Gamete and embryo donation guidance

The Practice Committee of the American Society for Reproductive Medicine and the Practice Committee for the Society for Assisted Reproductive Technology

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This document provides the latest recommendations for the evaluation of potential sperm, oocyte, and embryo donors, as well as their recipients, incorporating recent information about optimal screening and testing for sexually transmitted infections, genetic diseases, and psychological assessments. This revised document incorporates recent information from the US Centers for Disease Control and Prevention, the US Food and Drug Administration, and the American Association of Tissue Banks, with which all programs offering gamete and embryo donation services must be thoroughly familiar, and replaces the document titled "Recommendations for gamete and embryo donation: a committee opinion," last published in 2013. (Fertil Steril® 2024;122:799–813. ©2024 by American Society for Reproductive Medicine.)

El resumen está disponible en Español al final del artículo.

Key Words: Sperm, oocyte, donor insemination, donor screening, quarantine

Sperm, oocyte, and embryo donation use have increased over the past several decades (1–3). The availability of donor gametes allows individuals and couples who otherwise may not be able to conceive the opportunity to build a family. In an effort to optimize safety and outcomes, the US Food and Drug Administration (FDA), the American Association of Tissue Banks, the US Centers for Disease Control and Prevention (CDC), and the American Society for Reproductive Medicine (ASRM) have each developed their own guidance for screening donor tissue and recipients.

This document aimed to summarize the current guidance for donor eligibility determination, which is mandated by the FDA before the use of donor oocytes, donor sperm, or donor embryos. Donors are defined as individuals who are not sexually intimate partners of the recipients; donor eligibility determination is required for donor sperm, donor oocytes, donor embryos, and sperm and oocyte sources when planning to use a gestational carrier. This guidance also reviews the screening of donors and recipients that is recommended by the CDC and ASRM. Although the FDA donor eligibility determination focuses on infectious risk, the ASRM guidance also incorporates prenatal optimization, psychoeducational counseling of donors and recipients, and genetic risk assessment.

This guidance for the screening and testing of gametes and embryo donors applies to all potential donors in the US. Because the prevalence of sexually transmitted infections (STIs) may vary in other locales, this guidance may not be appropriate for other countries or for individuals who come to the United States from other countries. When a donor is deemed "ineligible" on the basis of the FDA guidance detailed below, the tissue cannot be used for a nondirected (anonymous) donation. However, for a directed or known donation, the "ineligible" tissue may be used when both parties are aware of the theoretical infectious or genetic risk and consent to move forward with the donation.

Throughout this document, "anonymous" donors are referred to as "nondirected." The transition in language from "anonymous" to "nondirected" reflects the realization that anonymity is decreasing with the prevalence of and access to nonmedical genetic testing.

Oocyte donation, and thereby this document, does not apply to lesbian couples who are undergoing reciprocal in vitro fertilization (IVF) treatment, in which one partner provides the oocyte(s) and the other partner is the carrier. In this setting, the partner is not donating her oocytes. The oocytes should be considered shared between sexually intimate partners because sperm is shared between heterosexual couples presumed to be sexually intimate.

Although the FDA does not require screening or testing of the recipients of donated gametes, the ASRM recommends the evaluation of recipients as described. Other areas where the ASRM recommendations may be more stringent than the FDA minimum requirements are noted in the text. Additionally, state requirements may be more restrictive than those of the FDA, and clinics are encouraged to check with government officials in the state where their practice is located to determine the minimum screening and testing requirements for their state.

The promulgation of FDA regulations has added considerable oversight

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to gamete and embryo donation, including mandatory registration of all assisted reproductive technology (ART) programs with the federal government, federal inspections of programs that are performing donation, required documentation, and written protocols related to donor screening, testing, selection, rejection, and follow-up. Complete records of all donor cycles, including documentation of adherence to FDA regulations, must be made available to FDA inspectors at their request. Federal regulations and frequently asked questions and answers may be viewed at the following websites:

- https://www.fda.gov/regulatory-information/search-fda-guidance-documents/eligibility-determination-donors-human-cells-tissues-and-cellular-and-tissue-based-products
- https://www.fda.gov/vaccines-blood-biologics/tissue-tissue-products/donor-eligibility-final-rule-and-guidance-questions-and-answers

DONORS – INDICATIONS, SCREENING, AND SELECTION

Sperm donation

Sperm donation for use in donor insemination (DI) or IVF treatment may be undertaken with known or nondirected donors, depending on the clinical circumstances. Donor sperm use has increased over the past 20 years (3).

Indications for donor sperm insemination Indications for donor sperm insemination may include, but are not limited to.

- The male partner has azoospermia, severe oligozoospermia, or other significant sperm or seminal fluid abnormalities.
- The male partner has ejaculatory dysfunction.
- Prior failure to fertilize during IVF treatment after insemination with intracytoplasmic sperm injection.
- The male partner has a significant genetic defect; previously, the couple has produced an offspring affected by a condition for which carrier status cannot be determined or has a strong family history of a heritable disease.
- The female partner is Rh-negative and severely Rh-isoimmunized, and the male partner is Rh-positive.
- Females without male partners or with transmale partners.

Donor sperm screening. There is no method to completely ensure that infectious agents will not be transmitted by DI. However, the following guidance (Table 1, [4–8]), combined with an adequate history and specific exclusion of individuals at high risk for human immunodeficiency virus (HIV) and other STIs, should significantly reduce these risks.

- Medical history—see Medical History Questionnaire list (4, 5)
- Physical examination—see FDA Physical Examination (6)
- Laboratory testing—see Laboratory Testing within 7 days of semen production (4)

Donor sperm selection.

- The main qualities to seek in selecting a donor for DI are an assurance of good health and normal semen analysis. There are no uniformly accepted standards, but, in general, the minimum criteria for normal semen quality can be applied (9).
  - Genetic evaluation: the donor should undergo appropriate genetic evaluation, as reviewed in the genetic counseling section (see Genetic screening and counseling).
- The donor should be of legal adult age in their state, ideally 21 years or older, and should ideally be young enough that

TABLE 1

Donor sperm, the US Food and Drug Administration requirements and the American Society for Reproductive Medicine recommendations (4–8).

Nondirected (anonymous) sperm donor	**FDA requirement** ✓ Donor physical examination ✓ Donor questionnaire ✓ Medical history ✓ Donor infectious laboratories at FDA-approved laboratories (including CMV and HTLV-I and -II IgM and IgG on sperm source) within 7 d (before or after) of sperm acquisition ✓ 6-mo quarantine with repeat infectious-disease testing ✓ Must be eligible to use tissue
ASRM recommendation (in addition to FDA requirements)	✓ Psychoeducational screening ✓ Genetic screening ✓ Infectious-disease testing of the recipient and the recipient's sexually intimate partner(s)
Directed sperm donor	**FDA requirement** ✓ Donor physical examination ✓ Donor questionnaire ✓ Donor infectious laboratories at FDA-approved laboratories (including CMV and HTLV-I and -II IgM and IgG on sperm source) within 7 d of sperm acquisition ✓ May use ineligible tissue, but must label and consent appropriately
ASRM recommendation (in addition to FDA requirements)	✓ Psychological screening ✓ Genetic screening ✓ Infectious-disease testing of the recipient and the recipient's sexually intimate partners ✓ Medical history ✓ Quarantine >35 d followed by repeat infectious-disease testing ✓ Legal consultation and laws may vary by state

Note: CMV = cytomegalovirus; HTLV = human T-cell lymphotropic virus; IgG = immunoglobulin G; IgM = immunoglobulin M.

Gamete and embryo donation. Fertil Steril 2024.

the risks to offspring associated with increased paternal age, such as autism, are minimized. Donors aged <21 years should have a psychological evaluation by a qualified mental health professional, and the decision to proceed with a donor aged <21 years should be made on an individualized basis with help from a qualified mental health professional.
- Psychological evaluation and counseling by a qualified mental health professional is strongly recommended for all sperm donors (see Psychoeducational Counseling).
- Donors should be healthy and have no history to suggest hereditary disease. Proven fertility in the donor is desirable but not required.
- No owner, operator, laboratory director, trainee, or employee of a facility providing donor sperm or performing DI may serve as a donor in that practice.

Directed (nonanonymous/known) donation. A directed (nonanonymous or known) donation is acceptable when all parties agree. Directed donors must undergo the same infectious-disease screening and testing as nondirected donors. Directed donors who test positive or demonstrate a risk factor for a hereditary disease are determined "ineligible" for nondirected donation. However, they are not prohibited from being used for directed donation according to current FDA rules, provided that both parties are aware of the theoretical infectious or genetic risk and consent to move forward with the donation. Although the FDA does not require informing the recipients of the test results other than their eligibility status, in the opinion of the ASRM, the recipients must be informed and counseled appropriately with donor consent before the use of the samples.

In addition, directed donor specimens are exempt from quarantine under the current FDA guidance, which requires only testing within 7 days of donation. However, in the opinion of the ASRM, quarantine of directed donor specimens for 35 days followed by retesting for infectious diseases is recommended. Current evidence suggests that the chance of having undetected HIV or hepatitis B 35 days after an initial negative quantitative test is extremely low; the risk of undetected HIV infection was <1/1 million for HIV after 14 days, for hepatitis B after 35 days, and for hepatitis C after 7 days from the time of potential exposure until the day of a negative NAAT results (10).

Use of fresh semen. In the opinion of the ASRM, the use of fresh semen can be justified only for sexually intimate partners. It is possible for HIV and other infectious organisms to be transmitted by fresh donor semen before the donor has become seropositive. Consequently, the potential for transmission of infections by fresh semen cannot be eliminated.

Oocyte donation

Oocyte donations may be undertaken with known or nondirected donors. Oocyte donation requires that the donor undergo ovarian stimulation with monitoring and oocyte retrieval, involving significant inconvenience, discomfort, and risks for the donor. Women may choose to donate oocytes more than once, increasing the potential risk to the health of the donor (the ASRM Practice Committee document titled "Repetitive oocyte donation: a committee opinion" for further information on this topic (11)). Women donating oocytes for reproductive purposes should be compensated on the basis of ethical grounds (the ASRM Ethics Committee document titled "Financial compensation of oocyte donors: an Ethics Committee opinion" for further discussion (12)).

Indications for use of donor oocytes Indications may include, but are not limited to.
- Women with hypergonadotropic hypogonadism.
- Women of advanced reproductive age.
- Women who have diminished ovarian reserve.
- Women who are known to be affected by or known to be the carriers of a significant genetic defect or who have a family history of a condition for which carrier status cannot be determined.
- Women with poor oocyte and/or embryo quality or multiple previous failed attempts to conceive using ART therapy.
- Men who do not have a female partner or who have a transfemale partner and are planning to use a gestational carrier.

Oocyte donor screening. There is no method to ensure completely that infectious agents will not be transmitted through the use of donor oocytes. However, the following guidance (Table 2, [4, 5]), combined with an adequate history and the specific exclusion of individuals at high risk of HIV and other STIs, should significantly reduce these risks.

- Medical history—Medical History Questionnaire List (4, 5)
- Physical examination—FDA Physical Examination (6)
- Laboratory testing—Laboratory Testing within 30 days before or up to 7 days after acquisition (4)

Oocyte donor selection.
- Oocyte donors should be of legal age in their state, preferably between the ages of 21 and 34 years old. Donors aged <21 years should have a psychological evaluation by a qualified mental health professional, and the decision to proceed with such a donation should be determined on an individual basis. When a prospective donor is aged >34 years, the age of the donor should be revealed to the recipient as part of the informed consent discussion concerning cytogenetic risks and the effect of donor age on pregnancy rates.
- Donors should be healthy and have no history to suggest hereditary disease. Proven fertility in the donor is desirable but not required. A pelvic ultrasound for assessment of pelvic anatomy, including the ovaries, for antral follicle count is recommended. Additional measurement of serum biomarkers of ovarian reserve is warranted to anticipate a response to oocyte stimulation.
- Psychoeducational counseling by a qualified mental health professional is strongly recommended for all donors (see Psychoeducational Counseling).
- The donor should undergo an appropriate genetic evaluation, as reviewed in the genetic counseling section (see Genetic Screening and Counseling).

TABLE 2

Donor oocyte the US Food and Drug Administration and the American Society for Reproductive Medicine recommendations (4, 5).

Oocyte donor	
	FDA Requirement
	✓ Donor physical examination
	✓ Donor questionnaire
	✓ Donor infectious laboratory tests at an FDA-approved laboratory 30 d before, or up to 7 d after[a], oocyte acquisition
	✓ Nondirected (anonymous): must be eligible to use tissue
	✓ Directed: may use ineligible tissue, but must label and consent appropriately
	ASRM recommendation (in addition to FDA requirements)
	✓ Psychoeducational counseling
	✓ Genetic screening
	✓ Medical history
	✓ Infectious-disease testing of the recipient and the recipient's sexually intimate partners
	✓ Legal consultation, particularly for directed donations

[a] May not be resulted in time for fresh donation.

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Directed (nonanonymous/known). Oocyte donation

Directed oocyte donors must undergo the same screening and testing as nondirected (anonymous) donors. Directed donors who test positive or demonstrate a risk factor for a relevant communicable disease are determined "ineligible" for nondirected donation but are not prohibited from use for directed donation according to the current FDA rules, provided that both parties are aware of the theoretical infectious or genetic risk and consent to move forward with the donation. Although the FDA does not require informing the recipients of the test results other than their eligibility status, in the opinion of the ASRM, the recipients must be informed and counseled appropriately with donor consent before the use of the samples.

Quarantine of oocytes Quarantine of oocytes is not required by the FDA for nondirected or directed donation. Requirements of clinics providing oocyte donation services

- When the sharing of oocytes from an ART treatment cycle is contemplated, informed consent must be obtained before the start of the cycle of retrieval. The conditions governing the sharing of oocytes should be specified in advance, be included in the informed consent, and comply with existing ASRM Ethics Committee opinion documents (13).
- No owner, operator, laboratory director, trainee, or employee of a facility screening for or performing oocyte donation may serve as a donor in that practice.
- When an agency is used to recruit oocyte donors, no individual who has a financial interest in that agency may be used as an oocyte donor.
- Ensure that the oocyte donor has medical insurance or that the practice has a policy to cover donation-related medical expenses or complications.

Embryo donation

In the current clinical practice of ART therapy, more embryos that can be transferred safely at one time are often generated and may be cryopreserved for later transfer. Couples who become pregnant and do not desire another pregnancy or have other reasons for choosing not to use their embryos may have the option of discarding these embryos, donating them to other individuals, or donating them for research (1). It is the purpose of this document to present guidance for embryo donation. It should be noted that this guidance represents minimum standards for screening, testing, and counseling of potential embryo donors and recipients. The US federal government has published minimum requirements for embryo donation (14). Some states and other localities may have laws or regulations pertaining to embryo donation that may supersede this guidance.

Guidance for ART therapy practices that offer embryo donation.

- The practice should be knowledgeable in the storage, thawing, and transfer of frozen embryos.
- The practice may charge a professional fee to the potential recipients for embryo thawing, the embryo transfer procedure, cycle coordination and documentation, and infectious-disease screening and testing of both recipients and donors. However, the selling of embryos per se is ethically unacceptable.
- Physicians and employees of an infertility practice should be excluded from participating in embryo donation as either donors or recipients within that practice.

Donor embryo screening. Donor screening requirements from the FDA and additional recommendations from ASRM are summarized in Table 3.

Donor embryo eligibility. Embryos derived from the gametes of a sexually intimate couple and created for use by that couple are exempt from the requirements for donor screening and testing before the creation of the embryos. The following guidance applies to sexually intimate couples who decide to donate unused embryos that are the product of their own biologic gametes:

- Embryo donors should provide a medical and genetic history (criteria described in Genetic Screening and Counseling).
- The gamete donors used to create the embryos should be screened for relevant risk factors for HIV and other transmissible infections, as well as transmissible spongiform encephalopathy (15).

TABLE 3

Donor embryo, the US Food and Drug Administration requirements, and the American Society for Reproductive Medicine recommendations (4, 5).

Embryo donor (directed or nondirected)	
	FDA requirement - Attempt, when feasible, to perform infectious-disease testing on both the oocyte and sperm source (including CMV and HTLV-I and -II IgM and IgG on the sperm source) - May use ineligible embryos when tissue is labeled appropriately and recipients consented ASRM recommendation (in addition to FDA requirements) - Psychological counseling of donors and recipients - Medical history - Genetic history - Infectious-disease testing of recipient and recipient's sexually intimate partners - Legal consultation

Note: CMV = cytomegalovirus; HTLV = human T-cell lymphotropic virus; IgG = immunoglobulin G; and IgM = immunoglobulin M.

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- There is no method to ensure completely that infectious agents will not be transmitted, but the following guidance, combined with an adequate medical history and the specific exclusion of individuals at high risk for HIV and other transmissible infections, should dramatically reduce these risks. The practice should determine when the cost of such tests will be borne by the donor couple, by the practice mediating the embryo donation, or by the potential recipients (discussed in Laboratory Testing).
- Often, screening and testing of the biologic source of the gametes used to create the embryos in sexually intimate partners was not done, and the decision to donate embryos occurred subsequent to their creation. When the decision to donate is made >180 days after cryopreservation of the embryos, the donors may be screened and tested. In this instance, the documentation that accompanies the embryos must include the following label: "Advise the recipient that screening and testing of the donors were not performed at the time of cryopreservation of the reproductive cells or tissue but have been performed subsequently."
- When the donors are not available or refuse to undergo the required screening and testing, the FDA guidance does not preclude the use of their embryos, provided that the documentation that accompanies the embryos includes the following labels: "NOT EVALUATED FOR INFECTIOUS SUBSTANCES," and "WARNING: Advise recipient of communicable disease risks." However, the ASRM recommends careful counseling regarding the risks of transfer of these embryos.
- Embryos that are shipped to another facility must be accompanied by a summary of records and must be appropriately labeled in accordance with FDA guidance. The receiving facility should not accept embryos that are not accompanied by a summary of records or that are not appropriately labeled (4).
- The embryo donors must sign an informed consent document indicating their permission to use their embryos for embryo donation. Issues to be addressed in the consent form include:
  - Relinquishing all rights of the donor(s) to the embryo(s) and any child or children that may result from the transfer of such embryo(s).
  - Recognition of inadvertent loss or damage to the embryo(s).
  - The right of the practice to refuse transfer to an inappropriate recipient.
  - The length of time that donated embryos will be maintained in cryostorage and the alternatives for their disposition thereafter.
  - Jurisdiction and process for medical/legal procedures and/or dispute resolution.
  - There is a possibility that the embryos will not be selected by potential recipients and that practices could then choose an alternative disposition, such as discarding the embryos.
- Proper chain-of-custody procedures must be followed and documented for the handling of all test specimens and donated embryos.
- Donors should receive no compensation for the embryos.
- The decision to proceed with embryo donation is complex, and patients may benefit from psychological counseling (as recommended in Psychoeducational Counseling).

Situations in which the gamete source was a donor, not an intimate partner. The eligibility of donors is determined by the gametes (donor oocyte or donor sperm), not the embryos being donated. For embryos derived from gametes obtained from a nondirected (anonymous) donor(s), the donor(s) must have met all FDA screening and testing requirements and must have been determined eligible for nondirected (anonymous) donation as described above for nondirected sperm and/or oocyte donation. In addition, the donor should have consented to a potential future embryo donation.

MANAGEMENT OF SPERM AND OOCYTE DONORS

- **Monitoring health status** The single most important method for reducing the risk of transmitting infectious agents is to screen carefully and test the potential donors, and to develop an ongoing procedure for monitoring their health status.
- **Payment to donors** Payment to donors varies from area to area but should not be such that the monetary incentive is the primary motivation for donating gametes. However, the donor may be compensated for time and expenses. Please see also the Ethics Committee opinion titled "Interests,

rights, and obligations in gamete donation: an Ethics Committee opinion" (16).

- **Limitations to donor use** Institutions, clinics, and sperm banks should maintain sufficient records to allow a limit to be set for the number of pregnancies for which a given donor is responsible. It is difficult to provide a precise number of times that a given donor can be used because one must take into consideration the population base from which the donor is selected and the geographic area that may be served by a given donor. It has been suggested that in a population of 800,000, limiting a single donor to no more than 25 births would avoid any significant increased risk of inadvertent consanguineous conception (11). This suggestion may require modification when the population using DI represents an isolated subgroup or when the specimens are distributed over a wide geographic area (16). Oocyte donors should be limited to six (6) treatment cycles per donor. The basis for this recommendation is rooted in concern over the cumulative risk for the donor after undergoing more than six ovarian stimulation and oocyte retrieval procedures (11). When splitting donor embryo batches, the potential risk of siblings in close geographic proximity should be considered. Additionally, donors should be informed about the potential future request for follow-up testing or receipt of follow-up medical information that stems from a medical diagnosis in a donor-conceived child.
- **Consent** It is essential for the donor to sign a consent form, which should include a firm denial of having any recognized risk factors for STIs and genetic diseases. It is recommended that the donor acknowledge in the consent form his or her responsibility to notify the donor program of any changes in health or risk factor status related to new diagnoses in the donor or his or her family members. In addition, the consent should consider addressing the donor's consent or dissent with the use of resultant embryos for embryo donation.
- **Counseling about the process** Donors should be counseled about the number and type of infectious-disease tests that will be performed and informed about how that information will be used and shared with others.
  - Oocyte donors should be informed about all relevant aspects of the medical treatment, including medications, monitoring, and oocyte retrieval, as well as potential risks, including ovarian hyperstimulation, cycle cancellation, and the risks of oocyte retrieval.
  - Oocyte donors should be counseled about the possibility of unintended pregnancy and offered options for prevention.
- **Record keeping** The FDA requires that records pertaining to each donor (screening and test results) be maintained for at least 10 years, and some states may require longer. However, in the opinion of the ASRM, a permanent record of each donor's screening and test results should be maintained. To the extent possible, the clinical outcome should be recorded for each donation cycle. A mechanism should exist to maintain such records as a future medical resource for any offspring produced.
- **Protection of confidentiality** Medical records detailing the donation should be maintained as stipulated by federal and local requirements.

RECIPIENTS AND THEIR PARTNERS – SCREENING AND TESTING

ASRM Recommended evaluation of recipients

A routine health and reproductive history. A routine health and reproductive history Should be obtained according to the general preconception screening standards that are applied to individuals anticipating pregnancy. The goal of prepregnancy care is to reduce the risk of adverse health effects for the woman, fetus, and neonate by working with the woman to optimize health, address modifiable risk factors, and provide education (17). This should include (but is not limited to): a review of medical, surgical, and psychiatric histories; review of current medications; evaluation for risk of family and genetic histories; substance use assessment; evaluation for exposure to violence; assessment of immunization status, nutritional status, weight, physical activity, and possible teratogenic exposures.

A complete general physical examination. A complete general physical examination should be performed, including a pelvic evaluation. For embryo or oocyte recipients, formal assessment of the uterine cavity with saline infusion ultrasonography or another suitable procedure is recommended before treatment to evaluate for any significant uterine abnormality.

Donor gamete or embryo recipient laboratory testing. Although there are no federal requirements for testing gamete or embryo recipients, the following tests are recommended to optimize perinatal care:

- Blood type, Rh factor, and antibody screen. Consideration should be given to blood type and Rh factor, particularly for Rh-negative recipients. When the use of donor gametes or embryo(s) creates the potential for Rh incompatibility, recipients should be informed of the obstetric implications of the condition.
- An assessment of vaccination status as per current guidance. Rubella and varicella immunity should be documented before pregnancy. When nonimmune, the vaccine should be administered, and pregnancy should be avoided for 4 weeks. Influenza and tetanus-diphtheria vaccinations should be completed before pregnancy but can be administered during pregnancy (18).
- Infectious-disease testing

Serologic test for syphilis, hepatitis B surface antigen, hepatitis C antibody, *Neisseria gonorrhoeae* and *Chlamydia trachomatis*, HIV, and cytomegalovirus (CMV) immunoglobulin G (IgG) antibody for women using donor sperm.

- Human T-cell lymphotropic virus types I and II may be also tested at the discretion of the clinician in the appropriate clinical setting.

- Positive testing for infectious-disease warrants treatment and, when appropriate, referral to an infectious-disease specialist. Positive testing should not preclude treatment assuming informed decision-making and a comprehensive treatment plan are in place before pregnancy attempts.

- Abnormalities detected from history, physical examination, or laboratory evaluation may require a more detailed evaluation and treatment. Additional guidance is available from ASRM regarding the provision of fertility treatment services to women at high risk of pregnancy complications (19, 20).

ASRM recommended recipient partner screening

Sexually intimate partners of individuals planning to receive oocytes, sperm, or embryos should be screened for infectious diseases. Although not required by the FDA, infectious-disease testing of the partner is recommended by the ASRM to address any potential medical or legal issues that could arise should the partner seroconvert during or after treatment. Such screening of the partner is optional, particularly when the risk of infectious-disease transmission is low, as is the case with same-sex female partners planning donor sperm insemination.

Testing for STIs, similar to that recommended for the recipient partner, is encouraged. This includes serologic tests for HIV, syphilis, hepatitis B surface antigen, and hepatitis C antibody; and *Neisseria gonorrhoeae* and *Chlamydia trachomatis* nucleic acid amplification testing (NAAT). It is worth noting that there are no FDA-licensed, approved, or cleared tests for screening these organisms in an asymptomatic, low-prevalence population. Human T-cell lymphotropic virus types I and II and CMV IgM as well as IgG may be obtained also at the discretion of the clinician in the appropriate clinical setting.

PSYCHOEDUCATIONAL COUNSELING – DONORS AND RECIPIENTS

ASRM recommends psychoeducational counseling for donors

A clinical evaluation by a qualified licensed mental health professional who has training and education in third-party reproduction is strongly recommended for all donors considering gamete donation. The decision to proceed with gamete donation is complex, and the following recommendations are intended to provide general guidelines for addressing the several moral, ethical, emotional, and social issues related to gamete donors, recipients, and donor-conceived persons:

- The evaluation includes a clinical interview and a standardized, empirically validated test that is designed for the assessment and/or screening of mental and behavioral disorders and should adhere to established standards of professional and ethical practice.
- A mental health history should include, at a minimum:
  - Family history.
  - Educational background.
  - Work history.
  - Financial stability.
  - Motivation to donate.
  - Current life stressors and coping skills.
  - Difficult or traumatic reproductive history.
  - Interpersonal relationships.
  - Sexual history.
  - Personal history of mental health issues, diagnoses, substance disorders, and treatment.
  - History of family-of-origin psychiatric and personality disorders and substance disorders.
  - Current or previous use of psychoactive medication.
  - Legal history.
  - History of abuse or neglect.
- The evaluation should also assess the donor'(s) understanding of:
  - Potential emotional and social risks.
  - Evidence of coercion (financial or emotional).
  - Information that will be disclosed to the donor or shared with others.
  - Risk of losing anonymity.
    - Social media and the future implications for identification.
    - Understanding of the likelihood and implications of contact through direct-to-consumer deoxyribonucleic acid (DNA) websites and implications for the donors, their children, current or future partners, and their extended families.
  - Implications of types of families and potential for multiple families receiving their gametes.
  - Aspects of gamete and embryo management and disposition.
  - Management of the donor's information and how it will be disclosed, stored, and secured, as well as future contact by the gamete program.
- For donors who undergo additional treatment cycles, a new full evaluation is strongly recommended when >24 months have elapsed since the prior evaluation.
- Relative exclusion criteria for a gamete donor include:
  - Donors with a serious mental illness or those with a first-degree relative with a serious mental illness, as defined by the Substance Abuse and Mental Health Services Administration, or donor candidates without a history of mental illness in the last 12 months but who report a history of severe mental illness or recurrent impairment in functioning because of mental health conditions.
  - Presence of significant psychopathology.
  - Positive family history of psychiatric disorders.
  - Current use of psychoactive medication.
  - Substance disorders.
  - Two or more first-degree relatives with substance disorders.
  - History of emotional, sexual, or physical abuse without professional treatment.
  - Excessive stress.
  - Relationship instability.
  - Inadequate cognitive functioning to support informed consent.

  - High-risk sexual practices.
  - Risks and concerns for the donor for future contact with donor-conceived offspring.
- For directed donors and recipients, partners should be included in the clinical interview. The goal is to provide information and education for family building, including discussion of the potential impact of the donation on their relationships, contact with the donor, role expectations, and the children's interests between and among each other.
- Candidates who are not approved for donation should be offered a referral for any psychological or safety concerns.

Psychoeducational consultation: gamete donation recipients (oocytes, sperm, and embryos)

The decision to proceed with oocyte, sperm, or embryo donation is complex, and intended parents benefit from counseling to aid in the decision. For these reasons, a psychoeducational consultation with a qualified licensed mental health professional who has training and education in third-party reproduction is strongly recommended.

The psychoeducational consultation addresses the implications of creating a family with gamete donations. The recipient(s) should be counseled about the potential emotional, moral, ethical, and social implications of building a family with gamete donations. Different circumstances may require counseling that focuses on one or more of the following issues:

- Disclosure.
- Implications of a long-term impact on the family.
- The needs of donor-conceived persons.
- Grief and loss.
- Limitations of donor screening.
- Desired qualities of the donor and their implications.
- Pregnancy, transition to parenthood, and parenting at an older age (when applicable).
- The challenges of anonymity arise because of direct-to-consumer DNA testing, technological advances, social media, and the implications for donor-conceived families.
- Future implications for the children of having persons who are linked through the same donor.
- Future implications of receiving new medical information related to the donor or another donor-conceived sibling.
- The impact of treatment failure, coping with treatment termination, and developing alternative plans for the future.

As the goal of this is psychoeducational, should information arise that indicates that there are concerns for the health, mental health, welfare, or safety of the recipient(s) or resulting children, a referral to an independent qualified professional should be made for an evaluation.

Psychoeducational consultation: gamete (sperm and oocyte) donation, with a directed donor

In addition to the above topics, directed donation consultation should include:

- In cases involving directed donors, the consultation strongly recommends separate sessions for the donor(s) and recipient(s) as well as a joint session with the donor, donor's partner, and recipient(s).
- Expectations for communication and relationship roles between and among donor, recipient, donor-conceived persons, partners, and other family members.
- That a donor may not be recommended for donation.
- Exploration of donor and recipient(s) preferences about the disposition of any remaining gametes or embryos.

Psychoeducational consultation: embryo donation, with a directed donor

Embryo donation requires special considerations for the recipients and donors and the psychoeducational consultation should include:

- Separate consultation sessions are strongly recommended for the donor(s) and recipient(s), as well as a joint session with the donor, donor's partner, and recipient(s) to discuss expectations, communication, and future relationships.
- Discussion with the recipient(s) about future implications for their children having full genetic siblings in other families.
- Exploration of contact and roles between and among the families.
- The impact of possible treatment failure.
- Donor and recipient(s) plan regarding the disposition of any remaining embryos.
- The challenges of anonymity because of direct-to-consumer DNA testing, technological advances, social media, and the implications for donor-conceived families.

GENETIC SCREENING AND COUNSELING – DONORS AND RECIPIENTS

Genetic carrier screening for heritable diseases

The decision to proceed with gamete donation is complex and the following recommendations are intended to provide general guidelines for genetic considerations.

Recommended nondirected donor carrier screening.

- Screening for cystic fibrosis, spinal muscular atrophy, and thalassemia/hemoglobinopathy carrier status should be performed on all oocyte and sperm donors.
- Routine carrier screening for fragile X syndrome carrier status may be considered for all oocyte donors, regardless of family history. Screening for fragile X syndrome carrier status should be performed on all oocyte donors with a family history of fragile X-related disorders or an intellectual disability suggestive of fragile X syndrome.
- Additional expanded carrier screening may be also appropriate. Pan-ethnic expanded carrier screening is recommended over ethnicity-based panels given the limitations of self-reported ethnicity, increasingly multiethnic populations, and the fact that rare recessive conditions can occur in any ethnic group despite lower carrier frequencies. It is important to note that different panels may test for different

conditions; ideally, the oocyte and sperm sources should be screened for the same conditions. When carrier screening is performed using different panels in the same or different laboratories, ideally, a professional should review the results to evaluate and disclose the reproductive risk to help determine whether additional screening is warranted.
- Embryo donors may not meet the above genetic carrier screening recommendations, particularly when the embryos were created with autologous oocytes and sperm. Updating genetic screening may be requested of embryo donors when desired, but it should not be considered a barrier to donating.
- Recipients using a directed donor should be offered the above carrier screening options for their directed donor.

Donor counseling.
- Donors should provide informed consent, ideally through a written consent form, before carrier screening.
- Informed consent should include a description of the test, the types and number of conditions included, the chance the donor will be found to be a carrier, the implications of being a carrier, the possibility for recontact for additional samples or testing in the future, and the possibility of results revealing a potential health risk to the carrier (e.g., homozygous for a recessive disease, carrier of a condition with health risks to carriers).
- Carrier screening results should be disclosed to the donor, and donors should be provided a copy of their results and given the opportunity to discuss their results with a genetic counselor.
- Informed consent should be obtained again before updating a donor's genetic testing on stored tissue samples.

Donor eligibility.
- Donors who are heterozygous carriers of autosomal recessive conditions, with no health risks to carriers, need not be excluded.
- Donors who are carriers for recessive conditions that confer significant health risks to carriers (e.g., ataxia telangiectasia, Nijmegen breakage syndrome) should be considered on a case-by-case basis.
- Eligibility of donors found to be homozygous, yet apparently asymptomatic, for autosomal recessive conditions (e.g., biotinidase deficiency, 21-hydroxylase congenital adrenal hyperplasia) should be considered on a case-by-case basis, with consideration toward the specific condition, the possible symptoms, the impact on fertility treatments, and the reproductive risk.
- Oocyte donors who are carriers of X-linked conditions should be excluded, with conditions such as glucose-6-phosphate-dehydrogenase deficiency (mild disease presentation) and Fragile X intermediate alleles (no risk for full expansion to the next generation) as possible exceptions.

Recipient counseling.
- Counseling regarding residual risk and reproductive implications of carrier screening is best provided by a certified genetic counselor or a professional boarded by the American Board of Medical Genetics and Genomics (ABMG) or the American Board of Genetic Counseling (ABGC).
- The recipient(s) should be counseled about their donor's carrier screen results. Counseling about positive results should include information about the natural history of the condition(s), carrier frequency, autosomal recessive inheritance, the detection rate of the screen, and the residual risk after a negative result.
- The recipient should be given the option of carrier screening for the reproductive partner. Some recipients may choose to decline carrier screening after adequate counseling; the declination of carrier screening should be documented.
- When a donor carries a recessive condition, the recipient and reproductive partner (as appropriate) should receive counseling regarding the implications of the carrier status specific to the condition and should provide informed consent before proceeding with the donor.
- Donor embryo recipients should be advised of any carrier screening results that are available for their embryo donors, including the limitations of their screening, or lack thereof.

Family history screening for nondirected (anonymous) donors

Recommended donor family history screening.
- All donors should provide a detailed three-generation family history, to the extent possible. Donors who are adopted, and who are unable to provide any family history information about their genetic relatives should be considered on a case-by-case basis.
- Providers reviewing the family history should be aware that some autosomal-dominant or X-linked disorders can have:
  - Variable expressivity: mutation carriers may exhibit different symptoms, even within one family, e.g., Fragile X syndrome, neurofibromatosis.
  - Reduced penetrance: mutation carriers may not develop symptoms, e.g., hereditary breast and ovarian cancer.
  - An age of onset that extends beyond the age of the donor and his or her first-degree relatives, e.g., Huntington's disease.
- Given the complexity of recognizing patterns that may signify an increased health risk to donor-conceived offspring, assessing reproductive risk, determining possible genetic testing options, and communicating relevant information to donors and recipients, family history review and assessment of donors should be performed by a certified genetic counselor or a professional boarded by ABMG or ABGC.

Donor counseling.
- Donors should be informed of their duty to update the clinic or agency with relevant family history changes over time, such as a new diagnosis of a genetic disease or a chronic

medical condition for the donor and their first-degree relatives.
- When the family history suggests the need for additional genetic testing for a donor, the donor should be referred to a certified genetic counselor or a professional boarded by ABMG or ABGC. Additional genetic testing without a referral to a genetics professional would be inappropriate.

Nondirected (anonymous) donor eligibility

Monogenic conditions.

- The donor should not be known to carry a mutation for an autosomal-dominant or X-linked disorder. Exceptions may be made for conditions considered to have more mild health risks to carriers, such as red-green color blindness or glucose-6-phosphate-dehydrogenase deficiency, as long as recipients are informed of potential health risks to offspring.
- Donors with a known family history of a dominant, recessive, or X-linked disorder may be referred for genetic counseling and potentially genetic testing for that specific disorder, when desired and appropriate.
- Donors with a known family history (in a first-, second-, or third-degree relative) of a dominant or X-linked disorder that has the potential to have been passed on to the donor should be excluded in the absence of risk-reducing genetic testing, as described below.
- Genetic test results, when available for the donor or their family members, may determine the appropriateness of using that donor. Donors with negative genetic testing for themselves or an appropriate intervening relative for a familial mutation are eligible to donate, pending review of the genetic test reports by a certified genetic counselor or professional boarded by ABMG or ABGC.
- Donors whose family history is strongly suggestive of an undiagnosed autosomal-dominant or X-linked disease (e.g., a family history suggestive of hereditary breast cancer, Marfan syndrome, retinitis pigmentosa, and others) should be excluded when the donor is at increased risk of that disorder. Donors may be referred for additional clinical screening, genetic counseling, or genetic testing, which could reduce the risk to offspring and make the donor eligible.

Congenital anomalies.

- Donors with a major malformation of complex cause (multifactorial/polygenic), such as a neural tube defect, limb deficiency, cleft lip, or cardiac malformation, should be excluded. A major malformation is defined by the CDC as an anomaly that carries serious function or cosmetic handicap, which typically requires medical follow-up or intervention (CDC website definitions). A noninclusive list of major malformations can be found at https://www.cdc.gov/ncbddd/birthdefects/data.html (21).
- Donors with isolated minor congenital anomalies, defined by the CDC as structural differences that do not have significant medical, social, or cosmetic consequences, may be approved as long as the history is not otherwise suggestive of an underlying genetic syndrome. A noninclusive list of anomalies that may be considered minor can be found in Appendix B of the CDC Birth Defects Surveillance Manual (22).
- Donors with a first-degree relative with a major malformation of complex cause (as described above) should be considered on a case-by-case basis, taking into account the severity of the malformation, the relative risk to second-degree relatives, and the general population frequency.

Multifactorial conditions.

- Risk assessment of multifactorial conditions is complex and should be performed by a certified genetic counselor or professional boarded by ABMG or ABGC.
- Donors with a personal history of an autism spectrum disorder or a first-degree relative with an autism spectrum disorder should be excluded.
- Donors with a personal history of intellectual disability or a first-degree relative with intellectual disability of undocumented etiology should be excluded.
- Donors with a personal history of cerebral palsy should be excluded. Donors with first-degree relatives with a diagnosis of cerebral palsy but insufficient evidence of perinatal anoxia, prematurity, or other risk factors should be excluded.
- Eligibility of donors with a personal history of, or a first-degree relative with, attention deficit hyperactivity disorder should be considered on a case-by-case basis, with consideration of factors such as the severity of symptoms, impact on daily function, and the results of the gamete donor psychological assessment. When approved, recipients should be informed of the potentially high heritability of attention deficit hyperactivity disorder as well as the increased risks for genetically related disorders. Additionally, the donor's severity of symptoms may not predict the severity of symptoms in future generations.
- Donors with a personal history of, or a first-degree relative with, serious mental illness, as defined by the Substance Abuse and Mental Health Services Administration (23), should be excluded. Serious mental illnesses typically include bipolar disorder, schizophrenia, schizoaffective disorder, and major depression, as diagnosed by a licensed mental health professional.
- Donors with a personal history of a medical condition that significantly impacts the donor's quality of life require lifelong medication or frequent medical follow-up should typically be excluded (e.g., diabetes, idiopathic epilepsy, severe hearing loss, severe vision loss, cardiac conduction abnormalities, and others).
- Multifactorial health conditions are common and are reported in most donors' family histories. Some examples of multifactorial conditions are hypertension, thyroid disorders, asthma, and arthritis. Most donors with a family history of multifactorial conditions can be approved, although recipients should be made aware of any increased risks for offspring.

- Factors to support the exclusion of a donor for a family history of a multifactorial condition may include having multiple (two or more) affected first- or second-degree relatives, young ages of onset, severe symptoms, reduced quality of life, limited treatment, significant impact on daily functioning, low prevalence in the general population, and high genetic risk to offspring.

Chromosomal conditions.

- Donors should not have a known karyotype abnormality, such as a translocation, inversion, or sex chromosome disorder, that may result in chromosomally unbalanced gametes.
- In the general population, the chance of having a chromosomal rearrangement that could be transmitted in an unbalanced form to offspring is small, provided family history is negative for risk factors. Therefore, routine karyotyping of all donors is optional.
- Karyotyping is recommended when the donor has a personal history of recurrent pregnancy loss, when a first- or second-degree relative is known to have a chromosome abnormality, or when the family history is suggestive of a chromosome rearrangement (such as multiple miscarriages, infertility, stillbirths, birth defects, or intellectual disability).
- When there is a known chromosome abnormality in the family, the test reports for the patient should be reviewed by an appropriate genetics professional to ensure the appropriate genetic test has been performed.

Recipient counseling.

- The donor's complete family history should be provided to the recipient, and recipients should be given the option of reviewing the family history with a certified genetic counselor or professional boarded by ABMG or ABGC.
- The intentions of the above eligibility criteria are to assist clinics and agencies in developing minimal standards for nondirected donor eligibility and to safeguard recipients from selecting a donor whose family history suggests excessive genetic risks for offspring without appropriate counseling or informed consent.
- Recipients should be advised of the limitations of a family history assessment. The effectiveness of these criteria is dependent on the accurate reporting of family history and genetic testing by the donor. Family history assessment may be limited by factors such as small family size or limited and partial information about the donor's genetic relatives. Many health conditions, birth defects, and genetic diseases are not predictable by family history assessment, and stringent adherence to these criteria does not guarantee that there will be no genetic risks to the genetic offspring of a particular donor.
- There may be situations in which a donor whose family history does not meet these criteria is still desired by a particular recipient. When a donor's family history does not meet the above criteria, recipients should be offered genetic counseling about the condition, the risk to donor-conceived offspring, the limitations of genetic testing results, When available, and recommendations for additional testing and screening for offspring. Recipients should provide informed consent to proceed with a donor whose family history contains significant health risks to the donor-conceived offspring.
- It may not be appropriate to apply the above donor eligibility criteria to embryo donors, given the key differences between embryo donation and oocyte and sperm donation. However, it is recommended that clinics and agencies attempt to collect three-generation family histories from embryo donors. Donor embryo recipients should receive the available family history, and they should be given the option of reviewing the family history and associated health risks with a certified genetic counselor or professional boarded by ABMG or ABGC.
- It may not be appropriate to apply the above donor eligibility criteria to directed egg and sperm donors; however, it is strongly recommended that clinics and agencies offer recipients the option of a family history assessment of their directed donor with a certified genetic counselor.

LEGAL CONSIDERATIONS – DONOR AND RECIPIENTS

Consultation with an attorney is strongly recommended for all participants in a directed donation and should be offered, but is not required, for all individuals receiving or donating gametes. Legal requirements may vary by state.

FDA DONOR ELIGIBILITY – QUESTIONNAIRE, PHYSICAL EXAMINATION, LABORATORY TESTING

FDA donor eligibility medical questionnaire (questions as of December 2019)

Donors should be healthy. A complete personal and sexual history should be obtained to exclude, as donors, individuals who might be at high risk for HIV, STIs, or other infections that might be transmissible via gamete donation. Prospective donors with any of the following factors should be deemed ineligible (as of January 2020):

- Males with a history of sex with another man, or females with a history of sex with a male who has had sex with another male in the preceding 5 years.
- Individuals who have injected drugs for nonmedical reasons in the preceding 5 years, including intravenous, intramuscular, and subcutaneous injections.
- Individuals who have had sex in exchange for money or drugs in the preceding 5 years.
- Individuals who have had sex in the preceding 12 months with any person meeting any of the criteria described immediately above or with any person having HIV infection, including a positive or reactive test to HIV infection, hepatitis B infection, or clinically active (symptomatic) hepatitis C infection.
- Individuals who have been exposed within the last 12 months through percutaneous inoculation or contact with an open wound, nonintact skin, or mucous membrane to blood that is known or suspected to be infected with HIV, hepatitis B, and/or hepatitis C virus.

- Individuals who have had close contact (e.g., living in the same household wherein sharing of kitchen and bathroom facilities occurs regularly) within 12 months preceding the donation with another person who has hepatitis B or clinically active (symptomatic) hepatitis C infection.
- Individuals who have been incarcerated in lock-up, jail, or prison for >72 consecutive hours within the previous 12 months.
- Individuals who had or have been treated for syphilis, gonorrhea, or chlamydia within the preceding 12 months. Deferral of donors is not necessary when there is evidence of successful treatments >12 months ago.
- Individuals who have undergone body piercing and/or tattooing procedures within the preceding 12 months in which sterile procedures were not used or it is unclear whether sterile procedures were used (e.g., contaminated instruments and/or ink were used, or shared instruments that had not been sterilized between uses were used).
- Individuals who have received a smallpox vaccination (vaccinia virus) for 21 days after vaccination or until the scab separates spontaneously and physical examination confirms the absence of a scab at the vaccination site (whichever is later). The donor should be deferred for 2 months when the scab is removed before spontaneous separation. If the donor experiences complications from vaccination, he should be deferred until 14 days after the complete resolution of those complications. When the donor became infected as a result of close contact with a person recently vaccinated for vaccinia, he may be considered eligible for donation when the scab spontaneously separated, when 14 days have elapsed since resolution of all the vaccinia-related complications, or 3 months after the scab was otherwise removed.
- Individuals who have had a medical diagnosis or suspicion of West Nile virus (WNV) infection (on the basis of symptoms and/or laboratory test results or confirmed WNV viremia) should be deferred for 120 days after the onset of symptoms or diagnosis, whichever is later.
- Individuals who have tested positive or reactive for WNV infection using an FDA-licensed or investigational WNV NAAT in the preceding 120 days.
- Individuals who have been diagnosed with variant Creutzfeldt-Jakob disease (vCJD) or any other form of CJD.
- Individuals who have been diagnosed with dementia or any other degenerative or demyelinating disease of the central nervous system or other neurologic disease of unknown etiology. Potential donors who have a diagnosis of delirium (e.g., delirium caused by toxic/metabolic diseases or recent head trauma) would not be considered necessarily to have a diagnosis of dementia and should be evaluated by the medical director.
- Individuals who are at increased risk for CJD. Donors are considered to have an increased risk for CJD when they have received a nonsynthetic dura mater transplant, human pituitary-derived growth hormone, or have one or more blood relatives diagnosed with CJD.
- Individuals who have a history of CJD in a blood relative unless the diagnosis of CJD was subsequently found to be in error, the CJD was iatrogenic, or laboratory testing (gene sequencing) demonstrates that the donor does not have a mutation associated with familial CJD.
- Individuals who spent 3 months or more cumulatively in the United Kingdom from the beginning of 1980 through the end of 1996.
- Individuals who are current or former US military members, civilian military employees, or dependents of a military member or civilian employee who resided at US military bases in Northern Europe (Germany, Belgium, and the Netherlands) for 6 months or more cumulatively from 1980 through 1990, or elsewhere in Europe (Greece, Turkey, Spain, Portugal, and Italy) for 6 months or more cumulatively from 1980 through 1996.
- Individuals who spent 5 years or more cumulatively in Europe from 1980 until present.
- Individuals who received any transfusion of blood or blood components in the United Kingdom or France between 1980 and the present.
- Individuals or their sexual partners who were born or lived in certain countries in Africa (Cameroon, Central African Republic, Chad, Congo, Equatorial Guinea, Gabon, Niger, or Nigeria) after 1977 (risk factor for HIV group O).
- Individuals who have received a blood transfusion or any medical treatments that involved blood in the countries listed in VIII.w. after 1977 (a risk factor for HIV group O).
- Individuals who have received xenotransplants (live cells, tissues, or organs from a nonhuman animal source or human body fluids, cells, tissues, or organs that have had ex vivo contact with live nonhuman animal cells, tissues, or organs) or have been in close contact with a xenotransplant recipient.
- Individuals who have received human organ or tissue transplants or treatments with human extracts.
- Medical diagnosis of Zika virus in the past 6 months.
- Residence in, or travel to, an area with an increased risk for Zika virus transmission within the past 6 months.
- Sex within the past 6 months with a person who has either of the risk factors listed in the items above.

Note: Recipients of human-derived clotting factor concentrates and sexual partners of recipients of clotting factors may be determined eligible when all other donor eligibility requirements are met.

RESOURCES:

- Guidance for Industry, Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCTPs):https://www.fda.gov/media/73072/download (4)
- Guidance for Industry: Donor Screening Recommendations to Reduce the Risk of Transmission of Zika Virus by Human Cells, Tissues, and Cellular and Tissue-Based Products:https://www.fda.gov/media/96528/download (4)

FDA donor eligibility laboratory testing

Laboratory requirements for FDA donor eligibility are outlined in Table 4.

TABLE 4

Laboratory tests required by FDA for gamete donors.

- Chlamydia
- Gonorrhea
- Hepatitis B virus NAAT
- Hepatitis B surface antigen
- Hepatitis B core antibody (IgG and IgM)
- HIV 1 antibody and NAAT
- HIV 2 antibody
- HIV group O antibody
- Hepatitis C antibody or HCV NAAT
- HIV 1/2 NAAT
- Serologic test for syphilis (nontreponemal or treponemal screening test)
- West Nile Virus NAAT
- HTLV-I and II (males only)
- CMV IgM and IgG (males only)

Note: Either year-round or seasonal testing when gametes are recovered between June 1 and October 31.
CMV = cytomegalovirus; HIV = human immunodeficiency virus; HTLV = human T-cell lymphotropic virus; IgG = immunoglobulin G; IgM = immunoglobulin M; NAAT = nucleic acid amplification testing; RPR = rapid plasma reagin for syphilis.

Gamete and embryo donation. Fertil Steril 2024.

Managing laboratory results.

- A positive test should be verified before notifying the potential donor. When a test is confirmed positive, the individual should be referred for appropriate counseling and management.
- Individuals who initially test positive (except for treated syphilis, *Neisseria gonorrhoeae*, or *Chlamydia trachomatis*, as described above) are not eligible for nondirected (anonymous) donations.
- Individuals whose specimen tests positive or reactive on a nontreponemal screening test for syphilis (rapid plasma reagin) and negative or nonreactive on a specific treponemal confirmatory test may be determined to be eligible, so long as all other required testing and screening are negative or nonreactive. A donor whose specimen tests positive or reactive on either a specific treponemal confirmatory test for syphilis or on a treponemal screening test is not eligible.
- Donors found to be positive for syphilis, *Neisseria gonorrhoeae*, or *Chlamydia trachomatis* should be treated, retested, and deferred from donation for 12 months after documentation that treatment was successful before being reconsidered. When evidence is presented that treatment occurred >12 months ago and was successful, no further deferral is needed as long as current testing does not indicate an active infection.
- Individuals who test positive for active infection with CMV (positive urine or throat culture or paired serum samples demonstrating a four-fold rise in IgG antibody and IgM antibody at least 30% of the IgG level) should be excluded. Because CMV is so common, insemination with semen from a CMV-seropositive man (without active infection) is permissible when the female partner is also CMV-seropositive or after informed consent from a seronegative woman. Although the practice is not entirely without risk, because there are many strains of CMV and superinfection is possible, the associated risk of newborn CMV infection is approximately 1%, and such infants appear to have no significant illness or other abnormality.

FDA donor eligibility physical examination

Before acceptance and every 6 months While remaining an active donor, donors should undergo a complete physical examination and should be declined when any of the following findings are present:

- Physical evidence for the risk of sexually transmitted disease, such as genital ulcerative lesions, herpes simplex, chancroid, or urethral discharge.
- Physical evidence for the risk of, or evidence of, syphilis.
- Physical evidence of anal intercourse, including perianal condylomata.
- Physical evidence of nonmedical percutaneous drug use, such as needle tracks; the examination should include examination of tattoos, which might be covering needle tracks.
- Physical evidence of recent (within 12 months) tattooing, ear piercing, or body piercing where sterile technique was not used.
- Disseminated lymphadenopathy.
- Unexplained oral thrush.
- Blue or purple spots are consistent with Kaposi sarcoma.
- Unexplained jaundice, hepatomegaly, or icterus.
- The large scab is consistent with the recent history of smallpox immunization.
- Eczema vaccinatum, generalized vesicular rash, severely necrotic lesion (consistent with vaccinia necrosum), or corneal scarring (consistent with vaccinial keratitis).

RESOURCES:

- Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCTPs):https://www.fda.gov/media/73072/download(4).
- Sample Donor Physical Exam Form:https://www.aatb.org/sites/default/files/AATB%20Guidance%20Document%20No.%201%2C%20v2%20%286.27.05%29.pdf(6).

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REFERENCES

1. Kawwass JF, Crawford S, Hipp HS, Boulet SL, Kissin DM, Jamieson DJ, et al. Embryo donation: national trends and outcomes, 2000 through 2013. Am J Obstet Gynecol 2016;215:747.e1–5.
2. Kawwass JF, Monsour M, Crawford S, Kissin DM, Session DR, Kulkarni AD, et al. Trends and outcomes for donor oocyte cycles in the United States, 2000-2010. JAMA 2013;310:2426–34.
3. Gerkowicz SA, Crawford SB, Hipp HS, Boulet SL, Kissin DM, Kawwass JF. Assisted reproductive technology with donor sperm: national trends and perinatal outcomes. Am J Obstet Gynecol 2018;218(421):e1–10.
4. US Department of Health and Human Services. Guidance for industry: eligibility determination for donors of human cells, tissues, and cellular and tissue-based products (HCT/Ps). Available at: https://www.fda.gov/media/73072/download. Accessed December 22, 2020.
5. US Department of Health and Human Services. Guidance for industry: donor screening recommendations to reduce the risk of transmission of Zika Virus by human cells, tissues, and cellular and tissue-based products. Available at: https://www.fda.gov/media/96528/download. Accessed December 22, 2020.
6. American Association of Tissue Banks. Guidance Document.Tissue Donor Physical Assessment form. Available at: https://www.aatb.org/sites/default/files/AATB%20Guidance%20Document%20No.%201%2C%20v2%20%286.27.05%29.pdf. Accessed December 22, 2020.
7. US Food and Drug Administration. Donor Eligibility Final rule and Guidance Questions and Answers. Available at: https://www.fda.gov/vaccines-blood-biologics/tissue-tissue-products/donor-eligibility-final-rule-and-guidance-questions-and-answers. Accessed December 22, 2020.
8. US Food and Drug Administration. Human cells, tissues, and cellular and tissue-based products; donor screening and testing; and related labeling 6/19/2007 final rule questions and answers. Available at: https://www.fda.gov/vaccines-blood-biologics/tissue-tissue-products/human-cells-tissues-and-cellular-and-tissue-based-products-donor-screening-and-testing-and-related. Accessed December 22, 2020.
9. World Health Organization. Laboratory manual for the examination of human semen and sperm-cervical mucus interaction. 5th ed. New York: Cambridge University Press; 2010:00–0.
10. Jones JM, Gurbaxani BM, Asher A, Sansom S, Annambhotla P, Moorman AC, et al. Quantifying the risk of undetected HIV, hepatitis B virus, or hepatitis C virus infection in Public Health Service increased risk donors. Am J Transplantation 2019;19:2583–93.
11. Practice Committee of the American Society for Reproductive Medicine. Repetitive oocyte donation: a committee opinion. Fertil Steril 2020;113:1150–3.
12. Ethics Committee of the American Society for Reproductive Medicine. Financial compensation of oocyte donors: an Ethics Committee opinion. Fertil Steril 2021;116:319–25.
13. Ethics Committee of the American Society for Reproductive Medicine. Financial ''risk-sharing'' or refund programs in assisted reproduction: an Ethics Committee opinion. Fertil Steril 2016;106:e8–11.
14. US Food and Drug Administration. Eligibility determination for donors of human cells, tissues, and cellular and tissue-based products: guidance for industry, AUGUST 2007. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/eligibility-determination-donors-human-cells-tissues-and-cellular-and-tissue-based-products. Accessed December 18, 2019.
15. US Food and Drug Administration. Human cells, tissues, and cellular and tissue-based products; donor screening and testing, and related labeling. Available at: https://www.govinfo.gov/content/pkg/FR-2005-05-25/pdf/05-10583.pdf. Accessed December 22, 2020.
16. Ethics Committee of the American Society for Reproductive Medicine. Interests, obligations, and rights in gamete and embryo donation: an Ethics Committee opinion. Fertil Steril 2019;111:664–70.
17. American College of Obstetrics and Gynecologists. ACOG Committee Opinion No. 762: prepregnancy Counseling. Obstet Gynecol 2019;133:e78–89.
18. Practice Committee of the American Society for Reproductive Medicine. Current recommendations for vaccines for female infertility patients: a committee opinion. Fertil Steril 2018;110:838–41.
19. Ethics Committee of the American Society for Reproductive Medicine. Oocyte or embryo donation to women of advanced reproductive age: an Ethics Committee opinion. Fertil Steril 2016;106:e3–7.
20. Ethics Committee of the American Society for Reproductive Medicine. Provision of fertility services for women at increased risk of complications during fertility treatment or pregnancy: an Ethics Committee opinion. Fertil Steril 2016;106:1319–23.
21. Ethics Committee of the American Society for Reproductive Medicine. Informing offspring of their conception by gamete or embryo donation: an Ethics Committee opinion. Fertil Steril 2018;109:601–5.
22. Centers for Disease Control and Prevention. Birth defects surveillance toolkit. Available at: https://www.cdc.gov/ncbddd/birthdefects/surveillancemanual/chapters/objectives.html. Accessed December 18, 2019.
23. Substance Abuse and Mental Health Services Administration. Mental Health and Substance Use Disorders. Available at: https://www.samhsa.gov/find-help/disorders. Accessed December 18, 2019.

Guía para la donación de gametos y embriones

Este documento proporciona las recomendaciones más recientes para el estudio de candidatos a donación de semen, de ovocitos y de embriones, así como de sus receptores, incorporando información actualizada sobre el cribado y las pruebas óptimas para enfermedades de transmisión sexual, genéticas y evaluaciones psicológicas. Este documento revisado incluye información reciente de los Centros para el Control y la Prevención de Enfermedades de EE. UU., la Administración de Alimentos y Medicamentos de EE. UU. y la Asociación Americana de Bancos de Tejidos, con la cual todos los programas que ofrezcan servicios de donación de gametos y embriones deben estar completamente familiarizados. Este documento reemplaza al titulado "Recomendaciones para la donación de gametos y embriones: una opinión del comité", publicado por última vez en 2013.