Health Canada Santé Canada

Guidance Document

Safety of Sperm and Ova Regulations

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Foreword

Guidance documents are meant to provide assistance to industry and health care professionals on **how** to comply with governing statutes and regulations. Guidance documents also provide assistance to staff on how Health Canada mandates and objectives should be implemented in a manner that is fair, consistent, and effective.

Guidance documents are administrative instruments not having force of law and, as such, allow for flexibility in approach. Alternate approaches to the principles and practices described in this document ***may be*** acceptable provided they are supported by adequate justification. Alternate approaches should be discussed in advance with the relevant programme area to avoid the possible finding that applicable statutory or regulatory requirements have not been met.

This document should be read in conjunction with the accompanying notice and the relevant sections of other applicable Guidance documents.

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Introduction

Purpose/Overview

This Guidance document provides information on the interpretation and application of the *Safety of Sperm and Ova Regulations* (Safety Regulations) which are made under the *Assisted Human Reproduction Act* (AHR Act).

Scope and application

The Safety Regulations apply to donor sperm and ova intended for use in assisted human reproduction (AHR) by a recipient who is not the spouse, common-law partner or sexual partner of the donor. This includes the use of donor sperm in assisted human reproduction techniques (e.g., in vitro fertilization). The Safety Regulations also apply to ova that has been obtained from a donor and that is intended for the donor's use (i.e. via in vitro fertilization) as a surrogate mother.

It is important to note that the Safety Regulations do not apply to sperm and ova obtained from a spouse, common law partner, or sexual partner of the recipient. In addition, the Safety Regulations apply to donor sperm that is distributed by an establishment or health professional to a recipient for their personal use, however, they do not apply to that person's own use of donor sperm to self-inseminate.

The Safety Regulations apply to all establishments and health professionals who process, import, distribute or make use of donor sperm or ova for the purpose of AHR. In addition to this Guidance document, the AHR Act as well as the most up to date *Health Canada Directive: Technical Requirements for Conducting the Suitability Assessment of Sperm and Ova Donors* (Directive) should be consulted for a more detailed understanding of the Safety Regulations.

It is the responsibility of the regulated party to ensure that they have access to the most recent version of the AHR Act, the Safety Regulations, the Directive, and this Guidance document.

Policy objectives

The purpose of this regulatory framework is to help minimize the potential health risks to individuals in Canada who use donor sperm or ova for the purpose of AHR to help them build their families. This includes the risk of infectious disease transmission from the donor or during processing, to the recipient as well as to the child born of AHR, and the risk of genetic disease transmission from the donor to the child.

Policy statements

The Safety Regulations are risk-based in their design, meaning that the level of regulatory oversight corresponds to the level of risk an activity poses to the health and safety of individuals in Canada who use AHR to build their families. The Safety Regulations are focused on the safety of the donated sperm or ova and were designed in a way that

recognizes and complements the role the provinces and territories play in overseeing the practice of health professionals who are authorized to make use of sperm or ova in Canada.

Background

The AHR Act received royal assent on March 29, 2004. The Act was based on recommendations made by the 1993 Royal Commission on New Reproductive Technologies, which had the mandate to examine the ethical, legal, social, and economic implications of reproductive technologies and their impact on Canadian society, and in particular on women, children and families.

The AHR Act was written to be a comprehensive legislative framework that established provisions to protect and promote the health, safety, dignity, and rights of Canadians who use or are born of AHR technology. The goal of the AHR Act is to protect Canadians by setting out prohibited activities related to AHR that may pose significant human health and safety risks to Canadians or that are deemed to be ethically unacceptable or incompatible with Canadian values.

The current version of section 10 of the AHR Act was introduced in 2012, as part of amendments made to the Act following the Supreme Court of Canada's 2010 ruling that significant portions of the Act were unconstitutional due to their intrusion into provincial jurisdiction.

Section 10 of the AHR Act prohibits the distribution, use, and importation of donor sperm and ova for the purpose of AHR unless: (a) tests have been conducted in respect of the sperm or ova in accordance with the Safety Regulations, and the sperm or ova have been obtained, prepared, preserved, quarantined, identified, labelled, and stored and their quality assessed in accordance with the Safety Regulations; and (b) the donor of the sperm or ova has been screened and tested, and the donor's suitability has been assessed, in accordance with the Safety Regulations.

Guidance for implementation

In this Guidance document, the word "should" indicates a recommendation made by Health Canada. Where standards are recommended, decisions regarding their implementation should be based on a risk benefit analysis within the context of the establishment or health professional's operations. It should also be noted that the Safety Regulations specify minimum safety standards that may be exceeded by establishments and health professionals.

The statements enclosed in the boxes are sections taken directly from the Regulations. If there is a discrepancy between the text in this Guidance and the Regulations, the Regulations will take precedence.

Interpretation

Definitions

1 (1) The following definitions apply in these Regulations.

accident means an unexpected event that is not attributable to a deviation from the standard operating procedures or applicable laws, including these Regulations and that could compromise human health and safety or the safety of sperm or ova. (*accident*)

activity, in respect of sperm or ova, means any of the following activities:

(a) processing, which means

(i) performing the donor suitability assessment,

(ii) obtaining the sperm or ova from a donor,

(iii) preparing,

(iv) identifying,

(v) testing,

(vi) preserving,

(vii) assessing quality,

(viii) labelling,

(ix) quarantining, or

(x) storing;

(b) distributing; and

(c) importing. (*activité*)

Obtaining the sperm or ova from a donor

Obtaining is the collection or retrieval of sperm or ova from the donor. Sperm and ova must be obtained in a manner that reduces the risk to human health and safety and the safety of the sperm or ova. Specifically, measures must be taken to prevent contamination or cross-contamination and the transmission of an infectious disease, while also maintaining the quality of the sperm or ova.

Preparing

Preparation of sperm for use in AHR consists of the manipulation or treatment of sperm using a procedure to isolate sperm from semen, urine, testicular tissue or from an aspirate[1]. Commonly used methods of sperm preparation have two primary objectives: 1) to separate the sperm from the seminal fluid, and 2) to select the best quality sperm (i.e., motile sperm with normal morphology). Preparation of ova consists of the isolation of ova from surrounding cells, assessing the morphological quality and maturity of the isolated ova, and culturing of ova.

Preparation of sperm or ova for use in AHR presents the risk of contamination or cross-contamination and the risk of transmission of infectious diseases or disease agents to the recipient and the child born through assisted reproduction technology (ART)[2]. The risk of contamination or cross-contamination is even greater for establishments that prepare sperm or ova from a donor who has tested positive for infectious disease agents (e.g., HIV, HCV)[3].

Sperm and ova must be prepared in a manner that reduces the risk to human health and safety and the safety of the sperm or ova. Specifically, measures must be taken to prevent contamination or cross-contamination and the transmission of an infectious disease, while also maintaining the quality of the sperm or ova. Measures can include, but are not limited to, the use of appropriate equipment, and effective protocols such as density gradient centrifugation.

Preserving

Preserving is any procedure (e.g., cryopreservation) which has the purpose of maintaining the functionality of sperm or ova over a period of time. Establishments that preserve must do so using a method that prevents contamination and cross-contamination and that permits long term storage.

Sperm and ova must be preserved in a manner that reduces the risk to human health and safety and the safety of the sperm or ova. Specifically, measures must be taken to prevent contamination or cross-contamination and the transmission of an infectious disease, while also maintaining the quality of the sperm or ova.

Assessing quality

The quality of sperm can impact the health of the recipient (e.g., as it can reduce the chances of achieving a healthy pregnancy) as well as the health of the individual born of sperm that is of reduced quality[4, 5, 6]. An establishment that conducts a quality assessment of donor sperm should do so using a number of appropriate and effective methods, as recommended by various clinical guidelines. These include, but are not limited to, tests to assess sperm efficacy (motility, concentration, morphology), as well as tests to assess sperm quality before and after cryopreservation. When conducting a preliminary assessment of sperm quality, primary establishments must have in place minimum criteria for determining the acceptability of sperm samples.

The assessment of sperm motility is essential to establishing its quality. Sperm motility should be assessed as soon as possible after liquefaction of the sample to limit the deleterious effects of dehydration, pH or changes in temperature on motility[7]. In cases where sperm motility is low (less than 40%), an assessment of sperm vitality could be considered. Sperm vitality is estimated by assessing the membrane integrity of the cells to distinguish the immotile, live sperm cells from the dead sperm cells.

Sperm concentration, or sperm count, refers to the number of spermatozoa per unit volume of semen. It is a function of the number of spermatozoa emitted and the volume of fluid that dilutes them. According to the World Health Organization (WHO), a normal sperm count is considered to be over 15 million sperm per milliliter.

A morphological assessment of sperm should also be performed to assess its quality. This technical assessment includes an examination of the structure and shape of sperm cells as seen under a microscope using various nuclear and cytoplasmic stains. An establishment conducting the morphological assessment should employ a method that ensures consistent interpretations and diagnoses.

The methodology used to assess sperm efficacy, including sperm motility, concentration, and morphology, should comply with internationally recognized standards such as those set out in the WHO Laboratory Manual for the Examination of Human Semen[8].

In addition to assessing sperm efficacy, the quality of sperm before and after cryopreservation should be assessed given that cryopreservation is known to have an adverse effect on sperm motility. Cell survival after freezing and thawing depends largely on the minimization of intracellular water subject to ice formation. On average, approximately 50% of motile spermatozoa survive this process.

An establishment that assesses sperm quality post thaw must do so using appropriate and effective methods to minimize the damage caused by the cryopreservation process. The methodology used by establishments to assess sperm quality post thaw should comply with nationally or internationally recognized standards such as those set out by the Canadian Standards Association (CSA) National Standard on Tissues for Assisted Reproduction or in the WHO Laboratory Manual for the Examination of Human Semen.

Quarantining

Donor sperm and ova must be quarantined until certain conditions are met, including until the donor has been determined suitable under the regular process. Additionally, donor sperm and ova must also be quarantined in the event of an error, accident or adverse reaction.

There are two important concepts built in to the term quarantine, for the purposes of the Safety Regulations. First, all sperm and ova required to be quarantined must be identified as such and segregated from sperm and ova not under quarantine. Second, sperm and ova required to be quarantined must not be distributed or used.

For the purposes of the Safety Regulations, segregation can take the form of storing the donor sperm or ova in a physically separate area designated for such use or segregating through the use of a validated electronic segregation system (e.g., a validated computer system and barcode labeled sperm/ova containers).

It is important to note that the Safety Regulations also refer to segregated storage. While segregation is an important component of quarantining, these are to be understood as distinct concepts. Under certain situations (e.g., directed donation, exceptional access), donor sperm and ova that may pose a risk to human health and safety are permitted to be distributed and used. However, in those situations the sperm and ova must always be segregated from all other sperm and ova in order to mitigate risk.

adverse reaction means the unexpected presence of an infectious disease agent or the unexpected occurrence of an infectious disease in a recipient of sperm or ova or a child created from that sperm or those ova. (*effet indésirable*)

Directive means the document entitled *Technical Requirements for Conducting the Suitability Assessment of Sperm and Ova Donors*, published by the Department of Health, as amended from time to time. (*Directive*)

donation code means the unique group of numbers, letters, symbols or a combination of any of them that identifies the sperm or ova donation. (*code d'identification du don*)

donor identification code means the unique group of numbers, letters, symbols or a combination of any of them that is assigned to a donor. (*code d'identification du donneur*)

donor suitability assessment means an assessment of a donor that is based on the following:

(a) donor screening;

(b) physical examination of the donor; and

(c) donor testing. (*évaluation de l'admissibilité du donneur*)

error means a deviation from the standard operating procedures or applicable laws, including these Regulations, that could compromise human health and safety or the safety of sperm or ova. (*manquement*)

establishment means a person, partnership, unincorporated entity or a part of any of them that conducts an activity but only includes a health professional if the health professional conducts an activity that is not referred to in the definition *health professional*. (*établissement*)

health professional means a person who is authorized under the laws of a province to make use of sperm or ova in that province and who:

(a) makes use of sperm or ova or distributes sperm to a recipient for their personal use;

(b) prepares, quarantines, labels or stores sperm or ova for the purpose of their use by that person; or

(c) prepares, quarantines, labels or stores sperm for the purpose of its distribution by that person to a recipient for their personal use. (*professionnel de la santé*)

Directive

The Directive sets out the minimum technical requirements for conducting the donor suitability assessment, including donor screening, physical examination, and donor testing. It includes the technical requirements for screening the donor for the risk of infectious and genetic disease transmission and testing the donor for the presence of infectious disease

agents. The Directive is informed by national and international standards and regulations, including the CSA standard on Tissues for Assisted Reproduction[9].

Establishment

An establishment is an entity that imports or distributes donor sperm or ova or conducts any processing activity (see definition of "activity" as set out in section 1 of the Safety Regulations) with regard to such sperm or ova. A primary establishment is also considered to be an establishment.

An establishment that conducts a processing activity in respect of sperm or ova must do so in accordance with the Safety Regulations. If they are conducting that activity on behalf of a primary establishment they must be listed on the registration of that primary establishment.

For example, a testing lab may conduct donor testing on behalf of a primary establishment. That testing lab is considered an establishment, and is subject to the requirements of the Safety Regulations, but is not required to register with Health Canada. However, this testing lab is required to be listed on the registration of all primary establishments for which it conducts donor testing.

In some circumstances, an establishment may be considered to be independently conducting a processing activity, where it is not doing so on behalf of a primary establishment and is not itself a primary establishment. An example of this is when a fertility clinic merely stores donor sperm or ova prior to making use of them. Such an establishment must conduct its activities in accordance with the Safety Regulations, but is not required to register with Health Canada or be listed on a primary establishment's registration.

Health Professional

A health professional is a person who is authorized by the laws of their province or territory to make use of donor sperm or ova in AHR. A health professional is not considered an establishment when the health professional only conducts the following activities:

- makes use of donor sperm or ova;
- distributes donor sperm to a recipient for their personal use;
- prepares, quarantines, labels or stores donor sperm or ova only for the purpose of making use of that sperm or ova; or
- prepares, quarantines, labels or stores donor sperm only for the purpose of distributing that sperm to a recipient for their personal use.

As an integral part of the health and safety framework, health professionals are required to meet certain regulatory requirements with regard to records to permit the traceability of the donor sperm or ova, as well as requirements related to communicating risk, errors, accidents, and adverse reactions.

Where a person that is authorized to make use of donor sperm or ova conducts any activity, as defined by the Safety Regulations, other than those listed in the definition of a health professional, that person would be considered an establishment and subject to the relevant establishment requirements that correspond to the activities being carried out.

Furthermore, where a health professional or a group of health professionals has incorporated their practice, the corporation is considered an establishment and is subject to the relevant regulatory requirements.

There are some scenarios where the Safety Regulations equally apply to both the health professional and the establishment that may lead to some potential confusion. These could include situations where a health professional works for an establishment or where a health professional structures their practice by creating a corporation, in which case the health professional is not considered an establishment when they label, prepare, quarantine or store as an individual, yet the corporation is considered an establishment if it conducts any processing activity.

Regulatory obligations that are imposed on both health professionals and establishments apply equally to both parties in the scenarios described above. However, in these cases, Health Canada is of the view that the requirements on both the health professional and the establishment could be satisfied by a single or shared action on the part of both parties. For example, both the health professional and establishment have a requirement to maintain records with respect to the sperm and ova it uses. Where the health professional works for an establishment, for example, these requirements could be satisfied in the form of a single set of records that is maintained in the establishment's record management system.

The reason for the design of the Safety Regulations is to ensure that certain requirements that are at the core of the health and safety framework apply to health professionals who only make use of sperm or ova (e.g., family physician who performs intrauterine insemination) or distribute sperm to a recipient for their personal use (e.g., a family physician who serves as the shipping address for donor sperm to be used for self-insemination). These include requirements related to the communication of risk to the recipient, records to permit the traceability of the donor sperm or ova, as well as requirements related to errors, accidents, and adverse reactions.

human health and safety means the health and safety of a recipient of sperm or ova or a child created from that sperm or those ova to the extent that their health and safety relate to the safety of the sperm or ova. (*santé et sécurité humaines*)

medical director, in respect of a primary establishment, means a person who is authorized under the laws of the jurisdiction in which the primary establishment is situated to practise the profession of medicine and who is responsible for all medical and technical procedures carried out during the processing of sperm or ova. (*directeur médical*)

Medical Director

The medical director is a person in the primary establishment who is authorized under the laws of the jurisdiction in which the primary establishment is situated to practise medicine and who is responsible for all medical and technical procedures carried out during the processing of sperm or ova.

The medical director plays a number of key roles during processing that are critical to the safety of the donation.

First, the medical director, or a physician or nurse practitioner designated by the medical director, is responsible for conducting and documenting the donor suitability assessment, including donor screening, physical examination of the donor as well as donor testing.

The medical director is also responsible for preparing a structured questionnaire used to screen the donor, but may designate a physician or, in the case of genetic screening, a qualified professional to prepare it on their behalf.

Under the Regular Process for donation, based on the information obtained from the donor suitability assessment, the medical director is responsible for determining the suitability of a donor and documenting that the donation may be released from quarantine, which allows the donation to be distributed. Finally, the medical director is responsible for creating a summary document that contains information such as donor test results and a confirmation of the donor's suitability.

Under the Directed Donation Process, as set out in section 30 to 40 of the Safety Regulations, the medical director is responsible for reviewing and documenting the information obtained from the donor suitability assessment and, if applicable, the donor reassessment. In addition, the medical director is responsible for documenting any exclusion criteria that were met by the donor or parts of the donor suitability assessment that were not conducted, for review and consideration by the health professional.

primary establishment means an establishment that conducts all processing activities in respect of sperm or ova, whether it conducts them itself or another establishment conducts any of the activities on its behalf. (*établissement principal*)

quarantine, with respect to sperm and ova, means the quarantine described in subsection 28(2) conducted by an establishment or a health professional. (mise en quarantaine)

standard operating procedures means the component of a quality management system that comprises instructions that set out the processes applicable to the components of the system and to the activities carried out by an establishment. (*procédures d'opération normalisées*)

Primary Establishment

A primary establishment is the entity responsible for ensuring that, prior to distribution or use in Canada, donor sperm and ova are processed in accordance with the Safety Regulations. They are responsible for all processing activities, whether they conduct them themselves or another establishment does any of the processing activities on their behalf.

In many cases, the primary establishment will be a commercial sperm or ova bank. However, in certain instances, a fertility clinic or an individual physician may register as a primary establishment and take on the responsibility for all processing activities that it conducts itself or that is done on its behalf in order to facilitate a donation.

Amendments to Directive

(2) The document referred to in the definition of *Directive* is deemed to be amended for the purposes of these Regulations if the amendment is not inconsistent with the purpose of reducing risks to human health and safety.

The purpose of this subsection is to set out the circumstances under which the Directive may be amended.

The Directive is incorporated by reference on an ambulatory basis into the Safety Regulations, meaning it can be amended from time to time. This provides the Department with the ability to quickly update the requirements based on emerging scientific advances in the field of AHR and to effectively address urgent circumstances, for example, in the event of an emerging disease.

General Requirements

Primary establishment — conformity of processing

2 (1) A primary establishment must ensure that sperm or ova are processed in accordance with these Regulations before distributing or making use of them.

Primary establishment — activities on its behalf

(2) The primary establishment must ensure that every establishment that conducts any processing on its behalf meets the requirements of these Regulations.

The primary establishment has a central role in ensuring the safety of donor sperm and ova. This section establishes the two fundamental responsibilities of the primary establishment, namely to ensure that the sperm or ova that they distribute or make use of are processed in accordance with the Safety Regulations prior to doing so, and to ensure that every establishment that conducts a processing activity on its behalf does so in accordance with the Safety Regulations.

Some ways that a primary establishment can help ensure that an establishment conducting activities on their behalf is in compliance with the Safety Regulations, include the following:

- have written agreements or contracts in place that clearly outline the responsibilities and compliance with the Safety Regulations;
- ensure that the responsibilities are listed and understood as they relate to the requirements;
- audit the establishment prior to making arrangements for them to conduct activities on their behalf to ensure they meet the requirements of the Regulations;
- ensure that the establishment is conducting the audits as required by section 45 of the Safety Regulations and review the results of those audits;
- review test kit package inserts that are being used by establishments conducting donor testing on their behalf;
- review standard operating procedures applicable to the requirements in the Safety Regulations;
- review previous compliance history or actions; and
- ensure that the establishment has the appropriate quality management requirements in place, in relation to the activities they conduct under the Safety Regulations.

If a primary establishment becomes aware or has information to suggest that an establishment conducting activities on their behalf is not meeting the requirements, the primary establishment must:

- determine whether the deficiency meets the definition of an error or accident and could compromise human health and safety or the safety of sperm and ova as set out in section 59 to 68 of the Safety Regulations; and
- take reasonable steps to ensure that the establishment complies with the requirements. For example, review the establishment's corrective action plan and verify that corrective actions have been taken under the establishment's quality program.

If a primary establishment determines that the establishment is not meeting the requirements of the Safety Regulations, the primary establishment must take appropriate action to ensure that sperm or ova is processed in accordance with the Safety Regulations prior to distribution or use.

It is important to note that Health Canada has the ability to suspend a registration immediately, in whole or in part, if there are reasonable grounds to believe human health and safety or the safety of sperm or ova has been or could be compromised. For example, Health Canada could suspend a part of the primary establishment's registration, to mitigate

the risk posed by an establishment that is not conducting their activities in compliance with the Safety Regulations provided that the reasonable grounds threshold is met.

Establishment that imports

3 An establishment that imports sperm or ova must ensure that the sperm or ova are processed by a primary establishment that is registered in accordance with these Regulations.

Establishments that import donor sperm and ova play an important role in maintaining the safety of the distribution chain within Canada. It is for this reason that this section requires an establishment that imports donor sperm or ova to ensure that the sperm or ova are processed by a primary establishment that is registered with Health Canada.

There may be cases where a primary establishment is also importing donor sperm or ova. This means that either they must ensure that the donor sperm or ova are processed by a primary establishment that is registered with Health Canada or they must take on the responsibility for ensuring that the sperm or ova they import has been processed in accordance with the Regulations.

Registration

Application, Issuance and Refusal

Requirement to register — primary establishment

4 A primary establishment that processes sperm or ova must be registered and may process sperm or ova, subject to any change under paragraph 11(1)(a), only in accordance with its registration.

Who is required to register?

Primary establishments that are responsible for all of the processing activities must be registered with Health Canada by submitting an application for registration to Health Canada, as set out in section 5 of the Safety Regulations, and must only process sperm or ova in accordance with their registration. Establishments conducting processing activities on behalf of a primary establishment are not required to register, but need to be listed on the application for a registration and must conduct the processing activities in accordance with the Safety Regulations.

It is important to note the Safety Regulations have been developed to allow for cases where an establishment or a health professional can take on the responsibility for all of the processing activities, even if another establishment conducts any of them on their behalf, and register with Health Canada as a primary establishment.

Example Scenario

Take for example a case where one sister, who lives in another country, decides to donate her ova for use by the other sister, who lives in Canada. Rather than the sister in the foreign country unnecessarily traveling to facilitate the donation, she could have her ova retrieved at a local fertility clinic. Provided that clinic conducts their processing activities (e.g., performing the donor suitability assessment, obtaining, preparing, preserving, and so on) in accordance with the Safety Regulations, the sister in Canada could approach a Canadian primary establishment to list the foreign clinic on their registration, in which case the activities undertaken by the foreign clinic would be understood as being done on behalf of the primary establishment in Canada. The cryopreserved ova could then be imported by the primary establishment to complete the processing, at which point the medical director could determine and document that the ova can be released from quarantine and subsequently distributed or used.

In such cases, as part of the registration application, the primary establishment must submit the required information regarding any establishments conducting processing activities on their behalf, including any foreign establishments (e.g., sperm or ova bank) from which they wish to import sperm or ova. They must also ensure that they can meet the requirements of a primary establishment, including having their medical director determine the donor's suitability (e.g., in the case of a donation processed under the Regular Process), and must ensure that any establishment conducting activities on their behalf meet the requirements of the Safety Regulations.

The following are examples of establishments that are required to be either registered as a primary establishment, or listed on a primary establishment's registration.

Registered as primary establishment:

- establishments that are responsible for all of the processing activities (this can include both domestic and foreign establishments).

Listed on a primary establishment's registration:

- foreign establishments that process and distribute sperm or ova in Canada but are not registered as a primary establishment.
- a testing laboratory that is conducting the donor testing on behalf of a primary establishment.
- other establishments that conduct any of the processing activities on behalf of a primary establishment.

A foreign establishment may wish to register directly with Health Canada as a primary establishment to facilitate the distribution of sperm or ova to Canada. In addition, if the Canadian primary establishment lists the foreign establishment on their registration application and is importing from them, the Canadian establishment is also considered an establishment that imports sperm or ova.

Application

5 (1) A primary establishment must submit an application for registration to the Minister, in the form established by the Minister, that contains the following information:

(a) the applicant's name, telephone number, email address, postal address and, if different from the postal address, civic address;

(b) in the case of an applicant that previously conducted its activities under another name, either under these Regulations or the *Processing and Distribution of Semen for Assisted Conception Regulations*, that other name;

(c) the first name, last name, telephone number and email address of a person to contact for further information concerning the application and, if different, a person to contact in case of emergency;

(d) a statement indicating whether the applicant proposes to process sperm or ova;

(e) a list of the processing activities that the applicant proposes to conduct in each building and, if not already provided, the civic address of the respective buildings;

(f) a statement indicating whether the applicant proposes to have another establishment process sperm or ova on its behalf; and

(g) the name and civic address of any other establishment that the applicant proposes to have conduct any of the processing activities on its behalf, a list of the processing activities that are proposed to be conducted in each building and, if not already provided, the civic address of the respective buildings.

Signature and attestation

(2) The application must

(a) be signed and dated by a senior executive officer; and

(b) include an attestation from that senior executive officer of the following:

(i) that the applicant has evidence demonstrating that it is able to meet the requirements of these Regulations,

(ii) that any other establishment that is proposed to process sperm or ova on its behalf is able to meet the requirements of these Regulations,

(iii) that all information submitted in support of the application is accurate and complete, and

(iv) that the senior executive officer has the authority to bind the applicant.

Additional documents and information

(3) The applicant must provide to the Minister, on or before the date specified in the Minister's written request to that effect, any documents or information that the Minister considers necessary to complete his or her review of the application.

Subsection 5(1) of the Safety Regulations specifies the information that must be provided in the application for a registration.

Where to find the application form

The Sperm and Ova Establishment Registration Application and Notification form, along with instructions, can be obtained by sending a request to: AHR Registration at hc.ahrregistration-enregistrementpa.sc@canada.ca.

The applications for registration and notification are consolidated into one form in order to streamline the process to register or notify. Further instructions are provided within the form itself. Establishments will be informed by Health Canada of the location of the form when it is available on the Health Canada website.

The form must be dated and signed by a senior executive officer, including an attestation. A senior executive officer refers to an individual holding a position that has an assigned level of responsibility for activities the establishment conducts under the Safety Regulations and has the authority to bind the establishment applying for registration. The senior executive officer term refers to a function within the establishment and is not necessarily a specific position title.

It is the responsibility of the applicant to ensure that the information provided in the Sperm and Ova Establishment Registration Application and Notification form is accurate and complete in accordance with the requirements of section 5 of the Safety Regulations before filing it with the Biological Product Compliance Program of the Regulatory Operations and Enforcement Branch within Health Canada. Submission of complete applications within the required timelines will help prevent delays in processing the forms.

Where to file the application form

By email: AHR Registration at hc.ahrregistration-enregistrementpa.sc@canada.ca

Please contact the Biological Product Compliance Program at hc.bpcp-pcpb.sc@canada.ca should you have any questions or require assistance.

Registration number

6 If the Minister determines, after reviewing an application for registration, that the information provided in the application is complete, the Minister must register the primary establishment and issue a registration number.

Inspection

Health Canada may inspect establishments prior to and/or after the issuance of a registration number. This includes both the primary establishment, as well as any establishments conducting activities on behalf of the primary establishment that is listed on the registration application.

Disclosure of information related to primary establishments

The information related to registered primary establishments, or establishments listed on a primary establishment's application may be made publicly available. For example, the listing of registered primary establishments may be accessible via the Health Canada website and public information may be shared in response to specific inquiries made to the Department.

Registration Expiry

Subject to sections 13, 15, and 16 of the Safety Regulations, there is no expiry for a registration number and hence no renewal process. However, a registration must be updated if any amendments or changes, as set out in sections 8 and 11 of the Safety Regulations respectively, are made to the primary establishment's registration.

In addition, an annual attestation as set out in section 20 of the Safety Regulations is required to be completed for all registered primary establishments and other establishments that distribute or import sperm or ova.

Refusal

7 The Minister may refuse to register an applicant if

(a) the Minister has reasonable grounds to believe that the applicant has submitted, in the application for registration, false, misleading, inaccurate or incomplete information;

(b) the applicant has not complied with subsection 5(3) or the documents and information that the applicant has provided under subsection 5(3) are not sufficient to complete the review of the application; or

(c) the Minister has reasonable grounds to believe that registering the primary establishment could compromise human health and safety or the safety of sperm or ova.

If Health Canada refuses to issue a registration for an applicant due to one or more of the criteria set out in section 7 of the Safety Regulations, the applicant will be notified of this decision.

For instance, Health Canada may refuse to register an applicant if there are reasonable grounds to believe that the health and safety of a recipient of sperm or ova or a child created from that sperm or those ova to the extent that their health and safety relate to the safety of the sperm and ova, could be compromised as a result of the registration.

Amendments

Amendments — application

8 (1) A primary establishment that processes only one of sperm or ova and proposes to begin processing the other must, before doing so, submit an application to the Minister to amend its registration, in the form established by the Minister, that contains a description of the proposed amendment, as well as the information referred to in section 5 that is relevant to the proposed amendment.

Signature and attestation

(2) The application must

(a) be signed and dated by a senior executive officer; and

(b) include an attestation from that senior executive officer of the following:

(i) that the applicant has evidence demonstrating that it is able to meet the requirements of these Regulations,

(ii) that any other establishment that is proposed to process sperm or ova on its behalf is able to meet the requirements of these Regulations,

(iii) that all information submitted in support of the application is accurate and complete, and

(iv) that the senior executive officer has the authority to bind the applicant.

Additional documents and information

(3) The primary establishment must provide to the Minister, on or before the date specified in the Minister's written request to that effect, any documents or information that the Minister considers necessary to complete his or her review of the application.

Amendment

9 If the Minister determines, after reviewing the application for the amendment to the registration, that the information provided in that application is complete, the Minister must amend the registration.

If a primary establishment only processes either sperm or ova but intends to begin processing the other, the primary establishment must submit an application to amend their registration.

Where to find the application form

The Sperm and Ova Establishment Registration Application and Notification form, along with instructions, can be obtained by sending a request to: AHR Registration at hc.ahrregistration-enregistrementpa.sc@canada.ca.

Establishments will be informed by Health Canada of the location of the form when it is available on the Health Canada website.

It is the responsibility of the applicant to ensure that the information they provide in the Sperm and Ova Establishment Registration Application and Notification form is accurate and complete in accordance with the requirements of section 5 of the Safety Regulations before filing it with the Biological Product Compliance Program. Submission of complete applications within required timelines will help prevent delays in processing the forms.

Where to file the application form

By email: AHR Registration at hc.ahrregistration-enregistrementpa.sc@canada.ca

Please contact the Biological Product Compliance Program at hc.bpcp-pcpb.sc@canada.ca should you have any questions or require assistance.

Refusal

10 The Minister may refuse to amend the registration of the primary establishment if

(a) the Minister has reasonable grounds to believe that the primary establishment has submitted, in the application for amendment, false, misleading, inaccurate or incomplete information;

(b) the primary establishment has not complied with subsection 8(3) or the documents and information that it has provided under subsection 8(3) are not sufficient to complete the review of the application; or

(c) the Minister has reasonable grounds to believe that the amendment of the registration could compromise human health and safety or the safety of sperm or ova.

If Health Canada refuses to amend the registration of an applicant based on the grounds set out in section 10 of the Safety Regulations, the applicant will be notified of this decision and the applicant will be given an opportunity to be heard.

Changes or Cessation

Notice to Minister

11 (1) A primary establishment must notify the Minister in writing, in the form established by the Minister, within 30 days after the day on which

(a) there is any change to the information provided in the application for registration — other than a change that is the subject of an application for an amendment to the registration — including the cessation of all activities with respect to either sperm or ova if the registration is for both sperm and ova; or

(b) the primary establishment has ceased all of its activities.

Contents of Notice

(2) The notice must contain the following information:

(a) the primary establishment's name, telephone number, email address, postal address and, if different from the postal address, civic address;

(b) the primary establishment's registration number;

(c) the date on which the change or cessation became effective; and

(d) in the case of cessation, details of the disposition of the sperm or ova that are in the possession or control of the primary establishment.

Signature and attestation

(3) The notice must

(a) be signed and dated by a senior executive officer; and

(b) include an attestation from that senior executive officer of the following:

(i) that if the primary establishment has not ceased all of its activities, it has evidence demonstrating that it meets the requirements of these Regulations,

(ii) that if the primary establishment has not ceased all of its activities, any other establishment that processes sperm or ova or is proposed to process sperm or ova on its behalf meets the requirements of these Regulations,

(iii) that all information submitted in support of the notice is accurate and complete, and

(iv) that the senior executive officer has the authority to bind the primary establishment.

Update to registration

12 The Minister must update the registration to reflect the notice.

Changes to registration information can be filed with the Biological Products Compliance Program using the Sperm and Ova Establishment Registration Application and Notification form with an accompanying cover letter summarizing the changes. Please refer to the form for further instructions. Changes include both changes to the primary establishment as well as additions or removals of the names of establishments conducting regulated activities on behalf of the primary establishment.

Where to find the application form

The Sperm and Ova Establishment Registration Application and Notification form, along with instructions, can be obtained by sending a request to: AHR Registration at hc.ahrregistration-enregistrementpa.sc@canada.ca.

Establishments will be informed by Health Canada of the location of the form when it is available on the Health Canada website.

It is the responsibility of the applicant to ensure that the information they provide in the Sperm and Ova Establishment Registration Application and Notification form is accurate and complete in accordance with the requirements of section 5 of the Safety Regulations before filing it with the Biological Product Compliance Program. Submission of complete applications within required timelines will help prevent delays in processing the forms.

Where to file the application form

By email: AHR Registration at hc.ahrregistration-enregistrementpa.sc@canada.ca

Please contact the Biological Product Compliance Program at hc.bpcp-pcpb.sc@canada.ca should you have any questions or require assistance.

It is recommended that primary establishments notify the Biological Product Compliance Program as soon as possible, to allow these changes to be processed and updated on their registration in a timely manner.

Suspension

Suspension without notice

13 (1) The Minister may suspend, in whole or in part, without prior notice, a primary establishment's registration, if the Minister has reasonable grounds to believe that human health and safety or the safety of the sperm or ova has been or could be compromised.

Notice

(2) If the Minister suspends a registration, the Minister must send a notice to the primary establishment that

(a) gives the reasons for the suspension and its effective date;

(b) indicates that the primary establishment has an opportunity to be heard; and

(c) if applicable, indicates that corrective action must be taken by the primary establishment and the date by which it must do so.

Action following suspension of registration

(3) On the suspension of its registration, the primary establishment must immediately notify every establishment, health professional or recipient to which it has distributed the implicated sperm or ova during the period specified in the notice of the reasons for its suspension, the effective date of the suspension and the parts of the registration that are the subject of the suspension.

Action upon notice

(4) An establishment that has been notified under subsection (3) or under this subsection must immediately notify to the same effect any establishment, health professional or recipient to which it distributed the implicated sperm or ova.

Written notice

(5) If the Minister or the establishment gives a notice verbally under this section, that notice must be confirmed in writing as soon as feasible.

If Health Canada has reasonable grounds to believe that the human health and safety or the safety of sperm or ova has been or could be compromised, Health Canada may suspend, without prior notice, a primary establishment's registration, in whole or in part.

If Health Canada suspends a primary establishment's registration, in whole or in part, Health Canada will send a notice to the primary establishment outlining the reasons for the suspension and the effective date, inform the primary establishment that it has an opportunity to be heard, and if applicable, indicate the corrective actions that must be taken and by which date.

Health Canada may suspend a portion of a registration to address specific issues or elements of a registration while not impacting all registered activities. This could include suspending in part to remove from the registration an establishment conducting activities on behalf of the primary establishment (e.g., removing a testing establishment when there are reasonable grounds to believe that the sperm or ova has been or could be compromised). This could also include removing activities in relation to one of either sperm or ova, but the other elements of the registration would still be valid (e.g., issues were identified in the processing of sperm, but not ova).

Reinstatement of registration

14 (1) The Minister must reinstate a registration, in whole or in part, if the primary establishment makes a request to the Minister, in the form established by the Minister, and provides evidence that demonstrates that

(a) the primary establishment has corrected the situation that gave rise to the suspension; or

(b) the situation that gave rise to the suspension did not exist.

Notice

(2) The reinstatement takes effect immediately after the Minister sends to the primary establishment a notice to that effect.

Exception — compliance history

(3) The Minister may refuse to reinstate a primary establishment's registration if its compliance history demonstrates an inability to consistently conduct its activities in accordance with these Regulations.

Partial reinstatement

(4) If the Minister does not reinstate any part of a registration that was suspended, the Minister must remove that part of the registration.

If Health Canada has suspended a registration, in whole or in part, the Safety Regulations provide a mechanism for the primary establishment to request for their registration to be reinstated. The primary establishment must provide evidence to Health Canada to demonstrate that:

- the primary establishment has corrected the situation that gave rise to the suspension (i.e., the reason for the suspension); or
- the situation that gave rise to the suspension did not warrant a suspension.

Health Canada may refuse to reinstate all or part of a primary establishment's registration if the primary establishment's compliance history indicates an inconsistency in their ability to conduct their activities in accordance with the Safety Regulations.

If the primary establishment does not demonstrate willingness or consistently refuses to implement corrective actions for non-compliance or the corrective actions fall short of rectifying the non-compliance, or has a history of recurring non-compliance, Health Canada may not reinstate the primary establishment's registration.

Cancellation

Cancellation Initiated by Primary Establishment

Cessation of activities

15 The Minister must cancel a registration if the Minister receives a notice under section 11 that the primary establishment has ceased carrying out all of the activities that are the subject of its registration.

Cancellation Initiated by Minister

Circumstances

16 (1) The Minister may cancel a registration in any of the following circumstances:

(a) the primary establishment has not provided the annual statement that is required under section 20;

(b) the primary establishment has not complied with the requirements set out in section 21 to provide additional documents or information;

(c) any information provided by the primary establishment to the Minister in accordance with these Regulations proves to be false or misleading;

(d) the primary establishment fails to take corrective action, within the required period, in accordance with subsection (2) or paragraph 13(2)(c);

(e) the corrective action that was taken by the primary establishment in accordance with subsection (2) or paragraph 13(2)(c) has not corrected the situation that gave rise to a notice of suspension or cancellation of the registration;

(f) the registration has been suspended for a period of more than 12 months;

(g) the Minister has reasonable grounds to believe that the primary establishment does not meet the requirements of these Regulations.

Notice

(2) Before cancelling a registration, the Minister must send to the primary establishment a notice that

(a) gives the reasons for the proposed cancellation and its effective date;

(b) indicates that the primary establishment has an opportunity to be heard; and

(c) if applicable, indicates that corrective action must be taken by the primary establishment and the date by which it must do so.

Action following cancellation of registration

17 (1) If the registration is cancelled under section 16, the primary establishment must immediately take the following action:

(a) cease carrying out all of the activities that are the subject of its registration; and

(b) notify any establishment, health professional or recipient to which it has distributed the implicated sperm or ova during the period specified in the notice of the cancellation and the effective date.

Action upon notice

(2) An establishment that has been notified under paragraph (1)(b) or under this subsection must, in turn, immediately notify to the same effect any establishment, health professional or recipient to which it distributed the implicated sperm or ova.

Written notice

(3) If an establishment gives a notice verbally under this section, that notice must be confirmed in writing within 24 hours after it is given.

A primary establishment is not permitted to conduct any activities requiring a registration, for which its registration was cancelled. If a primary establishment intends to commence

activities requiring a registration for which a registration was cancelled, it must file a new Sperm and Ova Establishment Registration Application and Notification Form.

Notification

Notice before distribution or importation

18 (1) Before distributing or importing sperm or ova, an establishment must send to the Minister a notice, in the form established by the Minister, that contains the following information:

(a) the establishment's name, telephone number, email address, postal address and, if different from the postal address, civic address;

(b) in the case of an establishment that previously conducted its activities under another name, either under these Regulations or the *Processing and Distribution of Semen for Assisted Conception Regulations*, that other name;

(c) the first name, last name, telephone number and email address of a person to contact for further information concerning the notice and, if different, a person to contact in case of emergency;

(d) a statement indicating whether the establishment proposes to distribute or import sperm or ova and the projected start date;

(e) the civic address of the buildings in which the establishment proposes to conduct the activities, if not already provided; and

(f) the name and registration number of each primary establishment that processes that sperm or those ova.

Signature and attestation

(2) The notice must

(a) be signed and dated by a senior executive officer; and

(b) include an attestation from that senior executive officer of the following:

(i) that the establishment has evidence demonstrating that it is able to meet the requirements of these Regulations,

(ii) that all information submitted in support of the notice is accurate and complete, and

(iii) that the senior executive officer has the authority to bind the establishment.

If an establishment intends to import or distribute sperm or ova, it must submit a notification form to Health Canada. The form must be signed by a senior executive officer and must include an attestation that the establishment has evidence to demonstrate that it is able to meet the requirements of the Safety Regulations, all the information in support of

the notice is accurate and complete, and the senior executive officer signing the attestation has the authority to bind the establishment notifying Health Canada. There may be cases where a primary establishment must also fill out the applicable notification section for distribution or import, within the same Sperm and Ova Establishment Registration Application and Notification form. Additional instructions are provided on the Sperm and Ova Establishment Registration Application and Notification form.

Where to find the Notification Form

The Sperm and Ova Establishment Registration Application and Notification form, along with instructions, can be obtained by sending a request to: AHR Registration at hc.ahrregistration-enregistrementpa.sc@canada.ca.

Establishments will be informed by Health Canada of the location of the form when it is available on the Health Canada website.

Where to file the Notification Form

By email: AHR Registration at hc.ahrregistration-enregistrementpa.sc@canada.ca

Please contact the Biological Product Compliance Program at hc.bpcp-pcpb.sc@canada.ca should you have any questions or require assistance.

Change or cessation

19 (1) An establishment that distributes or imports sperm or ova and makes any change to the information provided under section 18, including the cessation of distribution or importation, must send to the Minister, within 30 days after the day on which the change occurs, a notice, in the form established by the Minister, that contains the following information:

(a) the name of the establishment, telephone number, email address, postal address and, if different from the postal address, civic address;

(b) the date on which the change or cessation became effective; and

(c) in the case of cessation, details of the disposition of the sperm or ova that are in the possession or control of the establishment.

Signature and attestation

(2) The notice must

(a) be signed and dated by a senior executive officer; and

(b) include an attestation from that senior executive officer of the following:

(i) that the establishment has evidence, if it is still distributing or importing sperm or ova, demonstrating that it meets the requirements of these Regulations,

(ii) that all information submitted in support of the notice is accurate and complete, and

(iii) that the senior executive officer has the authority to bind the establishment.

If an establishment that has notified Health Canada under section 18 of the Safety Regulations, makes any change to the information provided, or stops any of its activities, the establishment must file these changes with the Biological Products Compliance Program using a Sperm and Ova Establishment Registration Application and Notification form, and should include an accompanying cover letter summarizing the changes. Please refer to the form for further instructions.

It is recommended that establishments notify the Biological Product Compliance Program as soon as possible, to allow changes to be processed in a timely manner.

Annual Attestation

April 1

20 (1) A primary establishment and any other establishment that distributes or imports sperm or ova must send to the Minister, in the form established by the Minister, an annual attestation

(a) on or before April 1 of the calendar year following the year of registration or the year in which the notice of distribution or importation is sent; and

(b) on or before April 1 of each subsequent calendar year.

Signature and attestation

(2) The attestation must

(a) be signed and dated by a senior executive officer; and

(b) certify that

(i) the establishment has evidence demonstrating that it meets the requirements of these Regulations,

(ii) in the case of a primary establishment, any other establishment that processes sperm or ova on its behalf meets the requirements of these Regulations,

(iii) all information submitted in support of the attestation is accurate and complete, and

(iv) the senior executive officer has the authority to bind the establishment.

Additional documents and information

21 An establishment must provide to the Minister, on or before the date specified in the Minister's written request to that effect, any additional relevant documents or information to demonstrate that the activities it conducts are in compliance with these Regulations.

Although a primary establishment's registration, or an establishment's notification does not expire, all establishments who have registered or notified must submit an annual attestation of compliance by April 1st of each year. Establishments must submit their annual attestation of compliance using the Sperm and Ova Establishment Registration Application and Notification form. Additional instructions are provided with the form.

If a primary establishment, or an establishment that imports or distributes does not provide their annual attestation, Health Canada may cancel a registration as stated in section 16 of the Safety Regulations, or take other compliance and enforcement measures.

Donor Suitability

Regular Process

Donor Suitability Assessment and Determination

The Regular Process requirements, set out in sections 22 to 29, are intended to apply to all donor sperm and ova to be used for the purpose of AHR. However, in cases where the donor and the recipient know each other, the Directed Donation Process requirements, set out in sections 30 to 40 of the Safety Regulations, may be followed instead.

Donor sperm and ova used in AHR pose a potential risk to human health and safety because of their inherent nature to transmit infectious and genetic diseases. As such, the Regular Process for donation sets out the minimal standard requirements for assessing and determining donor suitability to minimize the risk to the health and safety of the recipient and the individual born of the donation.

All sperm and ova donors subject to the Regular Process must undergo the donor suitability assessment, and if applicable, donor reassessment, to identify any risk factors for infectious and genetic disease transmission, which could impact the safety of the sperm and ova.

In the case of a repeat donor (i.e., a sperm or ova donor who donates more than once), donor reassessment must be conducted in accordance with section 26 of the Safety Regulations, to monitor for any risk of infectious and genetic disease transmission since the initial donor suitability assessment was conducted.

A primary establishment is responsible for ensuring that the donor suitability assessment and donor reassessment is conducted in accordance with the Safety Regulations, including if it is carried out, in part or in whole, by another establishment on its behalf.

The medical director at the primary establishment must determine if the donor is suitable to donate and if the donation can be released from quarantine, in accordance with section 27 of the Safety Regulations by reviewing the information obtained from the donor suitability assessment and, if applicable, donor reassessment. The medical director must also create and sign a summary document that confirms this determination. The donation must be kept in quarantine, in accordance with section 28 of the Safety Regulations, until

the medical director has determined that the donor is suitable and documented that the sperm or ova can be released from quarantine.

If the medical director at the primary establishment has determined the donor to be unsuitable or if the donor suitability assessment has not been completed, the donation cannot be released from quarantine unless it is subject to certain exceptions outlined in section 29 of the Safety Regulations.

The technical requirements for conducting the suitability assessment of sperm and ova donors are set out in the *Health Canada Directive: Technical Requirements for Conducting the Suitability Assessment of Sperm and Ova Donors*, which has been incorporated by reference in the Safety Regulations.

Donor suitability assessment

22 In order to determine whether a donor is suitable, a primary establishment must ensure that a donor suitability assessment is conducted.

The donor suitability assessment must be conducted and documented by the medical director or a physician or nurse practitioner designated by a medical director, and must be based on the following:

a) Donor screening, in accordance with section 23 of the Safety Regulations;
b) Physical examination, in accordance with section 24 of the Safety Regulations; and
c) Donor testing, in accordance with section 25 of the Safety Regulations.

Donor screening

23 An establishment that performs donor screening must do so in accordance with the requirements set out in the Directive under the heading “Donor Screening”.

Donor screening, as set out in clause 2.1 of the Directive, is intended to identify risk factors for infectious and genetic disease transmission that could impact the safety of the donation based on the donor's medical and social history as well as their clinical status.

The initial donor screening should be performed as close to the time of donation as feasible to accurately reflect the donor’s risk of infectious and genetic disease transmission. In the event that more than one month has elapsed since the initial donor screening was completed and the donation has not been obtained, Health Canada recommends rescreening the donor, in order to ascertain whether any of the information has changed.

Donor screening must be conducted using a structured questionnaire, based on the applicable donor screening criteria set out in clause 2.1 of the Directive, and should be

documented in the form of a checklist where the response/outcome for each criterion is recorded and followed up, as appropriate. The questionnaire must be structured in a way that collects the required information, including:

- donor's age at the time of obtaining the sperm or ova;
- infectious disease screening criteria; and
- genetic disease screening criteria.

In the case of infectious disease screening, the structured questionnaire must be prepared by the medical director or by a physician designated by the medical director. In the case of genetic disease screening, the medical director can designate a qualified health professional, such as a clinical geneticist, to prepare the structured questionnaire. Separate questionnaires for infectious and genetic disease screening may be developed and administered to collect the required information.

An establishment that conducts donor screening must develop and maintain standard operating procedures for all steps performed during the donor screening process.

Age of Donor

The donor's age at the time of obtaining the sperm or ova must be documented as this information is an important component of the summary document, which accompanies the donation, and which is meant to provide the health professional with the relevant health and safety information related to the donation.

Scientific evidence has shown that the use of sperm and ova from a donor who is above a certain age can increase the risk of an adverse reproductive outcome associated with that donation, including the risk to the health and safety of the recipient, or the individual born of that donation.

For instance, a number of studies have correlated age-related reduction in male fertility[10] with lower sperm quality[11]. The age-related reduction in sperm quality can be attributed to a number of factors including reduced sperm motility, abnormal sperm morphology, and decreased sperm concentration[12]. Additionally, the use of sperm from donors who are above the age of 40 years has been correlated with increased incidence of genetic diseases[13].

In the case of ova donors, in addition to a slow but steady decline in female fertility, the risk of chromosomal abnormalities during embryonic development has been shown to increase with the age of the donor[14, 15]. The most common chromosomal abnormality is trisomy 21, or Down syndrome. At 35 years of age, a female has approximately one in 365 chance of conceiving a child with Down syndrome[16], and this chance gradually increases to 1 in 84 by age 40[17].

Many studies have linked a female's age-related decline in fertility beyond a certain age threshold with a reduced quantity and quality of her oocytes[18, 19]. Despite this, the rate of ovarian aging varies among women, as both environmental and genetic factors contribute to the depletion of a female's ovarian reserve.

Recognizing the range of factors associated with age that can influence the safety of the donation, Health Canada has not set an upper age limit for sperm and ova donors. However, the donor's age must be documented, so that the health professional can use this information to assess any relevant health and safety risks that the donor's age may pose, and inform the recipient if such risks exist in their medical opinion, prior to making use of the donation or distributing the sperm donation for personal use. It is recommended that primary establishments should have standard operating procedures for assessing the risks associated with age, which set out an upper age limit for eligible donors.

Infectious Disease Screening

All sperm and ova donors must be screened for the risk of infectious disease transmission, based on their medical history, social history, and clinical status, using a structured questionnaire prepared by the medical director or a physician designated by the medical director. The donor screening must be conducted and documented by a medical director or a physician or nurse practitioner designated by a medical director. The structured questionnaire must at a minimum include the infectious disease screening criteria outlined in clause 2.1.1 of the Directive.

The medical director may also choose to include additional screening criteria to assess the risk of any relevant emerging infectious diseases at the time of donation. A relevant emerging disease is a disease transmissible via sperm or ova and whose incidence has increased within the last decade or threatens to increase in the near future. Emerging diseases can be caused by 1) newly identified pathogens; 2) mutated/variants of an existing pathogen; 3) pathogens with recent transfer to human host; or 4) pathogens with changes in geographic distribution.

The infectious disease screening criteria set out in clause 2.1.1 of the Directive have been organized as follows:

Clause 2.1.1 (I) and (II) (a) to (l) apply to all sperm and ova donors;

Clause 2.1.1 (II) (m) applies only to sperm donors subject to the Regular Process;

Clause 2.1.1 (II) (n) applies only to ova donors subject to the Regular Process;

Clause 2.1.1 (II) (o) applies to sperm and ova donors subject to the Directed Donation Process.

The screening criteria represent the minimum information that must be obtained to assess the donor for the risk of infectious disease transmission. The criteria are intentionally broad, to allow the medical director, or the physician designated by the medical director, to determine how best to collect the necessary information, including information to identify the risk of any emerging diseases that may be relevant at the time of screening.

The screening criteria set out in clause 2.1.1 (II) (f) requires that a donor be screened for being treated for or being diagnosed with *Neisseria gonorrhoeae* or *Chlamydia trachomatis* in the 2 months prior to donation. However, if the diagnosis and treatment occurred more than 2 months prior, evidence of successful treatment one-month post completion of

treatment must be documented. Health Canada considers the Canadian Guidelines on Sexually Transmitted Infections to be an acceptable resource for providing recommendations on the interpretation of results with respect to successful treatments.

The screening criteria set out in clause 2.1.1 (II) (i) requires that a donor be screened for infections of clinical significance. An infection would be considered clinically significant if: (a) it is potentially transmissible by sperm or ova and has sufficient incidence and/or prevalence to affect the potential donor population; (b) it is highly pathogenic to the recipient or the individual born of the donor's sperm or ova; or (c) reliable and valid screening tests for the infection are available.

The screening criteria set out in clause 2.1.1 (II) (m),(n), and (o) are specific for assessing the donor's risk for Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV) or Human T-cell Lymphotropic Virus (HTLV) transmission at the time of donation, including assessing the donor's social history for high risk behavior that has been correlated, based on scientific evidence, with greater prevalence and/or incidence of infection[20, 21, 22, 23 ,24, 25, 26, 27, 28, 29].

Donors subject to the Regular Process who meet any of the screening criteria set out in clause 2.1.1 (II) (a) to (l), (m) and (n) must be excluded from donating, as set out in the Exclusion Criteria [clause 4(a)] of the Directive. Donors subject to the Directed Donation Process are not excluded from donating even if they meet any of the screening criteria set out in 2.1.1 (II) (a) to (l), and (o), however, a medical director must review the information obtained from the donor suitability assessment, and donor reassessment if applicable, and prepare a summary document that is used by the health professional to inform the recipient of the risks that the use of the sperm or ova in question could pose to human health and safety.

Genetic Disease Screening

Donor sperm and ova, in addition to the risk of transmitting infectious diseases, carry an inherent risk of genetic disease transmission that can have a major impact on the health and safety of individuals born of donor sperm or ova.

A genetic disease, disorder, or condition is caused by one or more mutations or abnormalities in an individual's DNA. It can be caused by mutation/s in a single gene; by a combined effect of mutations in multiple genes (known as multifactorial conditions); or it can be due to chromosomal abnormalities.

Many medical conditions such as certain types of cancer, cardiovascular diseases, or neurological diseases are considered multifactorial conditions that are caused by the interaction of multiple genes (polygenic) and a combination of various lifestyle and environmental factors. The pattern of inheritance for such multifactorial conditions is unpredictable and/or less understood, which makes it difficult to determine a person's risk of inheriting or transmitting such diseases. Similarly, diseases due to chromosomal abnormalities are usually caused by random errors in cell division during the formation of sperm or ova and thus are usually sporadic rather than hereditary in nature, although may be impacted by other factors such as a donor's age at the time of donation.

On the other hand, single-gene diseases, such as cystic fibrosis or muscular dystrophy, are caused by mutation/s in a single gene and are generally inherited in a well-known and predictable pattern of inheritance (e.g., autosomal dominant, autosomal recessive, X-linked). For instance, a sperm or ova donor who is a carrier of a mutation in the gene responsible for cystic fibrosis, has a 25 % chance that an individual born of their donation will be at risk for the disease if the recipient is also a carrier of that mutation, due to its autosomal recessive pattern of inheritance.

X-linked genetic diseases can be classified as X-linked dominant or X-linked recessive, based on their pattern of inheritance. X-linked recessive diseases most often affect males, given that males have one copy of the X chromosome and as such, any disease-causing mutations on that X chromosome are sufficient to cause the disease. For instance, if an ova donor is a carrier of an X-linked recessive disease such as hemophilia, they have a 50% chance that a male individual born from making use of that ovum will be affected, while a female individual will either not inherit the mutated copy of the disease-causing gene or will be a carrier of the disease. As such, if the results of donor screening reveal that an ova donor is a carrier of a serious X-linked recessive disease, additional measures may be taken to reduce the risk of disease transmission (e.g., testing the recipient to determine if they too are a carrier). On the other hand, if a sperm donor is affected by an X-linked recessive disease (e.g., Duchenne muscular dystrophy), they will only pass the mutated copy of the disease-causing gene to all female individuals born of their donation, making them a carrier of the genetic disease.

In the case of an X-linked dominant genetic disease, only one copy of the disease-causing gene is sufficient to cause the disease. As such, if the sperm donor is affected by an X-linked dominant disease, all female individuals, but none of the male individuals, born from making use of their sperm will inherit the disease. On the other hand, if the ova donor is affected by an X-linked dominant disease, there is a 50% chance that an individual (male or female) born of their donation will inherit the disease.

Genetic Disease Screening Requirements

All sperm and ova donors must be screened for the risk of transmitting genetic diseases in accordance with clause 2.1.2 of the Directive.

The scope of the genetic disease screening requirements, as set out in the Directive, is limited to reducing the risk of transmitting serious single-gene genetic diseases that are inherited in an autosomal dominant, autosomal recessive, and X-linked pattern, through the genetic disease screening of sperm or ova donors. However, the medical director may choose to additionally, screen the donor for the risk of transmitting multifactorial conditions (e.g., certain types of cancer) or chromosomal abnormalities that could present a significant risk of transmission or that have a higher frequency in a specific population.

The term “genetic disease screening” and “genetic disease testing” have often been used interchangeably in literature. However, the Safety Regulations have been developed with a clear distinction between these two terms. The genetic screening of donors constitutes the

systematic application of inquiry or gathering of information regarding a donor's medical and family genetic history to identify and assess the risk of transmitting a specific genetic disease to an individual born of their donation. This includes screening a donor for any clinical evidence of having a genetic disease or to determine the donor's potential carrier status via their family genetic history. Genetic testing on the other hand, involves conducting a test to analyze the donor's DNA, RNA, chromosomes, proteins or metabolites for the purpose of detecting the presence of mutations or chromosomal changes in the donor that could indicate the risk of genetic disease transmission.

A donor of sperm and ova must be screened by the medical director, or by a physician or nurse practitioner designated by the medical director, for the risk of transmitting serious autosomal dominant, autosomal recessive and X-linked genetic diseases using a structured questionnaire. While conducting the genetic disease screening, the medical director should consider variation of manifestations and range of severity in the case of autosomal dominant and X-linked diseases, as the donor may not be aware that they are affected.

The medical director is responsible for developing the structured questionnaire, or they may choose to designate a qualified professional with training in medical genetics, such as a clinical geneticist or genetic counselor, to develop the genetic screening questionnaire.

The genetic disease screening must assess the donor's risk of transmitting serious genetic diseases, based on the donor's medical history and three generations of family genetic history. When conducting genetic disease screening, the results of the donor's physical examination should also be taken into consideration.

The family genetic history-based screening should include:

- three generations of the genetic history of the donor, donor's parents, and donor's offspring (if any) or donor's grandparents (if the donor doesn't have any offspring) for the presence of serious genetic diseases (a list of serious genetic diseases intended to guide donor screening has been provided below);
- three generations of the genetic history for risk factors such as intellectual disability, stillbirth, congenital anomalies or sudden death that may indicate history of a serious genetic disease; and
- three generations of the genetic history for the presence of genetic diseases more prevalent in the donor's ethnicity, if applicable (a list of serious genetic diseases prevalent in specific ethnicities and/or populations has been provided below).

Family history-based genetic disease screening plays a critical role in assessing the risk of transmitting a serious genetic disease and involves evaluating a donor based on known or suspected family history for a specific disease. A person with a family history of a genetic disease or a person from a population group in which the disease is prevalent is known to be at a significantly higher risk of being affected or being a carrier of the disease. The use of

family history screening is known to increase the likelihood of detecting individuals at an increased risk for diseases with known genetic components as compared to reviewing a patient's medical records alone[30]. A number of guidelines have been established to obtain a family genetic history that can be adapted to screen a sperm and ova donor, including administering a family history questionnaire/checklist and the pedigree method [31, 32, 33, 34, 35].

A particular genetic disease may be more prevalent in certain ethnicities or populations due to the "founder effect." As such, in screening a donor, special consideration should be given to the single-gene genetic diseases that are prevalent in the donor's ethnic background. For example, individuals from Southeast Asia, the Mediterranean region, and Africa are at increased risk of hemoglobinopathies. Similarly, people of Ashkenazi Jewish (AJ) descent (i.e., at least one grandparent of AJ background) are known to be more prone to certain diseases such as Tay-Sachs disease (carrier frequency 1/30), Canavan disease (carrier frequency 1/37 – 1/53), and familial dysautonomia (carrier frequency 1/32)[36].

List of Serious Genetic Diseases

The list of serious genetic diseases provided below is meant to guide the medical director when conducting the genetic disease screening of donors.

The list, which includes serious genetic diseases that are more prevalent in the general population as well as in specific ethnicities has been informed by the latest scientific evidence and the recommendations made by national and international professional societies/associations and standards[37, 38, 39, 40, 41]. Health Canada recognizes that there are over 3,600 human genes[42] that have a known phenotype corresponding to one or more single gene disorder/s[43], and more such genes are being discovered at a rapid pace.

Health Canada intends to update the list based on scientific advances in the field of human genetics.

As part of the genetic disease screening, the medical director should screen all donors for the risk of transmission of serious genetic diseases, including:

- Cystic fibrosis;
- Duchenne/Becker muscular dystrophy;
- Haemophilia A and B; and
- Spinal muscular atrophy.

In addition, the medical director should consider screening donors for the risk of transmission of serious autosomal dominant and X-linked dominant diseases with varying manifestations and range of severity (such as neurofibromatosis type 1, 22q11.2 deletion syndrome, fragile-X syndrome, and polycystic kidney disease), as donors may not be aware that they are affected.

Additionally, donors of Southeast Asian, Mediterranean, or African descent should be screened for the risk of transmission of the following hemoglobinopathies:

- Sickle cell anemia [or Sickle cell disease]; and

- Thalassemia (alpha and beta).

Donors of Ashkenazi Jewish descent should be screened for the risk of transmission of the following diseases:

- Tay-Sachs disease;
- Canavan disease;
- Familial dysautonomia;
- Gaucher disease;
- Niemann pick disease [or Niemann-Pick A];
- Fanconi anemia, type C;
- Bloom syndrome;
- Mucolipidiosis [type IV];
- Glycogen storage disease, type 1a;
- Familial hyperinsulinism;
- Maple syrup urine disease [type 1b];
- Dihydrolipoamide dehydrogenase deficiency;
- Usher syndrome;
- Nemaline myopathy;
- Joubert syndrome; and
- Walker-Warburg syndrome.

Donors of the Saguenay-Lac Saint-Jean/Charlevoix region should be screened for the risk of transmission of the following diseases:

- Tyrosinemia type I;
- Congenital lactic acidosis Saguenay-Lac-Saint-Jean type;
- Spastic ataxia, Charlevoix-Saguenay type; and
- Agenesis of the corpus callosum with peripheral neuropathy.

Donors of Bas-St-Laurent (Rimouski) and Gaspésie regions in Quebec, and adjoining New Brunswick territories should be screened for the risk of transmission of the following diseases:

- Tay-Sachs disease.

Donors who are of Cree ancestry should be screened for the risk of transmission of the following diseases:

- Cree encephalitis (Aicardi-Goutières syndrome); and
- Cree leukoencephalopathy.

Donors from Indigenous Manitoba populations should be screened for the risk of transmission of the following diseases:

- Cerebro-oculo-facio-skeletal syndrome.

Donors of Newfoundland region should be screened for the risk of transmission of the following diseases:

- Bardet-Biedl syndrome; and
- Neuronal ceroid lipofuscinosis.

Genetic Disease Testing in Lieu of Genetic Disease Screening

Although genetic testing is not required by the Safety Regulations, relevant test results, if available, can be used in lieu of donor screening to assess the donor's risk of genetic disease transmission. For example, if a donor's test results are available for cystic fibrosis, these results can be used instead of screening the donor for the risk of transmitting the same disease.

Recent technological advancements in high-throughput genotyping and sequencing allow for the testing of a large number of genetic conditions simultaneously. Expanded Carrier Screening (ECS) is one such form of genetic testing intended to detect carrier status for a broader array (> 100 diseases in most cases) of recessive diseases in a person [a donor] who, based on their family genetic history, may/may not have an *a priori* increased risk of being a carrier[44, 45]. Thus, ECS tests for the carrier status of donors regardless of their ancestry or geographic origins.

However, it is important to note that many national and international guidelines do not recommend conducting ECS unless the risk of transmitting a specific disease has been identified first through genetic disease screening. Additionally, despite scientific and technological advances in identification, understanding, and analysis of genetic diseases, there are a number of challenges with using ECS panels, including false positive results, ambiguous test results, over diagnosis or incidental findings; all of which should be taken into consideration when assessing the donor's risk of genetic disease transmission through the use of ECS.

Assessment of Risk

The medical director or a qualified professional designated by the medical director must assess the donor for the risk of genetic disease transmission, based on the donor's genetic disease screening, or their relevant genetic testing if available in lieu of screening, or both.

In assessing the risk, the medical director should take into consideration the information obtained from the donor's medical history, physical examination, and three generations of family genetic history that would indicate an increased risk of genetic disease transmission. Consideration should also be given to additional risk factors, such as:

- multiple affected family members with the same or related disease;

- pattern of inheritance (e.g., the affected sex and any relevant implications);
- onset of the disease (e.g., earlier onset than typically expected may demonstrate genetic predisposition of the donor to a specific disease);
- reduced penetrance, variable expressivity, and genetic variants, which are known to influence the effects of a particular genetic disease (e.g., many genetic diseases show variable expressivity by which, based on specific mutations in the disease-associated gene, a particular disease could present a range of signs and symptoms, or may have reduced penetrance by which not every person carrying a particular genetic mutation would exhibit signs and symptoms of the genetic disease);
- any relevant results of donor testing, if available;
- limitations of the information gained from the donor's genetic disease screening, or their relevant genetic testing if available in lieu of screening, or both.

The assessment of the risk of genetic disease transmission must be included in the summary document that accompanies the donation. In addition to reducing the risk of genetic disease transmission, the assessment of risk, as it relates to third party donors, aims to provide the recipient with the necessary information in the event they may wish to seek genetic counselling based on their own genetic history and unique risk factors.

If the donor's genetic disease screening indicates a risk of serious genetic disease transmission, Health Canada recommends that relevant follow up testing be conducted to rule out any risk of disease transmission. The medical director may also want to consider recommending follow up testing for any serious genetic diseases prevalent in the donor's ethnic background.

Health Canada recognizes that there may be cases where a donor may not know the three generations of their family history (e.g., if they were adopted). In such instances, Health Canada recommends that a donor undergo relevant genetic testing, to assess the risk of transmitting serious genetic diseases based on the donor's own medical history, physical examination, and ethnic background, if known. However, if testing is not conducted and the information related to the donor's family history is incomplete, the medical director should consider the lack of this information when assessing and documenting the risk of serious genetic disease transmission.

Physical examination

24 An establishment that performs physical examinations on donors must do so in accordance with the requirements set out in the Directive under the heading "Physical Examination".

A medical director or, a physician or nurse practitioner designated by the medical director, is responsible for performing a physical examination to assess any physical evidence that could indicate the presence or symptom/s of an infectious or genetic disease. For example, a potential donor subject to the Regular Process requirements whose physical examination reveals evidence of active genital herpes would be unsuitable to donate.

Based on the donor medical history, social history, and clinical status assessed through the donor screening questionnaire, a more tailored physical examination should be performed to confirm or rule out any potential risk factors that may have been identified during the donor screening.

Health Canada recommends that the initial physical examination be performed as close to the time of donation as feasible. In the event that more than one month (but not more than six months) has elapsed since the initial physical examination was completed and the sperm or ova has not been obtained, Health Canada recommends reviewing the donor's initial screening and physical examination results to determine if, based on clinical judgement, a new physical examination should be performed. If more than six months have elapsed since the initial physical examination was completed, the donor must undergo a new physical examination.

Donor testing

25 An establishment that performs donor testing must do so in accordance with the requirements set out in the Directive under the heading "Donor Testing".

A primary establishment must ensure that all infectious disease testing, including testing which is carried out on its behalf by another establishment, is carried out in accordance with the requirements outlined in clause 2.3 of the Directive.

Donor testing is intended to identify the risks of infectious disease transmission by testing the donor for the presence of infectious disease agents that could impact the safety of the sperm or ova. All sperm and ova donors must be tested for the infectious disease agents set out in clause 2.3.3 of the Directive. In addition, sperm donors subject to the Regular Process requirements, but not those subject to the Directed Donation Process requirements, must be retested in accordance with clause 2.3.4 of the Directive, to determine if they are suitable to donate.

General Requirements

An establishment that performs donor testing must:

- have standard operating procedures that describe all tests to be performed and the handling of positive and indeterminate test results;
- use appropriate and effective tests;

- ensure that donor testing is conducted by a laboratory that meets the applicable accreditation requirements of the province in which the laboratory is located, or if donor testing was conducted in another country, the testing laboratory is accredited by an organization that is considered an acceptable accreditation organization by the foreign jurisdiction where the donor testing was conducted;
- perform donor testing using in vitro diagnostic devices that are licensed in Canada, if the testing is carried out in Canada, or if the testing is performed outside of Canada, using in vitro diagnostic devices licensed in either Canada or the United States;
- conduct donor testing in accordance with the test kit manufacturer's instructions, including the requirements for specimen collection, performance and the interpretation of results;
- at the time of initial donor testing or at any time prior to the release of sperm and ova from quarantine, test all sperm and ova donors to determine their blood type (i.e., ABO group and Rh type).

Infectious Disease Agents

At the time of initial testing, all sperm and ova donors must be tested for the presence of the following infectious disease agents, as listed in clause 2.3.3 of the Directive:

a) Human Immunodeficiency Virus (HIV) -1 and -2;
b) Hepatitis C Virus (HCV);
c) Hepatitis B Virus (HBV);
d) Human T-cell Lymphotropic Virus (HTLV) -1 and -2 (sperm donor only);
e) *Treponema pallidum* (syphilis);
f) Cytomegalovirus (CMV) (sperm donor only);
g) West Nile Virus (WNV), if the donation is made during the time of year when WNV is potentially transmissible to humans in the donor's country of residence, or if in the preceding 56 days, a donor has lived in or travelled to an area where WNV is endemic;
h) *Chlamydia trachomatis*; and
i) *Neisseria gonorrhoeae*.

Please note that ova donors are not required to be tested for HTLV-1 and -2 and CMV.

Appropriate and Effective Tests

A test is considered appropriate and effective if it is:

- licensed for the detection of the infectious disease agent or marker;
- used in accordance with the test kit manufacturer's instructions; and
- used for the detection of an infectious disease marker that is relevant at the time testing is performed.

Health Canada considers the followings tests to be appropriate and effective infectious disease tests. This list may be revised when new infectious disease tests become licensed, or when new information necessitates an amendment.

a) HIV:
   - antibodies to HIV, types 1 and 2 (anti-HIV-1 and anti-HIV-2), and HIV antigen; or
   - anti-HIV-1, anti-HIV-2, and nucleic acid testing (NAT) for the detection of HIV-1;

b) HCV:

   b1) in the case of a donor subject to retesting at least 180 days after the date of donation:
   - at a minimum, antibodies to HCV (anti-HCV) for both initial testing and retesting;

   b2) in the case of a donor not subject to retesting at least 180 days after the date of donation:
   - both anti-HCV and NAT for the detection of HCV;

c) HBV:
   - HBV surface antigen (HBsAg) and total antibodies to HBV core antigen (anti-HBc, IgG and IgM);

d) HTLV-1 and HTLV-2:
   - serological assays for the detection of antibodies to HTLV type 1 and 2 (anti-HTLV-1 and HTLV-2);

e) *Treponema pallidum*:
   - treponemal-specific test; or
   - non-treponemal test;

f) CMV:
   - total antibodies to CMV (IgM and IgG);

g) WNV:
   - assays for the detection of WNV nucleic acid (WNV NAT);

h) *Chlamydia trachomatis*:
   - assays for the detection of *Chlamydia trachomatis* nucleic acid; and

i) *Neisseria gonorrhoeae*:
   - assays for the detection of *Neisseria gonorrhoeae* nucleic acid.

In Vitro Diagnostic Devices

All donor testing must be performed using in vitro diagnostic devices (test kits) that are licensed in Canada, if the testing is carried out in Canada, or if the testing is performed outside of Canada, using in vitro diagnostic devices that are licensed in either Canada or the

United States. Health Canada is the federal regulator responsible for licensing in accordance with the Medical Devices Regulations. For more information, please consult the Medical Devices Active License Listing (MDALL) database.

In vitro diagnostic devices include test kits that are licensed for screening or for diagnostic purposes. Screening tests are based on investigational testing in a population with a low disease prevalence, and place an emphasis on test sensitivity. In contrast, diagnostic tests are based on investigational testing often performed in a symptomatic population, with an emphasis on test specificity.

An establishment that conducts donor testing for any of the infectious disease agents listed in clause 2.3.3 of the Directive must do so using tests that are licensed for the purpose of screening donors, except in the case of *Treponema pallidum*, *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in which case either screening or diagnostic test kits can be used. Although the use of screening tests is preferred, the Safety Regulations allow for the limited use of diagnostic tests, to account for testing carried out by establishments outside of Canada, where certain screening test kits for *Treponema pallidum*, *Chlamydia trachomatis* and *Neisseria gonorrhoeae* may not be licenced or available.

In cases where a licenced screening or diagnostic test is unavailable for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* for the specimen being tested, the laboratory must have validation data to support the use of an alternative test method for the intended application. It is recommended that the establishment keep on file confirmation from the testing laboratory that the method has been validated.

An establishment that conducts donor testing using a licensed test kit must do so in accordance with the manufacturer's instructions, including with respect to the following:

- the collection, handling, and storage of the specimen;
- the timeframe within which the collected specimen must be tested;
- the procedure for testing; and
- the performance of the test and the interpretation of the test results.

Timeframe for Specimen Collection

The initial testing of sperm donors for the infectious disease agents set out in clause 2.3.3 of the Directive must be conducted using a specimen collected within 7 days of obtaining the donation.

In the case where a sperm donor from whom a specimen has already been collected for initial testing and for whom retesting is required in accordance with clause 2.3.4 (Donor Retesting) of the Directive, an establishment is not required to collect a new specimen at the time of each donation, unless as per the donor reassessment requirements outlined in clause 3 of the Directive.

The initial testing of ova donors for the infectious disease agents set out in clause 2.3.3, except 2.3.3 (d) and (f), of the Directive must be conducted using a specimen collected within 30 days before obtaining the ova or within seven days of obtaining the ova.

For WNV, testing of sperm and ova donors must be performed during the time of year when WNV is transmissible to humans in the donor's country of residence (i.e., seasonal basis) or, if in the preceding 56 days prior to the donation, during the time of year when WNV is not transmissible in the donor's country of residence, the donor has lived in or travelled to an area where WNV is endemic. It is up to the primary establishment to determine the appropriate frequency of WNV testing to effectively address the risk of WNV transmission. For WNV surveillance information specific to Canada and the United States, please visit the following websites:

- West Nile virus surveillance in Canada
- Centers for Disease Control and Prevention (United States)

Retesting of Sperm Donors

Prior to the determination of donor suitability and the release of the donation from quarantine, all sperm donors subject to the Regular Process must be retested in accordance with clause 2.3.4 of the Directive, in order to allow for the detection of any infections that manifest after the donation has been obtained from the donor. Sperm donors must be retested for the infectious disease agents set out in clause 2.3.3 of the Directive (except for WNV, *Chlamydia trachomatis,* and *Neisseria gonorrhoeae*) using a new specimen collected from the donor after a minimum of 180 days following the date of donation. The sperm donation must remain in quarantine until the medical director has determined the donor to be suitable, based on their review of the donor suitability assessment, and reassessment if available, including the results of the initial testing and retesting.

In some cases, a donor can contract an infectious disease agent that is not detected at the time of initial testing due to the "window period" between the time of infection and the time that the infectious agent can be detected. In such instances, the 180-day period allows for the period of time needed for a specific antibody to be developed and become detectable in the blood (i.e. seroconversion). In addition to detecting window period infections, donor retesting may detect specific infectious disease markers that were not present at time of initial testing.

Sperm donors subject to the Directed Donation process, as well as ova donors subject to the Regular or the Directed Donation process are not required to be retested and as such, the use of fresh (i.e., not cryopreserved) sperm and ova is permitted in these instances.

Interpretation of Test Results

In general, the initial testing is performed using one or more tests (e.g., one or more serological tests or a combination of serological and NAT) on a single blood specimen. The terms used by test kit manufacturers for the interpretation of test results are determined in part, by the testing algorithms used.

For instance, in the case of serological testing, a nonreactive specimen is considered a negative test result and, as such, the donor may be considered suitable to donate or, if the test is conducted as part of donor retesting, the donation may be released from quarantine.

In the case where a donor is tested for an infectious disease agent using more than one test, all tests must be nonreactive for a specimen to be considered negative.

In contrast, a reactive specimen obtained using serological testing, is considered initially reactive instead of positive because in such cases the same test is repeated in duplicate and the results may be considered repeatedly reactive or positive if one or both of the two replicates are reactive. On the other hand, the results may be considered false positive or negative if both of the replicate tests are non-reactive. However, some test kit manufacturers may only consider a specimen to be positive once confirmatory or supplemental testing with a different test kit is performed to confirm the results of the first test kit.

It should be noted that screening tests are more sensitive than confirmatory tests and, as such, less likely to result in a false negative. Thus, confirmatory tests should not be used for the purpose of initial donor testing because false negative confirmatory test results cannot be ruled out.

These additional steps are necessary to achieve the final serological testing outcome (i.e., "positive" or "false positive") in the event that a specimen is initially reactive. In such cases, the donor must be determined unsuitable and the donation must not be released from quarantine, even if the confirmatory or supplemental test results are negative and the original test is deemed a false positive.

However, a sperm or ova donor who has been determined unsuitable due to a false positive test result may be determined to be suitable if the donor tests negative following an appropriate donor re-entry algorithm that typically requires testing to occur after a specific period of time to allow for possible seroconversion prior to the performance of additional follow-up testing (serological testing or serological testing and NAT). Performing follow-up testing using a new specimen collected before obtaining another donation from the donor may prevent a potentially contaminated donation from being collected and placed in the distribution chain.

It is important to note that this testing algorithm is intended to serve only as an example. There may be a different algorithm used for the interpretation of test results depending upon the type of test used for donor testing (e.g., serological testing and/or NAT) and as such, establishments must apply the specific testing algorithm proposed by each test kit manufacturer.

To ensure that a consistent interpretation of infectious test results is applied:

1. a negative test result means the final outcome in which the test specimen is determined to be nonreactive by the test kit manufacturer.
2. a positive test result means the final outcome in which the test specimen is determined to be "reactive", "repeatedly reactive" or "positive" according to the testing algorithms proposed by the test kit manufacturer.

3. a confirmed positive test result means the outcome of a confirmatory or supplemental test performed using a different test kit, in which the tested specimen is determined to be reactive.

Although not required by the Safety Regulations, Health Canada recommends that primary establishments responsible for donor testing archive specimens from donors for the purpose of retrospective testing when new tests are made available. Establishments that archive specimens should have standard operating procedures for the collection, storage and the duration of storage of the archived specimens.

Donor reassessment

26 In order to determine whether a repeat donor is suitable, a primary establishment must ensure that the donor is reassessed in accordance with the requirements set out in the Directive under the heading “Donor Reassessment”.

Sperm and ova donors who donate more than once, referred to as repeat donors, must be reassessed in accordance with clause 3 of the Directive. The reassessment is intended to monitor the donor's risk of infectious or genetic disease transmission during the time when the donor is actively donating or has lapsed a significant period of time since their last donation. Section 26 of the Regulations is specific to donors subject to the Regular Process for donation. The reassessment requirements for sperm and ova donors subject to Directed Donation Process are outlined in section 35 of the Regulations.

Reassessment of Sperm Donors

Repeat sperm donors who are subject to the Regular Process requirements must be screened for the risk of infectious and genetic disease transmission at least every six months, or at the time of the subsequent donation following a lapse in screening exceeding six months, in accordance with the donor screening criteria set out in clause 2.1 of the Directive. This includes screening repeat sperm donors for the risk of the relevant emerging infectious diseases. Additionally, the age of the donor at the time of the reassessment must be known and documented. In the case of genetic disease screening, an abbreviated questionnaire can be used to gather any new medical information that may have become available since the previous genetic disease screening was conducted.

Repeat sperm donors must undergo a new physical examination at least every six months or at the time of the subsequent donation following a lapse in physical examination exceeding six months, in accordance with the physical examination requirements set out in clause 2.2 of the Directive.

Repeat sperm donors must be tested for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, using a new specimen collected from the donor, at least every six months or within seven days of the subsequent donation following a lapse in testing exceeding six months, in

accordance with the donor testing requirements set out in clause 2.3.1(I) to (III), (V), and (VI) of the Directive. However, an establishment conducting donor reassessment may choose to test repeat donors more frequently (e.g., every month, every three months, etc.), in order to detect new infections more quickly, given that any donations obtained between testing intervals in which infection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* cannot be ruled out, must be discarded. Additionally, testing repeat donors more frequently will reduce the risk of cross-contamination.

The donor reassessment requirements are limited to testing repeat sperm donors for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* because the donor is retested for all other infectious disease agents listed in clause 2.3.3 of the Directive, except WNV, prior to their donation being released from quarantine.

The results of donor reassessment, combined with the results of donor retesting, provide the medical director with the necessary information to determine if the donor remains suitable to donate at regular intervals.

Reassessment of Ova Donors

A repeat ova donor must undergo donor screening and testing at the time of each donation, in accordance with the clause 3.2.1 and 3.2.3 of the Directive, respectively. This includes screening donors for risk of infectious and genetic disease transmission and testing for infectious disease agents set out in clause 2.3.3 (I) of the Directive.

In the case of genetic disease screening of repeat ova donors, an abbreviated questionnaire can be used to gather any new medical information that may have become available since the previous genetic disease screening was conducted.

Also, repeat ova donors must undergo a physical examination at least every six months or at the time of the subsequent donation following a lapse in physical examination exceeding six months, in accordance with clause 3.2.2 of the Directive. In other words, repeat ova donors are required to undergo a physical examination only if more than six months have elapsed since the previous physical examination. Health Canada recommends that the physical examination be performed as close to the time of donation as feasible. If more than one month (but not more than six months) has elapsed since the previous physical examination was completed and the ova has not been obtained, Health Canada recommends reviewing the donor's most recent screening and physical examination results to determine if, based on clinical judgement, a new physical examination should be performed. If more than six months have elapsed since the previous physical examination was completed, the repeat ova donor must undergo a new physical examination.

Determination of donor suitability

27 (1) A primary establishment must ensure that its medical director determines whether a donor is suitable by reviewing the information obtained from the donor suitability assessment and, if applicable, from the donor reassessment.

Donor unsuitability

(2) A primary establishment must ensure that its medical director determines a donor to be unsuitable if

(a) the donor meets any criteria set out in the Directive under the heading "Donor Exclusion"; or

(b) the donor suitability assessment is not complete.

A primary establishment is responsible for ensuring that its medical director determines the suitability of sperm and ova donors by reviewing the results of donor screening, physical examination, and donor testing, including donor retesting. If applicable, the results of donor reassessment must also be reviewed by the medical director, in order to determine if the donor is suitable. Under the Regular Process, sperm and ova from donors who are determined to be unsuitable to donate must not be released from quarantine, except as outlined in section 29 of the Safety Regulations.

A donor subject to the Regular Process requirements who meets one or more of the donor exclusion criteria, set out in clause 4 of the Directive, is considered unsuitable to donate until they no longer meet the exclusion criteria, if applicable (e.g., donor no longer meets the timeframe for being at risk of Zika virus transmission). The donor is also considered unsuitable to donate if the donor suitability assessment was not completed in accordance with the Safety Regulations. The donor exclusion criteria include:

a) A sperm or ova donor who meets any of the infectious disease screening criteria set out in clause 2.1.1 (II) (a) to (n).

A donor who meets any of the infectious disease screening criteria outlined in clause 2.1.1 (II) (a) to (n) is at an increased risk of transmitting an infectious disease to the recipient of their sperm or ova, or the individual born of their donation. For this reason, donors must be considered unsuitable to donate on the basis of these contraindications.

b) A sperm or ova donor who is symptomatic or has previously been diagnosed with a serious autosomal dominant or X-linked genetic disorder.

Based on the results of genetic screening, the medical director must determine a donor to be unsuitable to donate if the donor is either symptomatic of or has previously been diagnosed with a serious autosomal dominant or X-linked genetic disease.

In the case of an autosomal dominant or X-linked dominant disease, only one copy of the disease-associated gene in each cell is sufficient for that individual to be affected. As such, a donor who is either symptomatic of, or has been diagnosed with a serious autosomal dominant or X-linked dominant disease is at an increased risk of transmitting it to the individual born of their donation.

In the case of an autosomal recessive disease, both copies of the disease-associated gene in each cell must have mutation/s in order for that individual to be affected. As such, a donor who is a carrier of an autosomal recessive disease is not excluded from donating, as they only present a risk of genetic disease transmission if the recipient is also a carrier for the same mutation. Thus, a more comprehensive and effective risk assessment, to mitigate the risk of autosomal recessive disease transmission to the individual born of the implicated sperm or ova, should include the assessment of genetic information from both the donor and the recipient.

X-linked recessive genetic diseases most often affect males, given that they only have one copy of the X chromosome and as such, any disease-causing mutations on that X chromosome are sufficient to cause the disease. As such, an ova donor who is either symptomatic or has been diagnosed with a serious X-linked recessive disease presents a risk of transmitting the disease to all male individuals born of their donation. On the other hand, a sperm donor who is symptomatic for a X-linked recessive genetic disease will only pass the affected disease-causing gene to female individuals born of their donation, making them a carrier of the genetic disease (in some cases, such as Hemophilia A and B, a carrier of an X-linked recessive disease can also be affected and can exhibit a range of symptoms).

Given the higher risk associated with the transmission of serious X-linked recessive or X-linked dominant genetic diseases, the medical director must exclude sperm or ova donors who have been diagnosed with or are symptomatic of a serious X-linked genetic disease.

c) With the exception of *Treponema pallidum* and CMV, a sperm or ova donor who tests positive for any of the infectious disease agents listed in clause 2.3.3 (I). Donations obtained between testing intervals in which infection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* cannot be ruled out shall be discarded.

A donor is considered unsuitable to donate if the donor, at the time of donor testing and if applicable, at the time of donor reassessment, tests positive for any of the infectious disease agents set out in clause 2.3.3(I) (a) to (d), and (g) to (i) of the Directive. If donor sperm or ova was obtained during a time period in which infections of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* cannot be ruled out (e.g., during the time period between initial donor testing and donor reassessment), that donation must not be released from quarantine.

d) In the case of *Treponema pallidum*, a sperm or ova donor who tests positive for *Treponema pallidum* using the treponemal-specific test. A sperm or ova donor may

be determined suitable if the non-treponemal test is negative or positive, but the treponemal-specific test is negative.

For *Treponema pallidum* (syphilis), a donor is considered suitable if the donor at the time of initial testing or, if applicable, at the time of donor retesting, tests positive using a nontreponemal test, but negative using a treponemal-specific confirmatory assay. It should be noted that if an establishment decides to use a treponemal-specific test for syphilis, and the donor tests positive (at the time of initial testing or if applicable, at the time of donor retesting), the donor must be determined unsuitable to donate. This is because a positive treponemal-specific test identifies both recent syphilis infections, and remote or treated syphilis infections. While a nontreponemal test can be performed to rule out a recent infection, false negative results are possible, particularly in the context of acute syphilis infection. Thus, appropriate testing algorithms need to be developed to resolve this issue.

e) In the case of CMV, a sperm donor who tests positive for CMV IgM until they become IgM negative. A sperm donor may be determined suitable if the CMV IgG test is negative or positive, but the CMV IgM test is negative.

For CMV, a sperm donor must be considered unsuitable to donate if a donor tests positive for CMV immunoglobulin M (IgM) until that donor tests negative for IgM. However, a sperm donor may be determined suitable if the CMV immunoglobulin G (IgG) test is negative or positive, but the CMV IgM test is negative. This is because a positive test for CMV IgG indicates that a donor was infected with CMV at some time during their life, but does not indicate when that donor was infected.

f) A sperm or ova donor, who has been determined unsuitable due to a positive test result, as specified in clauses 4(c) and 4(d), may be determined to be suitable if:
    - a confirmatory or supplemental test result is negative, and
    - the donor is retested according to an appropriate donor re-entry algorithm.

A donor who tests positive for any of the infectious disease agents listed in clause 2.3.3 (I) of the Directive may be determined to be suitable to donate if a confirmatory or supplemental test result is negative and the donor is retested according to an appropriate donor re-entry algorithm.

In some cases, donors may be excluded from donating due to false positives, or infection with treatable pathogens (e.g., *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Treponema pallidum*). In the case of treatable pathogens, donor re-entry may be possible provided appropriate treatment was received (as per current National or Provincial Guidelines) and the treatment was shown to be effective through a negative test of cure.

For instance, if a donor was previously determined to be unsuitable to donate due to infection with *Treponema pallidum, Chlamydia trachomatis,* or *Neisseria gonorrhoeae*, they may be allowed to become a donor following confirmed successful treatment. In these

cases, donor re-entry must follow the requirements set out in clause 2.1.1(II)(f) of the Directive.

Summary document

(3) If a donor has been determined to be suitable, the primary establishment must ensure that its medical director creates and signs a summary document that confirms this determination and that contains

(a) the age of the donor;

(b) a statement that the donor suitability assessment and, if applicable, donor reassessment have been conducted in accordance with these Regulations; and

(c) the dates and results of the donor testing and the assessment of the risk of genetic disease transmission.

Once a donor has been determined to be suitable, the medical director at the primary establishment must create a signed summary document that will accompany the donation throughout the distribution chain. The purpose of the summary document is to provide the health professional, who intends to make use of the sperm or ova or distribute it to a recipient for their personal use, with sufficient information to assess any risks associated with the donation.

The summary document must contain important information about the donor, namely:

- their age at the time of donation;
- a statement that the donor suitability assessment and, when applicable, the reassessment have been conducted in accordance with the Safety Regulations;
- the dates and results of all donor testing, including donor's blood group testing and donor retesting; and
- the assessment of the risk of genetic disease transmission.

Quarantine

Requirement

28 (1) An establishment must quarantine all sperm and ova that it processes in the manner set out in subsection (2) until the medical director of the primary establishment that is responsible for the quarantine of that sperm and those ova has

(a) determined the donor to be suitable; and

(b) determined and documented that the sperm and ova can be released from quarantine.

Segregation

(2) The establishment must quarantine the sperm and ova by

(a) clearly indicating that they are quarantined;

(b) segregating them from sperm and ova that are not quarantined; and

(c) ensuring that they are not distributed or used.

All sperm and ova must be quarantined until the medical director determines the donor to be suitable and has determined and documented that the sperm and ova can be released from quarantine. The sperm and ova required to be quarantined by an establishment must not be distributed or used.

To prevent improper release, the quarantined sperm and ova must be clearly identifiable as quarantined and kept segregated from donor sperm or ova that are not required to be quarantined. The segregation can take the form of storing the donor sperm or ova in a physically separate area designated for such use or through the use of a validated electronic segregation system (e.g., a validated computer system and barcode labeled sperm/ova containers) to prevent improper release.

Release from quarantine — exceptional access

29 (1) Despite paragraphs 28(1)(a), an establishment may release sperm or ova from quarantine if the primary establishment that is responsible for their quarantine receives a request from a health professional for exceptional access to that sperm or those ova and if one of the following conditions is met:

(a) the recipient has previously been exposed to sperm or ova from that donor and the risk profile of the requested sperm or ova, based on the results of any part of the donor suitability assessment, is at least equivalent to the risk profile of the sperm or ova to which the recipient has previously been exposed, based on the results of any of the donor suitability assessment that was conducted at that time; or

(b) sperm or ova from that donor have previously been used to create a child for an individual or a couple and the requested sperm or ova are to be used for the purpose of creating another child for that individual or couple.

Summary document

(2) Before the sperm or ova are released from quarantine, the primary establishment must ensure that its medical director creates a summary document that contains the following information:

(a) the age of the donor, if known;

(b) the conditions that have been met;

(c) the dates and results of any donor screening, physical examination or donor testing; and

(d) the reasons the donor was determined to be unsuitable and a detailed explanation for each reason.

Storage

(3) An establishment and a health professional must ensure that sperm or ova that are in their possession or control and are intended for exceptional access are segregated from sperm and ova that are not intended for exceptional access.

Access to donor sperm and ova that otherwise cannot be released from quarantine (i.e., because it was not processed in accordance with the Safety Regulations or is the subject of an error, accident or adverse reaction investigation) may be permitted under a narrow range of exceptional circumstances.

The two conditions for exceptional access are:

1. where the recipient has previously been exposed to sperm or ova from that donor and the results of the donor suitability assessment indicate that the risk profile of the requested sperm or ova is equivalent to the risk profile* of the sperm or ova to which the recipient was previously exposed; or,
2. where sperm or ova from the donor will be used to create a genetic sibling for the individual or couple.

** For the purposes of the Safety Regulations, "equivalent risk profile" means that the requested donation would not pose a greater risk to human health and safety as that posed by the donation to which the donor was previously exposed. At a minimum, the donor would have to be tested for the same infectious disease agents as they were previously tested for and would have to be subjected to the same donor screening they had previously been subjected to. In addition, the results of any other tests performed in respect of the donor would have to indicate that the sperm or ova are not contaminated by an infectious disease agent and any additional screening results would have to indicate that the donor is suitable to donate.*

In order for sperm or ova to be released from quarantine under exceptional access, a number of requirements must be met, such as:

- a health professional must request the sperm or ova from the primary establishment responsible for their quarantine, on behalf of the recipient. As part of the request, the health professional must indicate to the primary establishment which of the conditions for exceptional access applies;

- prior to releasing the sperm or ova under exceptional access, the primary establishment must have its medical director create a summary document that contains the information that is necessary for the health professional to meet their documentation requirements for communication of risk (outlined below) including:
    - the age of the donor at the time of donation (if known);
    - the conditions for exceptional access that have been met;
    - the dates and results of any donor screening, physical examination, and donor testing;
    - the reason(s) that the donor was determined to be unsuitable to donate as per the Donor Exclusion criteria set out in clause 4 of the Directive and a detailed explanation of each reason;
- segregated storage: establishments and health professionals must ensure that all sperm and ova released from quarantine under exceptional access is kept segregated from all other donor sperm or ova that are not intended for exceptional access;
- additional labeling requirements: a primary establishment must ensure that the immediate container of sperm or ova is accompanied by documentation that contains a statement that indicates that the donation is for exceptional access only as set out in section 50(c) of the Safety Regulations: and
- communication of risk to the recipient (as set out in section 29(4) of the Safety Regulations, described below).

Communication of risk

(4) A health professional must meet the following requirements before making use of the sperm or ova or distributing the sperm to a recipient for their personal use:

(a) create a document that states that, based on the summary document and any risk mitigating measures with respect to that sperm or those ova, in their medical opinion, the use of the sperm or ova would not pose a serious risk to human health and safety; and

(b) create a document that states that the health professional has informed the recipient of the risks that the use of the sperm or ova could pose to human health and safety and that the health professional has obtained written consent from the recipient.

Prior to making use of sperm or ova released under exceptional access or distributing sperm to a recipient for their personal use, the health professional must document that:

- based on the information contained in the summary document and any risk mitigation measures taken (e.g., sperm washing, anti-retroviral drugs to mitigate the risk of HIV transmission etc.) with respect to the sperm or ova in question, in their medical opinion the use of the donation would not pose a serious risk to human health and safety of the recipient and the individual born of that donation; and
- they have informed the recipient of the risks that the use of the sperm or ova donation could pose, such as instances where the effectiveness of a risk mitigation measure may be very high but not absolute, and that they have obtained written consent from the recipient to make use of the sperm or ova.

Directed Donation Process

Donor Suitability Assessment and Confirmation

Application

30 Despite sections 22 to 29, the requirements set out in sections 31 to 40 with respect to sperm or ova that are intended for directed donation may instead be met if

(a) the donor and recipient know each other; and

(b) the health professional requests the sperm or ova from a primary establishment in the context of a directed donation.

In the case where the donor and recipient know one another, the donor sperm or ova may be processed in accordance with the Directed Donation Process requirements as set out in sections 31 to 40 of the Safety Regulations. The Directed Donation Process provides the recipient with more flexibility in selecting their donor, while still prioritizing the safety of the donation. In order for sperm or ova to be processed via the Directed Donation Process, a health professional must request the sperm or ova from a primary establishment on behalf of the recipient.

There are some similarities in the requirements for the Regular Process and the Directed Donation Process. For example, a sperm or ova donor subject to either the Regular Process or Directed Donation Process must undergo a donor suitability assessment. The requirements that are the same for both processes have been explained under the Regular Process sections of this Guidance and will not be repeated in this section.

However, there are a number of differences between the Regular Process and the Directed Donation Process requirements that will be explained in this document, such as:

- testing requirements for sperm donors;
- reassessment of sperm donors;
- review of donor suitability assessment;
- additional labelling requirements;

- communication of risk to the recipient; and
- segregated storage requirements.

Donor suitability assessment

31 A primary establishment, in the context of a directed donation, must ensure that a donor suitability assessment is conducted.

Donor screening

32 An establishment that performs donor screening, in the context of a directed donation, must do so in accordance with the requirements set out in the Directive under the heading "Donor Screening".

Physical examination

33 An establishment that performs physical examinations on donors, in the context of a directed donation, must do so in accordance with the requirements set out in the Directive under the heading "Physical Examination".

Donor testing

34 An establishment that performs donor testing, in the context of a directed donation, must do so in accordance with the requirements set out in the Directive under the heading "Donor Testing".

Donor Screening, Physical Examination, and Donor Testing

Sperm and ova donors who are subject to the Directed Donation Process (henceforth known as directed donors) must undergo a donor suitability assessment, including:

- donor screening as set out in clause 2.1 and 2.1.1 (I), (II) (a) to (l) and (o) of the Directive;
- physical examination as set out in clause 2.2 of the Directive; and
- donor testing as set out in clause 2.3 of the Directive, except for clause 2.3.4 (donor retesting).

The donor screening, physical examination and donor testing requirements described for the Regular Process (as part of section 23-25 of the Safety Regulations), also apply to directed donors, except where specified otherwise.

Under the Directed Donation Process directed sperm donors are not required to be retested for infectious disease agents (i.e., at minimum a 180 days following the donation) and the use of fresh sperm is allowed. However, revised donor screening criteria have been included to account for certain risks that may be associated with the use of fresh sperm. For example, directed donors are screened for use of antiretroviral medications for prevention of HIV infection (including medications for pre-exposure prophylaxis (PrEP) or post-exposure prophylaxis (PEP)) within the preceding 4 months. In the rare event that an

individual acquires HIV infection despite taking PrEP or PEP, these medications can delay detection of HIV infection.

It is important to note that a directed sperm or ova donor is not determined unsuitable to donate even if their screening, testing or physical examination results would have excluded them from donating under the Regular Process as per the donor exclusion requirements set out in clause 4 of the Directive. Instead, the medical director must review and document the results of the donor suitability assessment, including the results of donor screening and testing, and this information must accompany the donation so that any risk identified can be communicated to the recipient.

Donor reassessment

35 A primary establishment, in the context of a directed donation, must ensure that a repeat donor is reassessed in accordance with the requirements set out in the Directive under the heading "Donor Reassessment".

Repeat donors who are subject to the Directed Donation Process requirements must undergo donor reassessment, including donor screening, physical examination, and donor testing in accordance with clause 3.1.4 to 3.1.6 (for sperm donors) and 3.2 (for ova donors) of the Directive.

Reassessment of Sperm Donors

Repeat sperm donors must be screened at the time of each donation, in accordance with the requirements set out in clauses 2.1 of the Directive. Any increase to the risk profile as a result of donor screening must be followed up by appropriate donor testing, using specimen collected within seven days of the donation, in accordance with the requirements set out in clause 2.3.1(I) to (III), (V), and (VI) of the Directive. For example, if during the screening the donor was identified to have been treated for *Chlamydia trachomatis* since their last donation, they must be tested using an appropriate and effective test to establish evidence of successful treatment prior to their subsequent donation.

An abbreviated questionnaire can be used to screen a directed sperm donor for the risk of genetic or infectious disease transmission, in order to reassess the donor based on any new medical information that may have become available since the previous screening was conducted.

A physical examination of a repeat sperm donor must be conducted at least every six months or at the time of the subsequent donation following a lapse in physical examination exceeding six months, in accordance with the physical examination requirements set out in clause 2.2 of the Directive.

Repeat sperm donors must undergo donor testing for infectious disease agents set out in clause 2.3.3 (I) at least every three months or within seven days of the subsequent donation following a lapse in testing exceeding three months, in accordance with the requirements set out in clause 2.3.1(I) to (III), (V), and (VI) of the Directive.

Reassessment of Ova Donors

A repeat ova donor must undergo donor screening and testing at the time of each donation, in accordance with the clause 3.2.1 and 3.2.3 of the Directive, respectively. This includes screening donors for risk of infectious and genetic disease transmission and testing for infectious disease agents set out in clause 2.3.3 (I) of the Directive.

An abbreviated questionnaire can be used to screen a directed ova donor for the risk of genetic or infectious disease transmission, to reassess the donor based on any new medical information that may have become available since the previous screening was conducted.

In addition, repeat ova donors must undergo a physical examination at least every six months or at the time of the subsequent donation following a lapse in physical examination exceeding six months, in accordance with clause 3.2.2 of the Directive. The physical examination requirements described for the reassessment of ova donors under the Regular Process (as part of section 26 of the Safety Regulations), also apply to directed ova donors.

Review by primary establishment

36 (1) A primary establishment, in the context of a directed donation, must ensure that its medical director reviews the information obtained from the donor suitability assessment and, if applicable, the donor reassessment.

Summary document

(2) A primary establishment must ensure that its medical director creates and signs a summary document that confirms the review and that contains

(a) the age of the donor;

(b) a statement that the donor suitability assessment and, if applicable, donor reassessment have been conducted in accordance with these Regulations;

(c) the dates and results of the donor testing and the assessment of the risk of genetic disease transmission; and

(d) a list of any criteria set out in the Directive under the heading “Donor Exclusion” that have been met.

Unlike a donor subject to the Regular Process requirements, a directed sperm or ova donor is not excluded based on the donor suitability assessment results. Instead, the medical director at the primary establishment must review the information gathered from the donor suitability assessment and, if applicable, donor reassessment. This includes a review

of information obtained from screening the donor for risk of infectious and genetic disease transmission as well as the results of donor's physical examination and donor testing.

Upon reviewing the information, the medical director must create a signed summary document that confirms the review and sets out important information about the donor for review by the health professional who intends to make use of the sperm or ova, including:

- the age of the donor at the time of donation;
- the dates and test results of all donor testing;
- the risk assessment of genetic disease transmission; and
- any reasons that the donor would have been determined to be unsuitable to donate as per the Donor Exclusion criteria set out in clause 4 of the Directive, if applicable. For example, if a directed donor is at risk of transmitting an infectious disease based on the screening criteria set out in clause 2.1.1 (II) (a) to (l) and (o), that information must be included in the summary document.

Donor suitability assessment cannot be conducted

37 (1) Despite sections 31, 35, and 36, a primary establishment, in the context of a directed donation, must ensure that its medical director meets the requirements set out in subsection (2) if

(a) a donation of sperm or ova has previously been obtained from the donor;

(b) the donor suitability assessment in respect of the donation was not conducted in accordance with these Regulations; and

(c) it is not medically possible to obtain another donation of sperm or ova from the donor or obtaining another donation of sperm or ova would pose a serious risk to the donor.

Requirements — medical director

(2) The medical director must meet the following requirements:

(a) review any available medical information about the donor;

(b) review any available results of any donor screening, physical examination or donor testing that was previously conducted;

(c) unless it is not medically possible to do so, take appropriate measures to complete the donor suitability assessment; and

(d) create and sign a summary document that confirms the medical director's review and that contains:

(i) the age of the donor,

(ii) the medical reasons for which another donation cannot be obtained or an explanation of the risk,

(iii) the dates and results of any donor screening, physical examination or donor testing,

(iv) a list of any criteria set out in the Directive under the heading "Donor Exclusion" that have been met, and

(v) a list of any parts of the donor suitability assessment that have not been conducted and, for each one, an explanation of the reasons it was not conducted.

Health Canada recognizes that there may be specific scenarios under the Directed Donation Process where it may not be possible to conduct the suitability assessment of a sperm or ova donor in accordance with the Safety Regulations. The Safety Regulations were designed to account for such scenarios in order to provide Canadians with more flexibility in pursuing their family-building needs, while still prioritizing the safety of the donation. This section of the Safety Regulations sets out requirements for cases where the sperm or ova has already been obtained but the donor suitability assessment was not conducted in accordance with the Safety Regulations and where it is not medically possible to obtain another donation of sperm or ova from the donor or obtaining another donation of sperm or ova would pose a serious risk to the donor.

Example Scenarios

A woman cryopreserves her ova for family building purposes. A complete donor suitability assessment is not conducted at the time of cryopreservation because the Safety Regulations do not apply to such a scenario. The woman fulfills her own reproductive needs and has excess cryopreserved ova that she would like to donate to a friend.

Similarly, a cancer patient cryopreserves his sperm prior to undergoing treatment under the premise that it would be for "personal use" (i.e. meant for the use of the donor's eventual spouse, common-law partner or sexual partner) and as a result, does not undergo a donor suitability assessment in accordance with the Safety Regulations. Later on, the patient decides to seek the help of a surrogate mother to create his family but it is not medically possible for him to obtain a fresh sperm sample and as a result, he must make use of the sample obtained previously for personal use.

In such cases, the Primary Establishment must ensure the sperm previously obtained was obtained, prepared, identified, preserved, quality assessed/tested, labelled, quarantined, and stored in accordance with the Safety Regulations.

In addition, the medical director at the primary establishment must review any existing medical information about the donor and any available results of donor screening, physical

examination, and donor testing that might have been previously conducted. Unless it is not medically possible to do so (e.g., if the donor is deceased), the medical director must take appropriate measures to complete the donor suitability assessment retroactively. The purpose of obtaining retroactive donor suitability assessment results is to assist the health professional who intends to make use of the sperm or ova in assessing the risk the donation poses to the recipient and the individual born of the donation.

Finally, the medical director must create a summary document that confirms the review and sets out important information about the donor for review by the health professional who intends to make use of the sperm or ova or distribute the sperm to a recipient for their personal use. The summary document must contain the following information:

- the age of the donor at the time of donation;
- the medical reasons for which another donation cannot be obtained or an explanation of how obtaining another donation would pose a serious risk to the donor;
- the dates and results of any donor screening, physical examination or donor testing that is either conducted retroactively or that may have been conducted at the time of donation;
- a list of any donor exclusion criteria (as set out in clause 4 of the Directive) that the directed donor meets; and
- a list of any parts of the donor suitability assessment that have not been conducted as per the clause 2 of the Directive and the reasons it was not conducted.

Quarantine

Requirement

38 An establishment that processes sperm or ova in the context of directed donation must quarantine that sperm or ova until the medical director of the primary establishment that is responsible for the quarantine of that sperm and those ova has

(a) confirmed the review of the donor suitability assessment, and if applicable, the donor reassessment; and

(b) determined and documented that the sperm and ova can be released from quarantine.

Under the Directed Donation Process, donor sperm and ova must be quarantined until the medical director of the primary establishment that is responsible for the quarantine of the donor sperm or ova has confirmed the review of the information obtained through donor suitability assessment and has determined and documented that the sperm and ova can be released from quarantine. In cases where the donor suitability was not conducted in

accordance with the Safety Regulations, the medical director must confirm the review of any existing medical information about the donor and any available results of donor screening, physical examination, and donor testing that might have been previously conducted as well as any results of the donor suitability assessment completed retroactively, and must determine and document that based on their review, the sperm or ova can be released from quarantine.

Storage

39 An establishment and a health professional must ensure that sperm or ova that are in their possession or control and are intended for directed donation are segregated from sperm and ova that are not intended for directed donation.

After the release of directed donations from quarantine, an establishment or a health professional must ensure that the sperm or ova intended for directed donation is kept segregated from sperm or ova not intended for directed donation throughout the distribution chain. The segregated storage for the directed sperm or ova donations is meant to prevent the risk of contamination and cross-contamination. Segregated storage of sperm or ova may be accomplished in a variety of ways, including storing sperm or ova in a physically separate area designated for such use or through the use of a validated electronic segregation system (e.g., a validated computer system and barcode labeled sperm/ova containers).

Communication of Risk

Before distributing or making use

40 A health professional must meet the following requirements, in the context of directed donation, before making use of sperm or ova or distributing sperm to a recipient for their personal use:

(a) create a document that states that, based on the summary document and any risk mitigating measures with respect to that sperm or those ova, in their medical opinion, the use of the sperm or those ova would not pose a serious risk to human health and safety; and

(b) create a document that states that the health professional has informed the recipient of the risks that the use of the sperm or ova could pose to human health and safety and that the health professional has obtained written consent from the recipient.

Prior to making use of a directed donation of sperm or ova or distributing it to a recipient for their personal use, the health professional must document that:

- based on the information contained in the summary document and any risk mitigation measures taken (e.g., sperm washing, anti-retroviral drugs to mitigate the risk of HIV transmission) with respect to the sperm or ova in question, in their medical opinion the use of the donation would not pose a serious risk to human health and safety of the recipient and the individual born of that donation; and
- they have informed the recipient of the risks that the use of the directed sperm or ova donation could pose, such as instances where the effectiveness of a risk mitigation measure may be very high but not absolute, and that they have obtained written consent from the recipient to make use of the sperm or ova.

Quality Management

Risk reduction

41 An establishment that conducts an activity must do so in such a way as to reduce the risks to human health and safety and the safety of sperm or ova by having appropriate quality management measures, including the taking of measures

(a) to prevent contamination or cross-contamination;

(b) to prevent the transmission of an infectious disease; and

(c) to maintain the quality of the sperm or ova.

Quality management is a wide ranging concept. Establishments must have appropriate quality management measures in place to ensure that they conduct their activities in a way that reduces the risks to human health and safety and the safety of sperm and ova. Establishments must ensure that appropriate quality management measures are in place, including measures to:

- prevent contamination or cross-contamination;
- prevent the transmission of an infectious disease; and
- maintain the quality of the sperm or ova.

Quality Management System

Organizational structure

42 An establishment must have an organizational structure that sets out the responsibility of management for all activities that it conducts and all measures that it takes in order to meet the requirements related to quality management.

Components of system

43 An establishment must, with respect to the activities that it conducts and the measures that it takes in order to meet the requirements related to quality management, establish and maintain a quality management system that includes the following components and must name an individual to be responsible for that system:

(a) standard operating procedures;

(b) a process control program that includes a system for verifying and validating any change to a process;

(c) a system that allows for process improvement and that includes complaint monitoring and the implementation of corrective and preventative actions including recalls; and

(d) a document control and records management system.

Establishments must have a comprehensive quality management system in relation to the processing, distributing or importing activities they conduct. This includes establishments that are conducting processing activities on behalf of a primary establishment. For example, establishments that are conducting donor testing on behalf of a primary establishment must have a quality management system in relation to donor testing.

To ensure compliance, the quality management system of a primary establishment should include oversight of all other establishments that conduct regulated activities on their behalf to ensure they are meeting the requirements of the Safety Regulations.

The quality management system is an integrated system that is aimed at reducing the risks to human health and safety or the safety of sperm and ova. The quality management system must be defined, documented, implemented and maintained by the establishment. For example, a way to define and document the system is to have a quality manual or equivalent documentation that contains a description of the system, including the management responsibilities.

The quality management system must include:

- standard operating procedures for all the activities the establishment conducts;
- a process control program that includes a system to ensure that any changes made to a process are verified and validated;
- a system that allows for process improvement that includes complaint monitoring and elements that enable the prevention, detection, and correction of deficiencies that may compromise human health and safety or the safety of sperm and ova, including recalls; and

- a document control and records management system to ensure that written policies, processes and procedures that cover the regulated activities are available and communicated to all relevant personnel.

The establishment must appoint an individual responsible for the quality management system and ensure that quality objectives are met. The individual responsible for the quality management system may delegate duties to qualified personnel in accordance with section 53 of the Safety Regulations, but remains accountable for those delegated duties and responsibilities.

Standard operating procedures

Establishments must have standard operating procedures for all of the regulated activities they conduct under the Safety Regulations. Standard operating procedures are an essential element to quality management that is composed of instructions that set out the processes for an establishment to follow in conducting its activities. Standard operating procedures provide personnel with instructions or directions, so that activities are performed and documented consistently and in compliance with the regulatory requirements.

An establishment must develop and maintain written standard operating procedures describing the significant steps for each regulated activity that it conducts. For example, an establishment must have standard operating procedures in place to outline the process to manage equipment, supplies, and/or services used in any regulated activity under the Safety Regulations.

Process Control Program

Establishments must have a process control program that covers their regulated activities and must ensure that all activities are conducted under controlled and defined conditions, according to written procedures prepared by qualified personnel. A process control program must demonstrate that processes and activities are capable of achieving planned results and predetermined specifications with a high degree of assurance (e.g., testing).

As part of the process control program, a change control system must be established and maintained to identify, document, review, approve and control all processes. Any changes to the processes, supplies, equipment and facilities that may impact human health and safety or the safety of sperm and ova must be properly documented, validated, thoroughly evaluated, approved, and managed.

A validation plan could include testing methods, equipment to be used, standard operating procedures, acceptance criteria, and supporting documentation. Alternatively, establishments can use established procedures or processes that are in standards developed by recognized professional organizations, based on established practice, or that are supported by information available in scientific literature.

The need for revalidation must be assessed when changes are made to a validated process. Depending on the nature and extent of the changes, a revalidation may be necessary. For example, changes that could affect the original validation, process characteristics, and/or human health and safety or the safety of sperm and ova will require revalidation.

Documentation must be maintained for both the initial validation as well as any revalidation that is completed.

System for Process Improvement

Establishments must have a system for process improvement that includes complaint monitoring and the implementation of corrective and preventative actions. Corrective actions focus on eliminating causes of existing nonconformities in order to prevent recurrence whereas preventative actions focus on eliminating the potential causes of nonconformities in order to prevent occurrence.

Establishments must have policies, processes, and operating procedures for the handling of complaints. All complaints must be reviewed, assessed by the appropriate department, documented, and investigated in accordance with the establishment's operating procedures, including identifying and implementing corrective and preventative actions, as applicable. This could include recalls. All decisions and follow-up actions, taken as a result of a complaint investigation, must be documented.

As part of the establishment's system for process improvement, if preventative action is required, it must be implemented and monitored to reduce the likelihood of recurrence and to take advantage of the opportunity for improvement. Once corrective and/or preventative actions are implemented, the effectiveness of these actions must be monitored and evaluated.

Recalls are an effective method of removing non-compliant sperm or ova that may represent a risk to human health and safety. Establishments must have a system to effectively conduct prompt recalls of sperm or ova. This system, at a minimum, must include the following elements:

- operating procedures to define steps for an effective removal of any non-conformant sperm or ova from distribution or use, including identifying the roles and responsibilities within the establishment for the following activities:
    - (i) obtaining information on the implicated sperm or ova;
    - (ii) initiating the recall; and
    - (iii) reviewing distribution records necessary for recall coordination;
- distribution records to allow for the prompt identification and location of the implicated sperm or ova; and
- effectiveness checks to verify that all required establishments or health professionals have received the notification about the recall and have taken appropriate action. Methods for contacting them can include personal visits or telephone calls, followed by written confirmation.

Document Control and Records Management System

Establishments must define, document, and maintain standard operating procedures to control all quality documents and information relevant to the activities they conduct with respect to the Safety Regulations.

The distribution and maintenance of operating procedures and other quality documents e.g., policies, forms, etc., must be controlled, such that only the current versions are available for use. Previous and obsolete versions of quality documents must be removed, archived, and replaced with the current approved version. A copy of every version of the operating procedures that was implemented must be retained in accordance with subsection 78(3) of the Safety Regulations.

Standard Operating Procedures

44 (1) The standard operating procedures must meet the following requirements:

(a) they are in a standardized format;

(b) they are approved by the individual responsible for the quality management system;

(c) they are easily accessible at each location where the relevant activities are conducted;

(d) all changes to them are approved by the individual responsible for the quality management system before they are implemented; and

(e) they are kept up-to-date.

Review of procedures

(2) An establishment must review its standard operating procedures every two years or after either of the following events and every two years after that event:

(a) following any amendment to these Regulations; and

(b) when a deficiency in the standard operating procedures is revealed as a result of an investigation into an error, accident or adverse reaction or as a result of an internal audit.

Internal Audit

45 An establishment must establish and maintain an internal audit system for quality management purposes and must carry out an internal audit every two years of the activities that it conducts to ensure that those activities comply with these Regulations and with its standard operating procedures, to be carried out by a person who is qualified to do so and who does not have direct responsibility for the activities being audited.

Standard Operating Procedures

Establishments must have standard operating procedures for all of the regulated activities they conduct under the Safety Regulations.

An acceptable format for an operating procedure includes the following elements:

- the title and purpose of the procedure;
- a unique number or code identifying the document and indicating the version;
- the date of implementation;
- the signature of the authorizing person and the date of authorization;
- appropriate page numbers;
- clear instructions to be followed that correspond to the tasks required to perform the activity and may include worksheets, forms or electronic fields to be completed;
- the responsible department for performing the operating procedure; and,
- references to publications cited, if applicable.

Standard operating procedures must be kept up-to-date. The procedures must be reviewed every two years, or after any amendments to the Safety Regulations or when a deficiency is identified in a standard operating procedure as a result of a routine inspection or as a result of an investigation into an error, accident, adverse reaction, or an internal audit.

All personnel responsible for carrying out a procedure must be trained prior to performing any tasks associated with a new or revised operating procedure. Operating procedures must be accessible at each location, where the individuals are conducting the activities.

In an urgent situation, a deviation from a current operating procedure is allowed if permitted by a senior executive officer, or designate, and the deviation is documented, signed, and dated. The reason for the deviation from the procedure must also be documented.

As set out in paragraph 43(d), the distribution and maintenance of operating procedures and other quality documents e.g., policies, forms, etc., must be controlled, such that only the current versions are available for use. Previous and obsolete versions of quality documents must be removed, archived, and replaced with the current approved version. A copy of every version of the operating procedures that was implemented must be retained in accordance with subsection 78(3) of the Safety Regulations.

Internal Audits

Establishments must perform an internal audit every two years on all regulated activities they conduct to verify those activities comply with the Safety Regulations and the establishment's standard operating procedures. The internal audit must include an assessment of all regulated activities to ensure that the activities are conducted:

- consistently, and in a manner that achieves planned results and predetermined specifications with a high degree of assurance;
- in compliance with the requirements of the Safety Regulations; and
- in accordance with the establishment's standard operating procedures.

The internal audit must be conducted in accordance with established policies, processes, and standard operating procedures. Audits can be performed by trained personnel within the establishment who are not directly responsible for the activities being audited or by an external auditor (qualified third party) who is performing an audit on behalf of the establishment and is knowledgeable in the subject matter being audited.

A primary establishment must ensure that they audit the activities being conducted by another establishment on their behalf to ensure that they are meeting the requirements of the Safety Regulations. Some ways a primary establishment can ensure that an establishment that is conducting activities on their behalf is in compliance with the Safety Regulations is to:

- conduct an audit of the activities themselves (e.g., onsite at the establishment, paper assessment, review standard operating procedures);
- review and assess results of audits conducted by the establishment; or
- review and assess audit reports from a third-party that are provided by that other establishment itself.

It is important to note that establishments that perform activities on behalf of the primary establishment are also subject to the requirement to conduct an internal audit. Therefore, if a laboratory is conducting donor testing for a primary establishment, then the laboratory must perform an audit to ensure its regulated activities are meeting the Safety Regulations and its operating procedures. Acceptable ways an establishment can audit its activities include:

- conduct the audit themselves;
- have the primary establishment conduct the audit, and review the primary establishment's audit report; or
- have a third party conduct an audit and review that audit report.

Primary establishments should have agreements in place with establishments conducting activities on their behalf and should include the requirement for an establishment to update the primary establishment on any significant changes or compliance issues identified by the establishment, or by other means (e.g., other regulatory bodies).

The findings from audits and follow up actions required must be documented and reviewed by management as well as the individual responsible for the quality management system. Preventative and corrective actions must be implemented in a timely manner. Establishments must retain records of audits, including the preventative and corrective

actions in accordance with the requirements for records set out in subsection 77(1) of the Safety Regulations.

Tracing and Identifying

Tracing system

46 An establishment must establish and maintain a system for tracing sperm and ova.

Donor identification code

47 A primary establishment must ensure that a donor identification code is assigned to each donor.

Donation code

48 A primary establishment must ensure that a donation code is assigned to each donation of sperm and ova that indicates the date of the donation and links the donation to the donor.

Establishments are required to have a system in place for tracing sperm and ova throughout the distribution chain that enables the tracking of sperm and ova from:

- the donor to the consignee or recipient; and
- the recipient to the consignee or donor.

As part of this system, establishments must keep accurate records, using the unique identification codes of the donor and specific donation in order to ensure that all sperm or ova can be traced to support any recalls, errors, accidents, adverse reactions, and investigations.

The ability to effectively trace sperm and ova throughout the distribution chain is key to protecting the health and safety of Canadians. As they are at the head of the distribution chain, the primary establishment has the responsibility for ensuring that the foundational elements of an effective tracing scheme are established.

The primary establishment is responsible for assigning a unique donor identification code to each donor, which will allow for the donor to be identified no matter where an individual donation may be in the distribution chain.

The primary establishment is also responsible for assigning a donation code to each donation. The donation code must make a link between the donor identification code and the date of donation. This allows for more targeted tracing, if the situation requires it (e.g., in the event of an adverse reaction).

Labelling and Storing

Establishment that labels

49 An establishment that labels an immediate container of sperm or ova must

(a) establish and maintain a labelling control system; and

(b) ensure that the donor identification code and the donation code appear on the label in a clear and indelible manner.

Label verification - primary establishment

50 A primary establishment must ensure that the immediate container of sperm or ova is already labelled in accordance with the requirements of paragraph 49(b) and that it is accompanied by documentation that contains the following documents and information in English or French before distributing or making use of the sperm or ova:

(a) the donor identification code and the donation code;

(b) the type of content, whether sperm or ova, unless this information already appears on the label of the immediate container;

(c) in the case of exceptional access, a statement that indicates that the donation is for exceptional access only;

(d) in the case of a directed donation, a statement that indicates that the donation is for directed donation only;

(e) the name of the primary establishment, its registration number and contact information;

(f) a copy of any summary document; and

(g) instructions for the handling and storage of the sperm or ova.

Another key component of an effective tracing scheme is labelling. The regulatory requirements for labeling were designed to reflect that it may not always be the primary establishment that labels the immediate container of sperm or ova. For example, an ova bank that is a primary establishment may use a separate medical facility to retrieve the ova from the donor. In this case, that facility would be an establishment conducing activities on behalf of the primary establishment. It may be the case that after obtaining, preparing, and preserving the ova, the facility also labels the immediate container prior to shipping the container to the primary establishment for long-term storage (prior to its distribution or use).

This section requires any establishment that labels to ensure that the donor identification code and the donation code appear on the label in a clear and indelible manner. While the Safety Regulations are not prescriptive about the mechanism by which this occurs, where the establishment that labels is not the primary establishment, some communication

between the two parties will be required to enable the establishment to fulfill its obligations, given that it is the responsibility of the primary establishment to assign the donor identification and donation codes.

This section also requires the primary establishment to ensure that the immediate container of sperm and ova are properly labeled and are accompanied by the required documentation prior to distributing or making use of the sperm and ova.

Containers

51 (1) An establishment that distributes, imports or makes use of sperm or ova must

(a) verify the integrity of the immediate containers and the shipping containers as well as the accuracy and legibility of their labels; and

(b) ensure that the documentation that accompanies the immediate containers contains the following information in English or French:

(i) the donor identification code and the donation code,

(ii) the type of content, whether sperm or ova, unless this information already appears on the label of the immediate container,

(iii) in the case of exceptional access, a statement that indicates that the donation is for exceptional access only,

(iv) in the case of a directed donation, a statement that indicates that the donation is for directed donation only,

(v) the name of the primary establishment, its registration number and contact information ,

(vi) a copy of any summary document, and

(vii) instructions for the handling and storage of the sperm or ova.

The immediate container is the innermost package that contains the sperm or ova, and the shipping container is the outermost package in which the sperm or ova is delivered or transported.

An establishment that distributes, imports, or makes use of sperm or ova must examine the immediate container and shipping container for damage, and any evidence of contamination or tampering or mislabeling. When any defect, improper labelling or abnormal appearance is observed, the sperm or ova must be immediately quarantined until an investigation is completed under the error and accident requirements, as set out in section 60 to 68 of the Safety Regulations.

An establishment that distributes, imports or makes use of sperm or ova must ensure that the appropriate documentation accompanies the sperm or ova, and includes all of the information set out in paragraph 51 (1) (b) of the Safety Regulations.

An establishment must have procedures in place to ensure the integrity of the sperm or ova it receives has been maintained. This process must be defined in the establishment's standard operating procedures and may include the following documented evidence:

- that the sperm and ova was maintained under appropriate conditions;
- that the integrity of the packaging material and the labels were not compromised;
- that there was no evidence of contamination or tampering; and
- that the unopened sperm and ova package was free of damage.

Shipping

(2) An establishment that ships sperm or ova must

(a) establish and maintain shipping standards

(b) verify the integrity of the immediate containers and the shipping containers before shipping as well as the accuracy and legibility of their labels; and

(c) use shipping containers that are capable of resisting damage, maintaining the safety of the sperm or ova and maintaining adequate environmental conditions during shipping.

Establishments that ship sperm and ova must establish and maintain shipping standards, including the appropriate environmental conditions for shipping sperm and ova that must be defined in a standard operating procedure. They also must ensure the labels are legible and accurate prior to shipping. When specified, controls for temperature, light, etc. must be in place. Documentation that the sperm and ova were maintained under the appropriate environmental conditions must be kept and available upon request.

An establishment that ships sperm or ova must ensure they use shipping containers that are appropriate for both maintaining environmental conditions and resisting damage during shipping. The shipping standards need to ensure that the manner in which sperm or ova is shipped will:

- maintain the appropriate environmental conditions during transportation in order to protect the safety of the sperm or ova. The appropriate environmental conditions are to be consistent with the instructions that accompany the sperm or ova; and
- protect the sperm or ova from any tampering, damage, or contamination that could affect the safety of the sperm or ova.

An establishment must have documented evidence that the packaging materials used are capable of maintaining the integrity of the sperm and ova. The documented evidence must be available upon request. Evidence could consist of specification sheets, certificates of analysis (COAs), or manufacturer's package inserts describing the packaging material.

The packaging materials must also be compatible with the sperm and ova in order to prevent any interactions which may cause the package to degrade or chemicals from the packaging to be absorbed by the sperm and ova. Only packaging materials assessed and released by the person responsible for the quality management system, or by a designated alternate, must be used in the packaging of sperm and ova. Any changes in the packaging materials must be approved prior to use. Materials that are outdated or rejected should be adequately segregated until their disposal, which should be recorded. All packaging materials must be visually examined for damage before being used.

Storage

52 An establishment that stores sperm or ova must establish and maintain standards for acceptable storage temperature ranges and ensure that sperm and ova are stored at a temperature within that range.

Sperm and ova must be stored according to the instructions and documentation that accompany the sperm and ova. Establishments that are storing sperm or ova must ensure that sperm or ova are stored at appropriate environmental conditions that maintain the appropriate temperature range.

Documentation showing that the sperm or ova were maintained under the appropriate environmental conditions must be retained.

Procedures describing the actions to be taken in the event of deviations from established criteria must be written, and such events must be appropriately documented and investigated.

Personnel, Facilities, Equipment and Supplies

Qualified personnel

53 In order to conduct its activities, an establishment must

- **(a)** have sufficient personnel who are qualified by their education, training or experience to perform their respective tasks; and
- **(b)** establish and maintain a program for the initial and ongoing training of personnel and for evaluating their competency.

All personnel performing, or responsible for regulated activities, must be qualified in accordance with the establishment’s policies, and have the necessary combination of

education training, and/or experience. Personnel should be aware of the Safety Regulations and their responsibilities to comply with the applicable requirements.

An establishment must prepare and maintain a current organizational chart with clear delineation of lines of responsibility as set out in section 42 of the Safety Regulations. Establishments will need to ensure that staff meets the qualifications necessary to conduct their respective tasks.

A sufficient number of personnel must be available to perform the tasks required. Lack of sufficient personnel or underqualified staff may increase the risk of errors and accidents.

Establishments must have a documented training program as well as a formal competency-evaluation program. Personnel must receive initial and ongoing training appropriate to their job responsibilities related to activities regulated under the Safety Regulations, as defined in their standard operating procedures.

The training must:

- include initial and ongoing training, including remedial and retraining as appropriate for their duties;
- include training for all activities carried out with respect to sperm and ova; and
- be provided by qualified personnel who have knowledge with regard to the functions involved.

Training must be provided prior to the initiation of job duties or performing the tasks outlined in a new procedure or any revision of an existing procedure. Training must be documented and must include information necessary to verify that individuals have been trained prior to the conduct of the activities. For example, training records will need to include details such as name of the personnel, the date of the training and name of the trainer.

An establishment must have and maintain a program for the evaluation of the competency of personnel. The elements of a competency program may include, but are not limited to:

- direct observation of performance;
- monitoring or recording;
- written tests;
- assessment of knowledge of operating procedures and theory; and
- for personnel who normally perform the routine testing, assessment of performance through proficiency tests.

Records of the qualifications, training, and continuing competency of individuals must be maintained as set out in subsection 78(2) of the Safety Regulations.

Facilities

54 The facilities in which an establishment conducts its activities must be constructed and maintained in a manner that allows for the following:

(a) the carrying out of its activities;

(b) the cleaning, maintaining and disinfecting of the facilities in a way that prevents contamination and cross-contamination; and

(c) controlled access to all areas where its activities are conducted.

Environmental control system

55 An establishment must

(a) establish and maintain a system for controlling and monitoring appropriate environmental conditions for all facilities and areas in which activities are conducted; and

(b) periodically inspect those systems in order to verify that the systems function properly and must take any necessary corrective action.

Program – procurement and maintenance

56 An establishment must establish and maintain a program for procuring and maintaining all critical equipment, supplies and services.

Facilities

Facilities must be located, designed, constructed, and adapted to suit the activities to be conducted. Their design and furnishing must minimize the risks of errors and accidents and the potential for contamination or cross-contamination. Facilities must allow for effective decontamination and to prevent cross-contamination during the movement of personnel and materials between different areas.

Facilities must control access to all areas where its activities are conducted, as appropriate, and where products and samples are stored. Establishments must ensure the products that are used for the cleaning, maintaining and disinfection are appropriate to prevent the contamination and cross-contamination in all areas where activities are conducted.

Environmental Control System

Establishments must have a system for controlling and monitoring appropriate environmental conditions and must monitor the system to ensure the established environmental parameters are maintained. Establishments must have environmental monitoring procedures, which should include acceptable limits for all environmental parameters. When values are found to be outside of the acceptable limits, then corrective actions must be taken and may require relocation of the sperm or ova or temporarily discontinue those specified activities.

All sperm and ova must be stored under defined and controlled environmental conditions. The appropriate environmental conditions for storing sperm and ova must be defined in standard operating procedures. Documentation that the sperm and ova were maintained under the appropriate environmental conditions must be kept and available upon request.

Environmental parameters for storage, such as temperature and humidity, must be controlled and monitored using calibrated monitoring devices. The documented evidence of the monitoring of these parameters must be maintained. Temperature monitoring probes or devices should be located at points that represent extreme temperature areas, as determined by a temperature mapping study, if applicable. Where necessary, the building should be equipped with an appropriate HVAC (heating, ventilation, and air conditioning) system to maintain temperature and air flow control.

If the storage area has an environmental alarm system with audible signals, alarm activation points should be set at temperatures that allow time for appropriate corrective actions to be taken before the sperm and ova reach unacceptable temperatures. The alarm warning should signal in a location that is continually monitored or staffed so that corrective action can be taken in a timely manner.

There must be written procedures describing the actions to be taken in the event of deviations from established storage criteria. Such an event must be appropriately investigated and documented.

Access to storage areas must be restricted to designated personnel. Where physical quarantine areas are used, they must be marked appropriately, with access restricted to designated personnel. Additionally, where electronic quarantine is used, electronic access must be restricted to designated personnel.

Program – Procurement and Maintenance

Establishments must have a program to identify, document, and track all critical equipment, supplies, and services. The term critical applies to equipment, supplies and services used in any activities that are regulated under the Safety Regulations. Critical, in respect of equipment, supplies, and services means that the equipment, supply, or service could, if it does not meet its specifications, compromise human health and safety or the safety of sperm or ova. Examples of critical equipment, supplies and services include, but are not limited to, those that are used in the collection of sperm and ova, the testing of sperm and ova, and storage. Within this system, each piece of equipment must have a unique identifier. A barcode system is one example of this type of system.

Written specifications must be available for all critical equipment, supplies, and services. Establishments must have defined processes and ensure that in the event of any changes to regulatory requirements or technology, the specifications continue to meet the applicable requirements of the Safety Regulations.

In cases where the specifications are not met, an establishment must have a system in place to ensure prompt effective remedial action, which could include the timely reporting of complaints, deviations or product defects to their supplier or service provider.

Critical equipment must consistently meet its specifications in order to ensure the safety of sperm and ova. Establishments must have a preventive maintenance program to keep the function of all critical equipment within required performance specifications.

The preventive maintenance program must:

- have defined processes that includes a predetermined schedule of maintenance to verify that the performance and calibration of each piece of equipment meets the specifications identified in the manufacturer's manual and/or the specifications required by the establishment's quality system.
- include the methodology used, frequency of calibration, and action to be taken when equipment performance deviates from defined limits. This requirement applies to all equipment, instruments and measuring devices critical to ensuring that sperm and ova conform to the requirements in the Safety Regulations.

Preventive maintenance must be conducted by qualified personnel. The preventive maintenance schedule must be maintained and all records and reports of maintenance services, including the actual test results indicating that equipment is qualified and calibrated according to the manufacturer's instructions must be retained for 10 years as per subsection 78(1). Sections 57 and 58 of the Safety Regulations describe the requirements for the equipment and supplies.

Equipment — general requirements

57 An establishment must ensure that the critical equipment that it uses is cleaned and maintained and that, whenever applicable, it is

(a) qualified for its intended purpose;

(b) calibrated;

(c) disinfected or sterilized before each use; and

(d) requalified or recalibrated, as appropriate, after any repair or change is made to it that results in a change to its specifications.

All critical equipment must be cleaned and maintained in accordance with standard operating procedures and schedules based on the manufacturer's instructions and qualification results and with the purpose to prevent contamination or cross-contamination. The equipment must be located in areas that enable the required cleaning and maintenance to be conducted.

The cleaning, disinfection, and/or sterilization procedure must be done before each use to reduce the risk of contamination and cross-contamination.

Equipment must be qualified and calibrated according to the manufacturer's instructions, to ensure that it consistently operates within established specifications.

Storage equipment should have an automated alarm system with audible signals for monitoring the required environmental conditions. If the storage area has an alarm system with audible signals, alarm activations points should be set at temperatures that allow time for appropriate corrective actions before the sperm or ova reach unacceptable temperatures. The alarm warning should signal in a location that is continually monitored or staffed so that corrective action can be taken immediately.

If equipment has been repaired, moved, or modified, then re-calibration and/or revalidation must be conducted in accordance with the establishment's standard operating procedures and/or the manufacturer's manual before further use. In addition, where appropriate, measures should be taken to prevent unintended adjustments on the equipment or instrument that may impact its calibration settings.

All qualification, calibration, maintenance, and repair activities, including actual results are to be documented and retained by the establishment as outlined in sections 77 and 78 of the Safety Regulations.

If an establishment uses electronic equipment for regulated activities (e.g., a computer system), it must be validated. There must be processes and procedures in place to support the maintenance, security and integrity of computer systems and their data. Controls must be in place to limit access to the computer system data to ensure unauthorized changes are not made to software or data.

An establishment's program for the validation of computer systems should have a system acceptance test to address the following points:

(a) system functionality;

(b) system performance;

(c) critical parameters; and

(d) operating procedures.

The tests must ensure that the computer operates as indicated and meets the user requirements.

Data of a critical computer system must be backed up periodically and securely stored for data recovery. Computer validation records must be maintained and used as a reference for any system updates, changes and data recovery in case of system failures. Evidence must be presented that the equipment is performing to its specifications prior to the return to its regular use.

Any modifications, repairs, and system updates to critical equipment must be assessed to re-validate the equipment.

Supplies

58 An establishment must ensure that the critical supplies that it uses are qualified or validated, as applicable, for their intended use and that they are stored under appropriate environmental conditions.

Critical supplies must be qualified or validated, as applicable, prior to being made available for use in conducting an activity. Making supplies available to be used must be based upon established specifications and may include visual examination, lot specific release, and review of certificates of analysis. Only supplies that meet the documented requirements must be used.

The conditions of use and storage of each supply must meet the conditions specified by the manufacturer. The expiry dates of supplies and ongoing storage conditions must be strictly observed. Any critical supplies not meeting the required specifications must not be used, or made available for use, in regulated activities.

Errors and Accidents

The regulatory requirements for errors and accidents, including investigations, reporting, and record keeping, apply to all establishments and health professionals regulated under the Safety Regulations. The requirements with respect to the handling of errors and accidents are set out in section 59 to 68 of the Safety Regulations.

Under the Safety Regulations, an error is a deviation from the standard operating procedures or applicable laws that could compromise human health and safety or the safety of sperm or ova. An accident is an unexpected event that is not attributed to a deviation from the standard operating procedures or applicable laws, that could compromise human health and safety or the safety of sperm or ova.

Notifications are essential to the error and accident requirements. Establishments and health professionals may suspect that an error or accident occurred during an activity that they conducted, or during an activity conducted by another establishment, or health professional, and therefore, it is critical that all involved establishments and health professionals communicate and follow the applicable requirements (e.g., investigation and reporting) to ensure that all affected parties are aware of the error or accident and any results of investigation.

All establishments must have standard operating procedures in place to ensure that errors and accidents are addressed and handled in accordance with the requirements set out in section 59 to 68 of the Safety Regulations.

The Safety Regulations are not meant to regulate or monitor the practice of medicine. Any issues identified that are not within the scope of federal jurisdiction will be referred to the appropriate regulatory authority.

For some examples of errors or accidents, please see the scenarios listed in the guidance provided under sections 67 and 68.

System – investigation by establishment

59 An establishment must establish and maintain a system that allows for the identification, investigation and reporting of errors and accidents.

Establishments must have defined processes and standard operating procedures to identify, gather information and address any errors and accidents that occur. The standard operating procedures must include the steps to conduct an investigation and the implementation of corrective actions, as appropriate.

In the course of an investigation, non-conformances may be identified and corrective actions required. The type and extent of corrective actions is dependent upon the severity and nature of the non-conformance.

For example, recalls are an effective method of removing non-compliant sperm or ova that may represent a risk to human health and safety. As outlined in paragraph 43(c) of the Safety Regulations, establishments must have a system to effectively conduct prompt recalls of sperm or ova.

The standard operating procedures should also outline the communication methods (e.g., fax, email) to be used to notify establishments or health professionals in the event of an error or accident. The standard operating procedures must also include the reporting requirements for errors and accidents to Health Canada, as set out in sections 67 and 68 of the Safety Regulations.

Establishments must document all recalls and retain the documentation as per the requirements for records set out in section 77 to 85 of the Safety Regulations.

Error or accident by another establishment

60 (1) An establishment and a health professional that have reasonable grounds to believe that an error or accident by another establishment has occurred during the processing, distributing or importing of that sperm or those ova must immediately

(a) determine the donor identification codes and donation codes of the implicated sperm or ova;

(b) quarantine any implicated sperm or ova that are in their possession or control;

(c) notify the following:

(i) the establishment from which they received the implicated sperm or ova, and

(ii) in the case of an establishment, every establishment, health professional or recipient to which it distributed the implicated sperm or ova; and

(d) in the case of a primary establishment that has reasonable grounds to believe that the error or accident occurred during the processing of sperm and ova conducted on its behalf, initiate an investigation into the suspected error or accident.

Contents of notice

(2) The notice must include the following information:

(a) the donor identification code and the donation code associated with the implicated sperm or ova; and

(b) the reason for the belief that an error or accident has occurred.

Action upon notice

(3) An establishment or health professional that is notified under subparagraph (1)(c)(ii) or under this subsection must immediately

(a) quarantine all implicated sperm or ova in its possession or control; and

(b) in the case of an establishment, notify to the same effect every establishment, health professional and recipient to which it distributed the implicated sperm or ova.

Written notice

(4) If an establishment or a health professional gives a notice verbally under this section, that notice must be confirmed in writing within 24 hours after it is given.

Establishment or health professional — own error or accident

61 (1) An establishment and a health professional that have reasonable grounds to believe that an error or accident has occurred during the processing, distributing or importing of that sperm or those ova that they conducted must immediately

(a) determine the donor identification codes and the donation codes of the implicated sperm or ova;

(b) quarantine any implicated sperm or ova that are in their possession and control; and

(c) subject to subsection (2), initiate an investigation into the suspected error or accident.

Exception

(2) An establishment that conducts a processing activity on behalf of a primary establishment that has or previously had in its possession or control any implicated sperm or ova can request that the primary establishment conduct the investigation by providing a notice to them that contains the following information:

(a) the donor identification codes and donation codes of all implicated sperm or ova; and

(b) the reason for the belief that an error or accident has occurred.

Notice of investigation

62 (1) An establishment that initiates an investigation must immediately notify either the primary establishment that has in its possession or control any implicated sperm or ova and on whose behalf the processing activity was conducted or every establishment, health professional or recipient to which it distributed implicated sperm or ova and must include the following information in the notice:

(a) the donor identification codes and donation codes of all implicated sperm or ova; and

(b) a description of the suspected error or accident and an explanation of how human health and safety or the safety of the sperm or ova might have been compromised.

Action upon notice

(2) An establishment or health professional that is notified under subsection (1) or under this subsection must immediately

(a) quarantine all implicated sperm or ova in its possession or control; and

(b) in the case of an establishment, notify to the same effect every establishment, health professional or recipient to which it distributed implicated sperm or ova.

Written notice

(3) If an establishment or a health professional gives a notice verbally under this section, the notice must be confirmed in writing within 24 hours after it is given.

An establishment and a health professional that has reasonable grounds to believe that an error or accident by another establishment has occurred during processing, distributing or importing must immediately follow the actions set out in subsection 60(1) of the Safety Regulations. The establishment and health professional must identify and quarantine any sperm or ova implicated in the error or accident and notify all relevant establishments that are set out in paragraph 60(1)(c) without delay.

In addition to meeting the requirements in paragraphs 60(1)(a)-(c), a primary establishment that has reasonable grounds to believe that an error or accident has occurred during an activity that is conducted on their behalf, must also immediately initiate an investigation into the suspected error or accident.

The notice under subsection 60(2) must include the donation code and donor identification code that is associated with the implicated sperm or ova and must include information regarding why they believe that an error or accident has occurred.

An establishment or a health professional that receives a notice under paragraph 60(1)(c) of the Safety Regulations must immediately quarantine all of the implicated sperm or ova in their possession, as per subsection 60(3). Furthermore, in the case of an establishment, they must notify every establishment, health professional or recipient to which it distributed the implicated sperm or ova. Section 61 of the Safety Regulations applies to situations where establishments (including primary establishments) and health professionals who have reasonable grounds to believe that an error or accident occurred during an activity that they conducted, or to establishments that receive a notice that an error or accident may have occurred at their establishment. Health professionals are required to follow section 61 of the Safety Regulations, when there are reasonable grounds to believe an error or accident occurred during an activity they conducted.

Upon receipt of a notice under paragraph 60(1)(c), or when an establishment or health professional has reasonable grounds to believe that an error or accident occurred during an activity they conducted, the establishment must immediately determine the donor identification and donation codes of the implicated sperm or ova and whether any other sperm or ova may be implicated in the same error or accident (e.g., other donations from the same donor). The establishment or health professional must also quarantine any implicated sperm or ova in their possession and control and initiate an investigation into the error or accident. However, in the case of an establishment conducting an activity on behalf of a primary establishment, they may request the primary establishment to conduct the investigation on their behalf as per subsection 61(2).

A primary establishment must always conduct an investigation into a suspected error or accident whether the error or accident occurred during an activity they conducted, or at an establishment conducting activities on their behalf as per paragraph 60(1)(d).

An establishment that is conducting processing activities on behalf of a primary establishment that has reasonable grounds to believe that an error or accident has occurred may elect to initiate an investigation into the suspected error or accident itself. As per subsection 62(1), establishments that initiate an investigation must notify either:

- all primary establishments on whose behalf they are conducting activities; or
- every establishment, health professional or recipient to whom they distributed the implicated sperm or ova.

Alternatively, subsection 612(2) allows establishments conducting processing activities on behalf of a primary establishment to conduct the investigation on their behalf. To make such a request, the establishment must provide a notice to the primary establishment that contains the donor identification code and donation codes of all implicated sperm or ova and the reason for the belief that an error or accident has occurred. Furthermore, upon request from the primary establishment, the establishment conducting processing activities on its behalf must provide any relevant documents or information in its possession in respect of the implicated sperm or ova.

All establishments must have standard operating procedures in place to define how errors and accidents will be handled.

In all cases, if a notice is given verbally, a written notice must follow within 24 hours of the verbal notice.

Requirement to cooperate

63 An establishment and a health professional must, on request, provide to any establishment or health professional that is conducting an investigation any relevant documents or information in its possession in respect of implicated sperm or ova.

Establishments and health professionals must cooperate with any establishment or health professional that is conducting an investigation into a suspected error or accident, and provide any relevant documents or information in its possession in respect to the implicated sperm or ova, as requested. This information includes, but is not limited to, an inventory list of implicated sperm or ova with their disposition (e.g., distributed, inseminated, etc.) and the names of the establishments, health professionals, or recipients to which the implicated sperm or ova has been distributed.

Establishments conducting activities on behalf of a primary establishment must provide the primary establishment with all relevant information or documents required, in order for the primary establishment to thoroughly investigate the error or accident.

It is critical that all involved parties communicate to ensure that the affected establishments or health professionals receive relevant information regarding the investigation.

Results of investigation

64 (1) An establishment that conducts an investigation must notify in writing either the primary establishment that has in its possession or control any implicated sperm or ova and whose behalf the processing activity was conducted or every establishment, health professional or recipient to which it distributed implicated sperm or ova of the results of the investigation and of any action that is required to be taken.

Action on receipt of notice

(2) An establishment that receives a notice under subsection (1) or a copy of such a notice under this subsection must send a copy of the notice to every establishment, health professional or recipient to which it distributed implicated sperm or ova.

The establishment conducting the investigation must have mechanisms in place to communicate with all establishments, health professionals, or recipients that may have had sperm or ova in their possession, in a timely and accurate manner.

An establishment that conducted an investigation into a suspected error or accident must notify, in writing, all of the establishments, health professionals or recipients that were previously notified under subsection 62(1) of the Safety Regulations, of the results of the investigation. Where it has been determined the safety of sperm or ova has not been compromised, the establishment or health professional may make recommendations with regards to the disposition of the implicated sperm or ova.

Where the results of the investigation show that the sperm or ova may be compromised, the implicated sperm or ova must remain in quarantine, and must not be distributed or used, unless the establishment or health professional responsible for their quarantine receives a request for exceptional access from a health professional and one of the conditions set out in subsection 66(1) of the Safety Regulations has been met.

Establishments that distributed implicated sperm or ova, subject to an investigation, to a recipient for their own personal use, must notify them of the results of the investigation. Patient notification by a health professional is not within the scope of the Safety Regulations.

Release from quarantine

65 An establishment or health professional that quarantines implicated sperm or ova must continue to do so until the results of the investigation reveal that the safety of the implicated sperm or ova is not compromised.

Implicated sperm or ova that are subject to an error or accident investigation must remain in quarantine until the investigation results determine that the safety of the sperm or ova has not been compromised.

Release from quarantine — exceptional access

66 (1) Despite section 65, an establishment and a health professional may release sperm or ova from quarantine if the establishment or health professional that is responsible for their quarantine receives a request from a health professional for exceptional access to that sperm or those ova and if one of the following conditions is met:

(a) the recipient has previously been exposed to sperm or ova from that donor and the risk profile of the requested sperm or ova, based on the results of any part of the donor suitability assessment is at least equivalent to the risk profile of the sperm or ova to which the recipient has previously been exposed, based on the results of any part of the donor suitability assessment that was conducted at that time; or

(b) sperm or ova from that donor have previously been used to create a child for an individual or a couple and the requested sperm or ova are to be used for the purpose of creating another child for that individual or couple.

Summary document

(2) Before the sperm or ova are released from quarantine, the establishment or health professional that is responsible for the quarantine must create a summary document that contains the following information:

(a) the age of the donor, if known;

(b) the condition that has been met;

(c) the dates and results of any donor screening, physical examination or donor testing; and

(d) a description of the suspected error or accident and an explanation of how human health and safety or the safety of the sperm or ova might have been compromised.

Storage

(3) An establishment and a health professional must ensure that sperm or ova that are in their possession or control and are intended for exceptional access are segregated from sperm and ova that are not intended for exceptional access.

Communication of risk

(4) A health professional must meet the following requirements before making use of the sperm or ova or distributing the sperm to a recipient for their personal use:

(a) create a document that states that, based on the summary document and any risk mitigating measures with respect to that sperm or those ova, in his or her medical opinion, the use of the sperm or ova would not pose a serious risk to human health and safety; and

(b) create a document that states that the health professional has informed the recipient of the risks that the use of the sperm or ova could pose to human health and safety and that the health professional has obtained written consent from the recipient.

The regulations require sperm and ova under quarantine as a result of an error or accident to remain so until the results of the investigation reveal that the safety of the sperm or ova is not compromised.

The only exception to this requirement is where the establishment or health professional responsible for the quarantine receives a request for exceptional access from a Health Professional and the conditions for exceptional access are met. For more information about exceptional access, please refer to section 66 of the Safety Regulations.

Preliminary and interim reports

67 The establishment or health professional that conducts an investigation into a suspected error or accident that could lead to an adverse reaction must send the following reports to the Minister, in the form established by the Minister, at the following times:

(a) within 72 hours after the start of the investigation, a preliminary report that includes a detailed description of the suspected error or accident and any relevant information that is available at that time; and

(b) within 15 days after the start of the investigation and every 15 days after that until the final report is made, an interim report that contains

(i) any new information with respect to the suspected error or accident,

(ii) the progress of the investigation, and

(iii) any measures taken during those 15 days to mitigate further risk.

Final report

68 An establishment or health professional that conducts an investigation into a suspected error or accident that could lead to an adverse reaction must send, within 72 hours of completing the investigation, a detailed final report to the Minister, in the form established by the Minister, that contains the following information:

(a) the results of the investigation;

(b) any corrective action taken; and

(c) details concerning the disposition of the implicated sperm or ova.

Establishments or health professionals that conduct an investigation into suspected errors or accidents that could lead to an adverse reaction (i.e., an unexpected presence of an infectious disease agent or unexpected occurrence of an infectious disease in a recipient of sperm or ova or child created from that sperm or those ova) are required to send a report to Health Canada.

If the error or accident was identified after the implicated sperm or ova was released from quarantine and made available for use or distribution and the error or accident has led to, or could lead to an adverse reaction, this would be reportable under section 67 of the Safety Regulations. However, when an error or accident has been identified before the implicated sperm or ova has been released from quarantine and made available for use or distribution, this would not be considered reportable, as the error or accident could not lead to an adverse reaction.

When a suspected error or accident could lead to an adverse reaction, an establishment or health professional must submit a preliminary report to Health Canada within 72 hours after the start of the investigation. Interim reports are to be submitted within 15 days after

the start of the investigation (and every 15 days after) until a final report is made as set out in section 68 of the Safety Regulations. The preliminary report must include:

- a detailed description of the suspected error or accident; and
- all available information regarding the suspected error or accident, such as:
    - the name of the infectious disease agent;
    - any risk assessments conducted;
    - number of implicated units of sperm or ova (including the number of units in inventory and number of units that have been distributed or used);
    - corrective actions taken to date (including any notifications sent to other establishments or health professionals); and
    - any anticipated corrective actions.

If an establishment or health professional that makes use of sperm or ova is conducting an investigation into a suspected error or accident that was identified after the sperm or ova was made available for use, and the error or accident could lead to adverse reaction, they must send Health Canada a report in accordance with section 67 of the Safety Regulations.

A primary establishment must ensure that establishments conducting activities on their behalf that are investigating an error or accident that could lead to an adverse reaction submit the required reports to Health Canada, within the timelines set out in section 67 of the Safety Regulations. A primary establishment can report on behalf of an establishment that is conducting activities for which they are responsible for (e.g., a foreign establishment that processes sperm or ova on behalf of the primary establishment).

Establishments must have clear standard operating procedures on how error or accidents will be investigated and reported, under the Safety Regulations.

Following the preliminary report, the establishment or health professionals must provide a written update on any new information about the suspected error or accident within 15 days after the start of the investigation. The report must include information on the progress made, measures taken and any new information. It may also include root cause analysis, status of implicated sperm or ova, the number of implicated establishments or health professionals contacted, and planned corrective actions, such as conducting a recall of the implicated sperm or ova.

A recall is the removal of sperm or ova from further distribution or use of distributed sperm or ova that presents risk to human health and safety or violates the AHR Act and its associated regulations. Please note that Health Canada has the authority under section 44 of the AHR Act to take or order any person to take all reasonable measures that Health Canada considers necessary to mitigate the effects of the contravention or prevent the contravention, when Health Canada has reasonable grounds to believe the AHR Act has been or is likely to be contravened. Such measures could include ordering a recall of sperm or ova.

Not all suspected error or accidents need to be reported to Health Canada (i.e., only those that could lead to an adverse reaction need to be reported), however establishments or health professionals are still required to investigate and meet the requirements set out in section 61 of the Safety Regulations for all suspected error or accidents that could compromise human health and safety or the safety of sperm and ova.

All error or accident investigations must be documented and the documentation retained even if it was not reported as required by subsection 83(1) of the Safety Regulations.

Error and Accident Scenarios

The following scenarios are for illustrative purposes only and provides further guidance on suspected error or accidents (E/A), and whether or not they would be considered an error or accident under the Safety Regulations and if so, if they would be reportable to Health Canada.

Regardless of the scenarios provided, establishments and health professionals are still expected to assess each suspected error or accident to determine if it meets the definitions under the Safety Regulations and take required action according to the requirements.

Even though some errors or accidents are not reportable to Health Canada, establishments and health professionals must take the appropriate actions under the Error and Accident sections of the Safety Regulations, such as investigation and notification. All error and accident records must be maintained as set out in subsection 83(1) of the Safety Regulations.

Please note, some error or accidents may be identified during the course of a Health Canada inspection, and establishments must still meet the applicable error or accident requirements.

Scenario #1 (reportable E/A):

An establishment that imports notices that two tanks containing available inventory malfunctioned over the weekend and as a result sperm or ova may not have been maintained at the required storage temperature. As such, the sperm or ova could result in the transmission of a bacterial infection to the recipient. Since the implicated sperm or ova were in released inventory and could lead to an adverse reaction (i.e., bacterial infection), this would be a reportable error or accident.

Scenario #2 (reportable E/A):

A recipient of a directed sperm donation presents with a bacterial infection to the primary establishment that conducted the insemination. The primary establishment reviewed its records and found that the storage equipment had not continuously maintained the required temperature. This would be considered a reportable error because it was identified after the sperm was used and led to an adverse reaction. The adverse reaction must also be reported, and actions taken in accordance with the applicable requirements for adverse reaction investigation and reporting.

Scenario #3 (not reportable E/A):

A vial of sperm was received at a health professional's office and the label on the vial was different than the supporting documentation that accompanied the vial. The physician quarantines the vial and contacts the primary establishment. This is an error and needs to be investigated by the primary establishment. If during the investigation it is determined that the vial that was sent to the health professional was otherwise processed in accordance with the Safety Regulations (i.e., the donor suitability assessment was appropriately conducted and revealed no risk of infectious disease transmission), it is not reportable because the error or accident could not lead to an adverse reaction.

**if the labelling error was in relation to sperm that was not properly labeled that was processed under the Directed Donation Process or was released under exceptional access , this could cause an adverse reaction since the sperm has not been processed in accordance with the requirements and is reportable to Health Canada.*

Scenario #4 (not reportable E/A):

A recipient has an allergic reaction to sperm and it is suspected that this is due to the fact that the sperm was not prepared (e.g., washed) in accordance with the standard operating procedures. This is an error and needs to be investigated; however, it is not reportable because the error or accident would not lead to an adverse reaction as defined in subsection 1(1) of the Safety Regulations (e.g., unexpected presence of an infectious disease agent or unexpected occurrence of an infectious disease).

**This could also be considered an accident, if the recipient was, for example, allergic to an agent used in preparing or preserving the sperm.*

Scenario #5 (not reportable E/A):

A primary establishment is made aware (after the fact) of a donor who has provided false information on their screening questionnaire regarding their genetic disease history. This is an accident and needs to be investigated; however, this is not reportable because the accident would not lead an adverse reaction, as adverse reaction is limited to the unexpected presence of an infectious disease agent or unexpected occurrence of an infectious disease.

Scenario #6 (reportable E/A):

During the primary establishment's audit of establishments conducting activities on their behalf, it was identified that the donor testing laboratory had not followed the manufacturer's instructions for infectious disease testing for the last two years. Specifically, the laboratory was not interpreting the results of infectious disease screening results in accordance with the test kit manufacturer's instructions (e.g., the results were misinterpreted as non-reactive). Some of the implicated sperm or ova were available for use in the released inventory. This is considered a reportable error as the sperm was released into inventory and the donor was reactive for an infectious disease agent and therefore could result in the transmission of an infectious disease.

Scenario #7 (reportable E/A):

During the primary establishment's audit of a foreign establishment that conducts processing activities for sperm on their behalf (including donor testing activities), it was noted that a donor had tested reactive on a screening test for Hepatitis C, but negative on confirmatory testing. The donor was accepted and his sperm was imported and made available for use in Canada. This would be considered a reportable error because the sperm had been made available and the error could lead to an adverse reaction.

Scenario #8 (reportable E/A):

A repeat sperm donor that has donated regularly over the last 2 years indicated during his last visit to the clinic that, in fact, he has been making frequent trips to Zika virus endemic areas during those 2 years. Sperm from this donor had been released. This is considered a reportable accident, because the accident was identified after the sperm was released and could lead to an adverse reaction.

Where to find the error or accident form?

The error or accident form will be available on the Health Canada website. This form is primarily designed to facilitate the submission of preliminary reports to Health Canada within 72 hours after the start of an investigation. This form should not be used for the interim or the final investigation reports, where more detailed and comprehensive information are to be reported. Although this form is recommended for preliminary reports, other formats will be accepted as long as the information under section 67 of the Safety Regulations is included. It is acknowledged that not all information may be available at the time of initial reporting and may be provided after it becomes available.

Where to submit an error or accident report?

Error or accident reports must be sent to Health Canada's Biological Product Compliance Program.

By email: hc.bpcp-pcpb.sc@canada.ca

Please contact the Biological Product Compliance Program at hc.bpcp-pcpb.sc@canada.ca should you have any questions or require assistance.

Adverse Reactions

The regulatory requirements for adverse reactions, including identification, investigation, and reporting, apply to all establishments and health professionals regulated under the Safety Regulations. The requirements with respect to the handling of adverse reactions are set out in sections 69 to 76 of the Safety Regulations.

An adverse reaction is defined in the Safety Regulations as the unexpected presence of an infectious disease agent or the unexpected occurrence of an infectious disease in a recipient of sperm or ova or an individual created from that sperm or those ova.

An establishment or health professional that has reasonable grounds to believe that an adverse reaction has occurred must, among other things, immediately quarantine any implicated sperm or ova (i.e., sperm or ova containing the same donor identification code and donation code) and notify the primary establishment responsible for processing the

implicated sperm or ova without delay. In addition, if the implicated sperm or ova were imported, the importing establishment must also be notified of the suspected adverse reaction, to ensure that any other implicated sperm or ova within their possession can be quarantined without delay.

Once notified, the primary establishment is responsible for conducting an investigation into the suspected adverse reaction, as they are best positioned to review all the information related to the processing of the implicated sperm or ova, including information used to determine donor suitability. The implicated sperm or ova must remain in quarantine until the results of the investigation reveal that its safety is not compromised, except in cases where it can be released under exceptional access, as set out in section 74 of the Safety Regulations. The primary establishment is responsible for notifying every establishment, health professional or recipient to whom it distributed the implicated sperm or ova of its investigation and the results of the investigation, and for sending a preliminary report, periodic interim reports on the status of the investigation, and a final report to Health Canada.

If the investigation reveals that an adverse reaction occurred as a result of an error or accident made by another establishment, the primary establishment must notify every establishment, health professional or recipient of the suspected error or accident as set out in the section 61 of the Safety Regulations.

System – investigation by establishment

69 An establishment must establish and maintain a system that allows for the identification, investigation and reporting of adverse reactions.

Action to be taken

70 (1) An establishment and a health professional that have reasonable grounds to believe that an adverse reaction has occurred must immediately

(a) determine the donor identification codes and donation codes of any implicated sperm or ova in their possession;

(b) quarantine any of the implicated sperm or ova in their possession and control; and

(c) notify the following:

(i) the primary establishment that processed the implicated sperm or ova, and

(ii) if the sperm or ova were imported, the establishment that imported the sperm or ova.

Contents of notice

(2) The notice must include the following information:

(a) the donor identification code and the donation code of the implicated sperm or ova;

(b) a description of the adverse reaction;

(c) the name of any suspected infectious disease or disease agent, if known; and

(d) an explanation of how the safety of the implicated sperm or ova might have been compromised, if known.

Action upon notice

(3) An establishment that is notified under subsection (1) or under this subsection must immediately

(a) quarantine any of the implicated sperm or ova that are in its possession or control; and

(b) notify to the same effect every establishment, health professional and recipient to which it distributed the implicated sperm or ova.

Written notice

(4) If an establishment or a health professional gives a notice verbally under this section, the notice must be confirmed in writing within 24 hours after it is given.

Establishments must have defined processes and standard operating procedures to identify, gather information and address adverse reactions that occur as a result of the sperm or ova. The standard operating procedures must include the steps to conduct an investigation and the actions required as set out in section 70 of the Safety Regulations. The standard operating procedures should outline the communication methods (e.g., fax, email) to be used to notify establishments in the case of an adverse reaction.

The standard operating procedures must also include the reporting requirements to Health Canada, as set out in sections 75 and 76 of the Safety Regulations.

An establishment and a health professional that has reasonable grounds to believe, that an adverse reaction has occurred in a recipient of sperm or ova or a child created from that sperm or those ova, must immediately identify and quarantine any implicated sperm or ova in their possession, and notify the primary establishment responsible for processing the implicated sperm or ova, as well as the importing establishment, if the implicated sperm or ova were imported. The notice must contain the information outlined in subsection 70(2) of the Safety Regulations, including the description of the adverse reaction, an explanation of how the safety of the implicated sperm or ova might have been compromised, as well as the donor identification code and the donation code of the implicated sperm or ova.

Based on the donor identification code and the donation code, an establishment that receives the notice of a suspected adverse reaction must immediately quarantine all of the implicated sperm or ova (e.g., any other donations from the same donor that may be at risk

of transmitting an infectious disease agent) in their possession or control and must notify every establishment, health professional or recipient to which it distributed the implicated sperm or ova.

In all cases, if a notice is given verbally, a written notice outlining the required contents set out in subsection 70(2) of the Safety Regulations must follow within 24 hours of the verbal notice.

Investigation

71 (1) On receipt of a notice, a primary establishment must immediately initiate an investigation into the adverse reaction.

Requirement to cooperate

(2) An establishment and a health professional must, on request, provide to any primary establishment that is conducting an investigation any relevant documents or information in its possession in respect of implicated sperm or ova.

Results of investigation

72 (1) A primary establishment that conducts an investigation must notify in writing every establishment, health professional or recipient to which it distributed implicated sperm or ova of the results of the investigation and of any action that is required to be taken.

Action on receipt of notice

(2) An establishment that receives a notice under subsection (1) or a copy of such notice under this subsection must send a copy of the notice to every establishment, health professional or recipient to which it distributed implicated sperm or ova.

Upon receipt of the notice, the primary establishment must immediately initiate an investigation into the adverse reaction. During an investigation, the primary establishment must determine whether any other sperm or ova are compromised and the status of the implicated sperm or ova. The primary establishment should also consider whether any additional tests may be required to determine the root cause of the adverse reaction (e.g., bacteriological testing, donor testing, etc.).

Any documentation pertaining to the investigation must be retained for a period of 10 years.

Establishments, including the ones conducting processing activities on behalf of a primary establishment, as well as health professionals, must cooperate with any primary establishment that is conducting the investigation into a suspected adverse reaction, and must provide any relevant information they may possess, as requested. This information includes, but is not limited to, an inventory list of implicated sperm or ova and their

disposition (e.g., distributed, used, etc.), and the names of the establishments, health professionals, or recipients to which the implicated sperm or ova has been distributed.

A primary establishment must notify in writing every establishment, health professional or recipient to which it distributed the implicated sperm or ova of the results of their investigation and outline any action that is required to be taken. Where the investigation determined that the safety of sperm or ova is not compromised, an establishment or health professional that had quarantined the implicated sperm or ova, may release it from quarantine.

Where the results of the investigation show that the sperm or ova may be compromised, the implicated sperm or ova must stay in quarantine and must not be distributed or used, unless the establishment or health professional that is responsible for their quarantine receives a request for its exceptional access from a health professional and one of the conditions set out in section 74 of the Safety Regulations are met.

An establishment that receives a notice of investigation must send a copy of it to every establishment, health professional or recipient to which it distributed implicated sperm or ova, to ensure that all parties are made aware of the outcomes of the investigation, and can take appropriate action without delay. All establishments that receive a notice must follow the directions from the primary establishment on actions to be taken.

Establishments that distributed implicated sperm or ova, subject to an investigation, to a recipient for their own personal use, must notify them of the results of the investigation. Patient notification by a health professional is not within the scope of the Safety Regulations.

Release from quarantine

73 An establishment or health professional that quarantines implicated sperm or ova must continue to do so until the results of the investigation reveal that the safety of the implicated sperm or ova is not compromised.

Implicated sperm or ova that are subject to an adverse reaction investigation must remain in quarantine until the investigation results determine that the safety of the sperm or ova has not been compromised.

Release from quarantine — exceptional access

74 (1) Despite section 73, an establishment and a health professional may release sperm or ova from quarantine if the establishment or health professional that is responsible for their quarantine receives a request from a health professional for exceptional access to that sperm or those ova and if one of the following conditions is met:

(a) the recipient has previously been exposed to sperm or ova from that donor and the risk profile of the requested sperm or ova, based on the results of any part of the donor suitability assessment, is at least equivalent to the risk profile of the sperm or ova to which the recipient has previously been exposed, based on the results of any part of the donor suitability assessment that was conducted at that time; or

(b) sperm or ova from that donor have previously been used to create a child for an individual or a couple and the requested sperm or ova are to be used for the purpose of creating another child for that individual or couple.

Summary document

(2) Before the sperm or ova are released from quarantine, the establishment or health professional that is responsible for the quarantine must create a summary document that contains the following information:

(a) the age of the donor, if known;

(b) the condition that has been met;

(c) the dates and results of any donor screening, physical examination or donor testing;

(d) a description of the adverse reaction;

(e) the name of any suspected infectious disease or disease agent, if known; and

(f) an explanation of how the safety of the implicated sperm or ova might have been compromised, if known.

Storage

(3) An establishment and a health professional must ensure that sperm or ova that are in their possession or control and are intended for exceptional access are segregated from sperm and ova that are not intended for exceptional access.

Communication of risk

(4) A health professional must meet the following requirements before making use of the sperm or ova or distributing the sperm to a recipient for their personal use:

(a) create a document that states that, based on the summary document and any risk mitigating measures with respect to that sperm or those ova, in his or her medical opinion, the use of the sperm or ova would not pose a serious risk to human health and safety; and

(b) create a document that states that the health professional has informed the recipient of the risks that the use of the sperm or ova could pose to human health and safety and that the health professional has obtained written consent from the recipient.

Similar to the exceptional access requirements for errors and accidents, the Safety Regulations require sperm and ova that are under quarantine because of an adverse reaction to remain so until the results of the investigation reveal that the safety of the sperm or ova is not compromised.

The only exception to this requirement is where the establishment or health professional responsible for the quarantine receives a request for exceptional access from a health professional and if the conditions for exceptional access are met as set out in section 74 of the Safety Regulations.

Preliminary and interim reports

75 A primary establishment that is conducting an investigation into an adverse reaction must send the following reports to the Minister, in the form established by the Minister, at the following times:

(a) within 72 hours after the start of the investigation, a preliminary report that includes a detailed description of the adverse reaction and any relevant information that is available at that time; and

(b) within 15 days after the start of the investigation and every 15 days after that until the final report is made, an interim report that contains the following information,

(i) any new information with respect to the adverse reaction,

(ii) the progress of the investigation, and

(iii) any measures taken during those 15 days to mitigate further risk.

Final report

76 A primary establishment must send, within 72 hours of completing the investigation, a detailed final report to the Minister, in the form established by the Minister, that contains the following information:

(a) the results of the investigation;

(b) any corrective action taken; and

(c) details concerning the disposition of the implicated sperm or ova.

A primary establishment that is investigating a suspected adverse reaction must submit a preliminary report to Health Canada within 72 hours after the start of the investigation that includes a detailed description of the adverse reaction and any other relevant information that is available at that time. This information should include, but is not limited to:

- the donor identification code and donation code;
- the date on which the sperm or ovum was used;

- the date and description of the adverse reaction;
- the suspected infectious disease and/or disease agent;
- the number of containers of implicated sperm or ova that have been distributed; and
- the risk mitigation measures that are required to be taken.

Following the preliminary report, the primary establishment must send an interim report to Health Canada within 15 days after the start of the investigation and every 15 days thereafter until the investigation is completed. The interim report must include the information outlined in paragraph 75(b) of the Safety Regulations, including any new information, the progress of the investigation and any measures taken during the past 15 days to mitigate further risk. Information regarding the progress of the investigation should include relevant and updated clinical information such as laboratory findings, the status of the recipient and/or individual born of the implicated sperm or ova, root cause analysis, and any corrective actions either already taken or planned to mitigate further risks, such as conducting a recall of the implicated sperm or ova. All updated information should be clearly marked in the report. Health Canada may also request an update at any time after the preliminary report.

Once the investigation is complete, a primary establishment must send within 72 hours of completing the investigation, a detailed final report to Health Canada that contain the results of the investigation, any corrective action taken and details concerning the disposition of the implicated sperm or ova.

Primary establishments must have clear operating procedures on how adverse reactions will be investigated and reported. All adverse reactions that are investigated must be documented and records kept in accordance with section 83 of the Safety Regulations, and may be subject to review during an inspection by Health Canada.

Where to find the adverse reaction form?

A new adverse reaction form will be developed for the reporting of adverse reactions associated with sperm and ova, and will be made available on the Health Canada website. Primary establishments will be informed once the new adverse reaction form for AHR is available.

Where to submit an adverse reaction report?

Adverse reaction reports must be sent to the Canada Vigilance Program.
The completed adverse reaction form must be faxed or mailed to Health Canada's Canada Vigilance Program:

Canada Vigilance Program
Health Product Surveillance and Epidemiology Bureau
Marketed Health Products Directorate
Health Products and Food Branch
Health Canada

Address Locator 1908C
Ottawa, Ontario
K1A 0K9

For questions, contact Health Canada's Canada Vigilance Program:

E-mail for enquiries: hc.canada.vigilance.sc@canada.ca **(do not send reports by email)**

Facsimile: 613-957-0335

Records

General

77 (1) An establishment and a health professional must keep records that contain all the documents and information required under these Regulations and all other records that demonstrate that they meet the requirements of these Regulations.

Donor identification codes and donation codes

(2) An establishment and a health professional must ensure that the donor identification code and the donation code are components of all of their records that relate to the processing, distribution, importation or making use of sperm or ova.

Retention period — general

78 (1) An establishment and a health professional must keep records for 10 years after their creation unless otherwise specified in these Regulations.

Retention period — employees

(2) An establishment must keep records containing records of the qualifications, training and competency of its employees for 10 years after the day on which an individual ceases to be an employee of the establishment.

Retention period — standard operating procedures

(3) An establishment must keep a copy of every version of its standard operating procedures for 10 years after the day on which they are superseded by a new version.

Records consist of the documents and information required under the Safety Regulations and are a critical component of quality management as they provide documented evidence of compliance. Records must be created and updated at the same time that each significant step in the processing, distribution, importation, and making use of donor sperm and ova is performed. As well, all records relating to the processing, distribution, importation, and making use of donor sperm and ova must include the donor identification code and the donation code for each unit of sperm or ova. All records must identify the person who conducted the activities and the dates of the various entries.

Processing

79 (1) A primary establishment must keep records that contain the following documents and information with respect to the sperm or ova it processes:

(a) the donor identification code and the donation code that appear on the label of each immediate container of sperm or ova;

(b) the number of immediate containers on which the same donation code appears;

(c) the type of donation, whether sperm or ova;

(d) the date of the donation;

(e) any documents and information with respect to the suitability of the donor;

(f) a copy of all documentation that is required under these Regulations to accompany the immediate container of the sperm or ova; and

(g) any information with respect to the disposition of the sperm or ova.

Establishment to cooperate

(2) An establishment that processes sperm or ova on behalf of a primary establishment must provide to the primary establishment all of the documents and information that it possesses to update the primary establishment's records.

Primary establishments must keep records of the documents and information set out in section 79 of the Safety Regulations in order to permit the tracing of donor sperm and ova throughout the distribution chain.

Where applicable, records of written agreement between the primary establishment and the establishment that obtains the sperm or ova should be maintained to provide relevant information such as roles and responsibilities of the parties involved.

In the case of a primary establishment, documentation of the request for exceptional access, where applicable, must be available in its records. Similarly, follow-up assessment and testing results of the donor are to be available in the primary establishment's records.

Processing Equipment Records

Records should be maintained for each piece of equipment that could affect the quality and the safety of the sperm or ova. These records should include, but are not limited to the following:

- identity of the equipment;
- serial number or other unique identifier;
- manufacturer's name and contact information;
- date the equipment was received, put into service, and if applicable, out of service;

- manufacturer's instructions, if available;
- equipment performance records that confirm the equipment's suitability for use, including calibration and/or verification records (which should incorporate such information as dates of tests, test results, adjustments made, acceptance criteria and frequency of checks);
- schedules of completed and anticipated maintenance activities;
- any damage, malfunction, modification or repair, of the equipment;
- out of service records;
- usage log sheet; and
- records of recall.

The records should be readily available for the life span of the equipment. Each item of equipment should be uniquely labelled, marked or otherwise identified.

Testing Records

Primary establishments must have records which indicate that all laboratory testing of transmissible disease markers are performed in accordance with the corresponding test kit manufacturer's instructions.

The primary establishment can help ensure that the testing lab will provide the relevant testing information to them by having written agreements in place with the testing lab. The relevant information should include:

- the appropriate tests performed for each sample;
- a stipulation that the laboratory is to follow the manufacturer's instructions and perform the tests within the limits and time frames suggested by the manufacturer;
- a stipulation that the test kits used to test donors for the transmissible disease agents comply with these Regulations;
- a current test kit list and requirement for notification upon test kit changes;
- testing validation data; and
- the method of reporting results to primary establishment and an interpretation of the results.

For testing laboratories, detailed testing records, logs and other supporting documents must be readily accessible to the primary establishment, and should include the following:

- the name of the test kit;
- the lot number;
- the name, lot number, and expiry date of the solutions and reagents used;
- the expiry date;

- the name of the manufacturer; and
- records of recall, if applicable.

Critical Supplies Records

Records should be maintained for each critical supply item that is used during processing and that could affect the quality and the safety of the product. These records include, but are not limited to the following:

- identity of the supply, including type, lot number;
- manufacturer's name;
- expiration date, if applicable (obtain clarification from the manufacturer in cases where the date is unclear);
- manufacturer's instructions, if available;
- records of recall, if applicable; and
- records to demonstrate that non-disposable instruments used in the processing are cleaned, disinfected and/or sterilized to prevent contamination and cross-contamination according to written procedures.

Requirement to Cooperate

When two or more establishments are involved in activities related to processing sperm or ova, the relationship and responsibilities of each should be delineated in writing and that documentation must be maintained at each establishment.

Furthermore, an establishment that processes sperm or ova on behalf of a primary establishment must provide the primary establishment with all of the documents and information it possesses to update the primary establishment's records.

Distribution and importation

80 An establishment that distributes or imports sperm or ova and a health professional who distributes sperm to a recipient for their personal use must keep records that contain the following documents and information with respect to that sperm or those ova:

(a) the donor identification code and the donation code that appear on the label of each immediate container of sperm or ova;

(b) the number of immediate containers on which the same donation code appears;

(c) the contact information for the establishment from which the establishment or health professional received the sperm or ova, if applicable;

(d) a copy of all documentation that is required under these Regulations to accompany the immediate container of the sperm or ova;

(e) the contact information for each establishment, health professional or recipient to which the establishment or health professional distributes the sperm or ova, if applicable; and

(f) any information with respect to the disposition of the sperm or ova.

Establishments that distribute or import and health professionals that distribute sperm to a recipient for their personal use must keep records of the documents and information contained in this section in order to permit the tracing of donor sperm and ova throughout the distribution chain.

Making use

81 (1) An establishment and a health professional must keep records that contain the following documents and information with respect to the sperm or ova of which it makes use:

(a) the donor identification code and the donation code that appear on the label of each immediate container of sperm or ova;

(b) the number of immediate containers on which the same donation code appears;

(c) the contact information and registration number of the primary establishment that processed the sperm or ova;

(d) if applicable, the contact information for the establishment from which the establishment or health professional received the sperm or ova, if they were not received from a primary establishment;

(e) a copy of all documentation that is required under these Regulations to accompany the immediate container of the sperm or ova;

(f) any information that allows for the identification of the recipient; and

(g) any information with respect to the disposition of the sperm or ova.

Establishment to cooperate

(2) An establishment must provide to the establishment and health professional all of the documents and information that it possesses to update the establishment and health professional's records

Establishments and health professionals who make use of donor sperm or ova must keep the documents and information contained in this section of the Safety Regulations to permit the tracing of donor sperm and ova throughout the distribution chain. This includes information that allows for the identification of the recipient.

In the case of donor sperm or ova processed in accordance with the directed donation process and in the case of donor sperm or ova released under exceptional access, the health professional must also keep a record of the documents required by subsection 29(4), section 40, and subsections 66(4) and 74(4) of the Safety Regulations.

An establishment that distributes sperm or ova to another establishment or a health professional who make use of that sperm or ova must provide the documents or information it possesses to enable the establishment or health professional to meet the record retention and traceability requirements.

Retention period — processing, distribution, importation and making use

82 An establishment and a health professional must keep records in respect of each immediate container of sperm or ova for a period of 10 years after the day on which they distribute, make use of or effect the disposition of the sperm or ova.

After processing, donor sperm and ova may be cryopreserved for an extended period of time prior to their distribution, use or disposition. For this reason, this section of the Safety Regulations extends the retention period to 10 years after the distribution, use or disposition of the sperm or ova. Health Canada recognizes that there may be factors beyond the scope of the AHR Act for which a longer record retention period may be justified. As such, Health Canada encourages establishments and health professionals to retain records specific to each donation for longer than the minimum period of time set out in the Regulations.

Investigation

83 (1) An establishment or health professional that has conducted or received a notice of an investigation respecting an accident, error or adverse reaction must keep records that contain

(a) any documents and information with respect to the investigation;

(b) any notices that were received and copies of those that were sent and a list of all the establishments, health professionals or recipients to which they were sent; and

(c) a copy of any reports sent to the Minister.

Retention period

(2) An establishment and a health professional must keep records for a period of 10 years after the date of the last recording in that record.

If an error, an accident or an adverse reaction occurs, a report must be written that describes the incident, the investigation, corrective actions taken, and any follow-up

activities required. An establishment or health professional must keep this report, as well as any notices received, copies of notices sent and copies of any reports sent to Health Canada related to the error, accident or adverse reaction for a period of 10 years.

Record qualities

84 (1) Records containing documents and information must be complete and kept in a manner that allows them to be audited at any time.

Information qualities

(2) The information must be accurate, legible and indelible.

Storage of records

85 An establishment and a health professional must store records in a location that has appropriate environmental conditions and that is secure against the entry of unauthorized persons.

An establishment that keeps electronic records must have an electronic system validated for its intended use to ensure the maintenance of the data integrity of those records. Any changes to the electronic system must be evaluated, documented and approved prior to implementation to ensure the integrity of the data and that the records can be retrieved during the required retention period. A history of any changes to electronic records must be available in an audit trail and an establishment must be able to retrieve and print a hard copy of information that is stored in an electronic record.

Records must be accurate, complete, legible, indelible, and readily accessible at all times. This will permit the audit of these records at any given time.

Transitional Provisions

Primary establishment not registered

86 (1) A primary establishment that, before the day on which these Regulations come into force, processes sperm or ova, may continue to do so, despite section 4, without a registration if it files an application for registration under section 5 within 90 days after that day.

Duration

(2) Subsection (1) applies until the determination of the application made under section 5.

Registration number

87 Despite paragraphs 11(2)(b), 18(1)(f) and 50(e), subparagraph 51(1)(b)(v) and paragraph 81(1)(c), a primary establishment's registration number does not have to be provided before the 180th day after the day on which these Regulations come into force.

Distribution or importation before coming into force of these Regulations — notice

88 An establishment that, before the day on which these Regulations come into force, distributes or imports sperm or ova may continue to do so, despite section 18, if it sends a notice to the Minister that meets the requirements of that section within 90 days after that day.

The Safety Regulations come into force on the day that section 10 of the Act comes into force. Any primary establishment that processes sperm or ova before the Safety Regulations come into force may continue to do so without a registration provided it submits an application for registration to Health Canada within 90 days after the day on which the Safety Regulations come into force. This applies until the registration number is issued by Health Canada or the application for registration is refused.

It is important to note the provisions related registration numbers, for example, the requirement that the registration number must be included in the documentation that accompanies the immediate container of sperm or ova, will come into force on the 180th day after which the Safety Regulations come into force.

Any establishment that imports or distributes sperm or ova before the Safety Regulations come into force may continue to do so without prior notification as long as it sends a notification to Health Canada within 90 days after the day on which the regulations come into force.

Distribution or importation — requirements

89 (1) An establishment that, on or before the day on which these Regulations come into force, distributes or imports sperm or ova must ensure that

(a) the sperm or ova were processed in accordance with these Regulations by a primary establishment; and

(b) the primary establishment has filed an application for registration under section 5 within 90 days after the day on which these Regulations come into force.

Duration

(2) Subsection (1) applies until the day on which the determination of the application made under section 5.

Until a primary establishment that has applied for registration receives its registration number, any establishment that distributes or imports sperm or ova processed by that primary establishment is responsible for ensuring that the sperm or ova was processed in accordance with the Safety Regulations and that the primary establishment has filed an application for registration within 90 days of the coming into force of the Safety

Regulations. This applies until the registration number is issued by Health Canada or the application for registration is refused.

Sperm obtained before these Regulations come into force

90 (1) This section applies to sperm that is obtained before the day on which these Regulations come into force and that may be distributed, imported and used — despite the requirements set out in sections 22 to 40 – only if

(a) the sperm is processed, within the meaning of the *Processing and Distribution of Semen for Assisted Conception Regulations*, in accordance with those Regulations; or

(b) the sperm is the subject of a special access authorization under section 20 of those Regulations.

Special access authorization

(2) Despite subsection (1), sperm that is the subject of a special access authorization may only be distributed and used for the purpose for which the authorization is granted.

Immediate container

(3) Before distributing or making use of the sperm, an establishment and a health professional must ensure that the identification code, within the meaning of the *Processing and Distribution of Semen for Assisted Conception Regulations*, appears in a clear and indelible manner on the label of the immediate container.

Documentation

(4) Before distributing or making use of the sperm, an establishment and a health professional must ensure that the immediate container of sperm is accompanied by documentation that contains the following information in English or French:

(a) the donation code;

(b) the name and business address of the processor within the meaning of the *Processing and Distribution of Semen for Assisted Conception Regulations*;

(c) the date of the donation, the tests performed in respect of the donor, the dates and results of the tests and, if necessary, an interpretation of the results; and

(d) a copy of the special access authorization, if any.

The distribution, use and importation of donor sperm that was processed in accordance with the *Processing and Distribution of Semen for Assisted Conception Regulations* (Semen Regulations) prior to the coming into force of the Safety Regulations is permitted, provided the requirements in section 90 of the Safety Regulations are met. This includes donor sperm that was subject to a Donor Semen Special Access Programme (DSSAP) authorization under the Semen Regulations and for which an authorization has already been issued before the

coming into force of the Safety Regulations. However, such donor sperm may be imported, distributed or used for only the purpose for which the authorization was issued.

As the Semen Regulations will be repealed upon the coming into force of the Safety Regulations, the DSSAP under the Semen Regulations will no longer exist. Under the Safety Regulations, the directed donation process and exceptional access were designed to account for the vast majority of scenarios that were previously accommodated under the DSSAP. Once the Safety Regulations come into force, Health Canada will no longer authorize the use of otherwise non-compliant donor sperm and ova. Rather, the Safety Regulations are intended to provide individuals with flexibility in choosing their donor, while ensuring that important information with respect to the risks that the use of a donation may pose is provided to their health professional.

It is important to note that sperm obtained before the Safety Regulations come into force may be distributed, imported or used only if it has been processed either as per the Semen Regulations or as per the Safety Regulations. In other words, donor sperm obtained before the coming into force of the Safety Regulations either has to meet all of the requirements of the Semen Regulations or all of the requirements of the Safety Regulations, in order for that donor sperm to be distributed, imported, or used. Donor sperm obtained at the time the Semen Regulations were in force, but not processed in accordance with the Semen Regulations (e.g., donor was not tested for chlamydia at the time of donation) may still be distributed, imported or made use of if, it meets all of the processing requirements of the Safety Regulations (e.g., donor was tested for chlamydia within a six month interval, and all other screening and testing requirements of the Safety regulations were met).

Records

91 An establishment and a health professional must keep records of all documents and information as required under the *Processing and Distribution of Semen for Assisted Conception Regulations*, in respect of each immediate container of sperm, unless otherwise required by these Regulations, for a period of 10 years after the day on which they distribute, make use of or effect the disposition of the sperm.

This section of the Safety Regulations sets out the record keeping requirements for sperm that is obtained prior to the coming into force of the Safety Regulations that, following their coming into force, is subsequently distributed, used or its disposition is effected.

Consequential Amendment to the Safety of Human Cells, Tissues and Organs for Transplantation Regulations

92 Paragraph 3(1)(j) of the *Safety of Human Cells, Tissues and Organs for Transplantation Regulations* is repealed.

Repeal

93 The *Processing and Distribution of Semen for Assisted Conception Regulations* are repealed.

Coming into Force

Coming into force of section 10 of Act

94 (1) Subject to subsection (2), these Regulations come into force on the day on which section 10 of the *Assisted Human Reproduction Act* comes into force.

180th day

(2) Section 3 comes into force on the 180th day after the day on which section 10 of the *Assisted Human Reproduction Act* comes into force.

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