracts are not enforceable by legislation



	<b>Infectious Disease Screening</b> HIV-1 & HIV-2 Antibody Hepatitis C Antibody Hepatitis B Surface Ag Hepatitis B Core Ab (IgG & IgM) Syphilis serology N. gonorrhoea/C. Trachomatis <sup>#</sup>	<b>Table 3 - Genetic History</b>	<b>Legal counsel</b>	<b>Counseling</b>	<b>Additional testing</b>
<b>Embryo donor (oocyte)</b>	Recommended at least 180 days after initial gamete donation	Recommended	Recommended	Recommended	ABO & Rh factor
<b>Embryo donor (sperm)</b>	Recommended at least 180 days after initial gamete donation	Recommended	Recommended	Recommended	ABO & Rh factor HTLV-1 and HTLV-2 Antibody CMV IgM & IgG
<b>Embryo donor-recipient</b>	Recommended within 6 months prior to embryo transfer	No	Recommended	Recommended	ABO, Rh & antibodies Rubella & varicella titres Uterine cavity assessment
<b>Embryo donor recipient partner</b>	Recommended within 6 months prior to embryo transfer	No	Recommended	Recommended	

**Table 7- Recommended steps for individuals involved in embryo donation PRIOR to treatment.**

<sup>#</sup> Cervical cultures or nucleic acid-based test on urine or swab from urethral meatus, cervix or vagina for Neisseria gonorrhoeae and Chlamydia trachomatis



1. Practice Committee of American Society for Reproductive Medicine, Practice Committee of Society for Assisted Reproductive Technology. Recommendations for gamete and embryo donation: a committee opinion. *Fertil Steril*. 2013;99:47-62.
2. The Practice Committee of the American Society for Reproductive Medicine and the Practice Committee for the Society for Assisted Reproductive Technology. Recommendations for practices utilizing gestational carriers: an ASRM Practice Committee guideline. *Fertil Steril*. 2012;97:1301-1308.
3. Directive 2004/23/EC of the European Parliament and of the Council, March 2004. Available at <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:102:0048:0058:EN:PDF>
4. Barratt C, Englert Y, Gottlieb C, Jouannet P. Gamete donation guidelines. The Corsendonk consensus document for the European Union. *Hum Reprod*. 1998;13:500-501.
5. CSA Group. CAN/CSA-Z900.2.1-12 Tissues for assisted reproduction, December 2012.
6. Assisted Human Reproduction (Section 8 Consent) Regulations (SOR/2007-137).
7. Wilson RD, Audibert F, Brock JA, et al. Genetic considerations for a woman's pre-conception evaluation. *J Obstet Gynaecol Can*. 2011;33:57-64.
8. Practice Committee of American Society for Reproductive Medicine, Practice Committee of Society for Assisted Reproductive Technology. 2008 Guidelines for gamete and embryo donation: a Practice Committee report. *Fertil Steril*. 2008;90:S30-44.
9. Wingfield M, Cottell E. Viral screening of couples undergoing partner donation in assisted reproduction with regard to EU Directives 2004/23/EC, 2006/17/EC and 2006/86/EC: what is the evidence for repeated screening? *Hum Reprod*. 2010;25:3058-3065.
10. Cobo A, Remohi J, Chang CC, Nagy ZP. Oocyte cryopreservation for donor egg banking. *Reprod Biomed Online*. 2011;23:341-346.



11. Pomeroy KO, Harris S, Conaghan J, et al. Storage of cryopreserved reproductive tissues: evidence that cross-contamination of infectious agents is a negligible risk. *Fertil Steril*. 2010;94:1181-1188.
12. Cobo A, Bellver J, de los Santos MJ, Remohi J. Viral screening of spent culture media and liquid nitrogen samples of oocytes and embryos from hepatitis B, hepatitis C, and human immunodeficiency virus chronically infected women undergoing in vitro fertilization cycles. *Fertil Steril*. 2012;97:74-78.
13. Devaux A, Soula V, Sifer C, et al. Hepatitis C virus detection in follicular fluid and culture media from HCV+ women, and viral risk during IVF procedures. *Hum Reprod*. 2003;18:2342-2349.
14. Yee S, Hitkari JA, Greenblatt EM. A follow-up study of women who donated oocytes to known recipient couples for altruistic reasons. *Hum Reprod*. 2007;22:2040-2050.
15. Janssens PM, Nap AW, Bancsi LF. Reconsidering the number of offspring per gamete donor in the Dutch open-identity system. *Hum Fertil (Camb)*. 2011;14:106-114.
16. Paulson RJ, Boostanfar R, Saadat P, et al. Pregnancy in the sixth decade of life: obstetric outcomes in women of advanced reproductive age. *JAMA*. 2002;288:2320-2323.
17. Chibber R. Child-bearing beyond age 50: pregnancy outcome in 59 cases "a concern?". *Arch Gynecol Obstet*. 2005;271:189-194.
18. Ethics Committee of the American Society of Reproductive Medicine. Oocyte or embryo donation to women of advanced age: a committee opinion. *Fertil Steril*. 2013; 100(2):337-340.
19. Baker VL, Brown MB, Luke B, Conrad KP. Association of number of retrieved oocytes with live birth rate and birth weight: an analysis of 231,815 cycles of in vitro fertilization. *Fertil Steril*. 2015 Apr;103(4):931-938.
20. Drakopoulos P, Blockeel C, Stoop D, Camus M, de Vos M, Tournaye H, Polyzos NP. Conventional ovarian stimulation and single embryo transfer for IVF/ICSI. How many oocytes do we need to maximize cumulative live birth rates after utilization of all fresh and frozen embryos?



Hum Reprod. 2016 Jan 2. [Epub ahead of print]

21. Papanikolaou EG, Pozzobon C, Kolibianakis EM, Camus M, Tournaye H, Fatemi HM, Van Steirteghem A, Devroey P. Incidence and prediction of ovarian hyperstimulation syndrome in women undergoing gonadotropin-releasing hormone antagonist in vitro fertilization cycles.

*Fertil Steril.* 2006 Jan;85(1):112-20.

22. Practice Committee of American Society for Reproductive Medicine. Repetitive oocyte donation.

*Fertil Steril.* 2008;90:S194-5.

23. Luk J, Arici A. Does the ovarian reserve decrease from repeated ovulation stimulations? *Curr Opin Obstet Gynecol.* 2010;22:177-182.

24. Bukulmez O, Li Q, Carr BR, Leader B, Doody KM, Doody KJ. Repetitive oocyte donation does not decrease serum anti-Mullerian hormone levels. *Fertil Steril.* 2010;94:905-912.

25. Dondorp WJ, De Wert GM, Janssens PM. Shared lesbian motherhood: a challenge of established concepts and frameworks. *Hum Reprod.* 2010;25:812-814.

26. Marina S, Marina D, Marina F, Fosas N, Galiana N, Jove I. Sharing motherhood: biological lesbian co-mothers, a new IVF indication. *Hum Reprod.* 2010;25:938-941.

27. Gilbert WM, Nesbitt TS, Danielsen B. Childbearing beyond age 40: pregnancy outcome in 24,032 cases. *Obstet Gynecol.* 1999;93:9-14.

28. Usta IM, Nassar AH. Advanced maternal age. Part I: obstetric complications. *Am J Perinatol.* 2008;25:521-534.

29. Kenny LC, Lavender T, McNamee R, O'Neill SM, Mills T, Khashan AS. Advanced maternal age and adverse pregnancy outcome: evidence from a large contemporary cohort. *PLoS One.* 2013;8:e56583.

30. Davies GA, Maxwell C, McLeod L, et al. Obesity in pregnancy. *J Obstet Gynaecol Can.* 2010;32:165-173.



31. Min JK, Claman P, Hughes E. Guidelines for the number of embryos to transfer following in vitro fertilization. *J Obstet Gynaecol Can.* 2006; 28(9):799-813.
32. Lanzendorf S, Ratts V, Keller S, Odem R. Disposition of cryopreserved embryos by infertility patients desiring to discontinue storage. *Fertil Steril.* 2010;93:486-489.
33. Hammarberg K, Tinney L. Deciding the fate of supernumerary frozen embryos: a survey of couples' decisions and the factors influencing their choice. *Fertil Steril.* 2006;86:86-91.
34. Cattapan A and Doyle, A. Patient decision-making about the disposition of surplus cryopreserved embryos in Canada. *JOGC.* In press.