Storage, transport, and disposition of gametes and embryos: legal issues and practical considerations

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Cryopreservation of reproductive material has dramatically improved clinical outcomes for patients all over the world. At the same time the practice has produced significant legal, ethical, and practical challenges to physicians and practices who use this technique. Failing to meet the expectations of patients, for example by losing material because of a freezer failure, has significant implications for the reproductive facility. Similarly, improperly transporting or receiving gametes or embryos can result in substantial risk to a practice. Perhaps the most widely publicized conundrum is how best to manage embryos that are abandoned. This paper will describe the legal principles and best practices that should be incorporated into the management of a fertility cryopreservation program. (Fertil Steril® 2021;115:274–81. ©2020 by American Society for Reproductive Medicine.)

Key Words: Cryostorage, embryos, gametes, transport of reproductive tissues

The field of freezing in human reproduction has come a long way since the Italian scientist Spallanzani first used snow to cool human sperm in 1776 (1). Since that time, cryopreservation advances have improved the use of artificial insemination and, in the 1980s, affected human pregnancy potential, and the field of reproductive medicine, dramatically with the introduction of human embryo cryopreservation. The first pregnancy was established in 1983 (2), followed by the first live birth from a thawed frozen embryo in 1984 (3). Fast forward another decade, and reproductive medicine achieved and accepted oocyte freezing as another tool to enhance fertility treatment. Today, improved processes of cryopreservation (or "freezing" as it is commonly known) of human sperm, oocytes, and embryos, using vitrification to reduce freezing time and improve survival rates (4), and better culture systems that integrate highly complex media, environmental controls, and technical equipment (5), have become a fundamental part of providing assisted reproductive technology (ART) procedures to patients worldwide (6).

However, the challenges and concerns accompanying all new technologies also apply to the cryopreservation of human reproductive tissue. There are inherent benefits and risks, not only associated with the freezing and thawing process itself but also involving actual and potential legal rights and obligations. There is no denying that gamete (sperm and egg) and embryo freezing have many benefits to patients, including preserving fertility for those facing fertility-compromising medical treatment, optimizing pregnancy success by reducing ovarian hyperstimulation, decreasing the incidence of multiple pregnancies by storing supernumerary embryos for later use, decreasing cost and medical risk of subsequent IVF cycles, increasing the availability of donor gametes and embryos, and allowing time for genetic testing of embryos through preimplantation genetic testing (7). Some researchers have also shown that embryo freezing has increased ongoing pregnancy rates and decreased the cost per live birth (8). However, each of these indications for freezing raises the practical questions of how best to store, transport, and, ultimately, dispose of extraneous gametes and embryos while minimizing the risks that providing cryopreservation imposes on the healthcare provider and the fertility clinic. Clearly, the extensive use of cryopreservation in reproductive medicine has outpaced knowledge of the consequences of its use (9).

As always, medical technology largely races ahead of the law (10). So it is not surprising that regulatory guidance regarding the storage, transport, and disposal of gametes and embryos is seen as disparate, vague, overreaching, or (unfortunately, in some jurisdictions) nonexistent. In the United States, for example, the federal government has a relatively small role in regulating technology such as cryopreservation

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(11). Guidance is often learned as the result of litigated issues rather than through legislative direction—a case of learning from the outcome of someone else's risk event. Even where guidance from professional organizations is available, its applicability to everyday clinic operations may fall short, leaving knowledge gaps. This article will review the various laws, legislative efforts, case law, and professional guidance that apply to storage, transport, and disposal of cryopreserved gametes and embryos. It will also discuss the potential risks and present practical considerations for developing working policies and procedures for the healthcare provider dealing with the day-to-day issues of cryopreservation in the fertility clinic.

THE IMPACT OF ETHICS

Reproductive medicine and law cannot co-exist without considering the ethical concerns raised by cryopreservation of gametes and embryos. Questions about "status" and "value" and "rights" are complex considerations when dealing with these issues (12, 13). Whereas the status of eggs and sperm appears to be somewhat less controversial, issues of value and ownership or control are often raised in instances where losses of irreplaceable gametes occur (14) or the gamete contributor dies (15). Debates over the status, value, and rights of embryos are even more passionately espoused as healthcare providers, ethicists, lawyers, and patients struggle with how to handle human reproductive material or decide who has ownership or control over it (16). This has led to a myriad of approaches from considering embryos as persons to considering them property, or conferring them with an "interim status" as having human potential but not yet life (17). Each approach dictates its own path but must, at a minimum, be considered to better understand the basis for legal determinations (either legislative or judicial), professional guidelines, and practical applications on the management of cryopreserved gametes and embryos.

CRYOSTORAGE OF GAMETES AND EMBRYOS

"§127. Responsibility. Any physician or medical facility who causes in vitro fertilization of a human ovum in vitro will be directly responsible for the in vitro safekeeping of the fertilized ovum." (18). The emphasized language of the Louisiana statute embodies the mantel of protection that placed in that state on fertility providers when it comes to storing gametes and embryos. But first, one must consider whether this practice is even allowed under current law. Regulations vary worldwide from the generally unregulated landscape of North America to European countries where all but a few have regulations on ART (19). Most countries allow for freezing of gametes and embryos; however, some countries ban egg freezing for nonmedical reasons (e.g., Austria, France, Hungary, Lithuania, Malta, Norway, Serbia, and Slovenia) (20), prohibit certain forms of embryo freezing (e.g., Germany permits freezing of "egg cells" at the 2 pronucleic stage only) (21), or limit the practice to certain patient populations only (e.g., Poland, where a recent change to Polish law prevents single women from accessing treatment and prevents them from using previously frozen embryos unless they have a male partner; in addition, their cryopreserved embryos can be given to a married couple without their consent after 20 years) (22). Where cryopreservation is routine, fertility clinics are cast as "keepers" of material that is full of hope and fraught with risks. Some of these risks include storage management, reduced or lost viability of specimens, rejection by gametes donors, and even contamination (6), and the associated costs. However, there are resources to assist in policy development to optimize the storage dilemma and reduce potential liabilities.

The initial storage of gametes and embryos in fertility clinic–linked laboratories is by far the clearest of issues presented by the larger topic of human reproductive tissue cryostorage. Most fertility clinics are well aware of the necessity to follow professional guidelines that recommend—and, in a few jurisdictions, regulatory guidelines that dictate—the use and maintenance of cryostorage tanks. With the recent exposure of several catastrophic gamete and embryo losses in the United States resulting from human error and cryotank failure (23), the field has become even more aware of its obligation to protect the tissue under its care.

Current Legal and Professional Guidance

Today, there is a resurgence of directives aimed at avoiding unintentional or negligent losses of cryopreserved gametes. The European Parliament and the Council of the European Union have encouraged further regulation in the form of a standardized approach to "ensure high standards of quality and safety" regarding cryopreserved tissue, including reproductive tissue. The European Society for Human Reproduction and Embryology, which provides professional guidelines, notes that most countries in the European Union (EU) have legislated assisted reproduction, many including specific regulations on cryostorage. For example, in Finland (24) and the United Kingdom (25), a facility must be licensed before cryostorage is allowed. Other countries may be moving in this direction. Responding to recent gamete and embryos losses in the United States, two states initiated legislation aimed at deterring similar risk events in the future. The New York State Department of Health issued standards for IVF laboratories that include inspections to ascertain that standards are met for the storage and handling of reproductive tissue, including requiring licensing requirements that dictate acceptable equipment and storage conditions and require adherence to relevant professional guidelines (26). At the time of this writing, New Jersey is poised to enact a state statute that would require licensing and regulation of embryo storage facilities, including fertility clinics (27).

Aside from the few noted legislative efforts, the everyday care and storage of gametes and embryos in the United States is generally guided by standards set by professional organizations. The College of American Pathologists, which accredits ART laboratories, upon request provides checklists and reviews of some practices aimed at quality control for cryostorage, namely, monitoring liquid nitrogen levels within cryotanks and monitoring any alarm system that may be in use for such cryotanks (28). The American Association of Tissue Banks (AATB) guidance for cryopreservation storage and

specimen handling arguably covers ART laboratories in its definition of a biorepository (29); however, many fertility clinics do not accept its recommendations as binding. The Practice Committee of the American Society for Reproductive Medicine (ASRM) recently provided more detailed guidance for cryostorage, which emphasized best practices, including limited access to cryostorage tanks, easily observed cryostorage rooms, adherence to manufacturer's recommendations for cryotank use, quality control for liquid nitrogen and oxygen monitoring, cryostorage tank alarm systems, and storage tank inventories (30).

One of the predominant concerns regarding cryostorage of embryos revolves around the length of time that embryos may be stored. Questions of reduced viability over time continue to be expressed, even in the face of studies that prove otherwise (31). Various authors present embryo storage data in the United States from a 2002 survey as roughly 400,000 embryos cryopreserved and a 2011 survey noting 615,000 embryos cryopreserved. Arguably, a straight linear projection of an increase of roughly 50% over 9 years would hold that today there may be upwards of 900,000 embryos cryopreserved. This number, however, does not consider the use of new treatment protocols for reducing ovarian response and the creation of fewer embryos per cycle, nor the increasing use of oocyte freezing. Therefore, with a calculated 900,000 to 1,000,000 embryos currently in storage in the United States alone, storage limitations and final disposition arrangements are significant factors in establishing practical approaches to the fill gaps left by current regulations and guidelines.

Practical Considerations for Fertility Clinics

Cryostorage processes for sperm, eggs, and embryos inside the fertility clinic should address the potential known and foreseeable risks associated with cryopreservation, such as specimen loss due to equipment failure or human error, loss as a result of mislabeling, accidental destruction, reduced viability over time, cross-contamination of specimens, and staff safety (32). General items to be included in the development of policies to manage cryostorage risk include the following:

- Identifying the applicable cryostorage law, regulation, or judicial outcome and appropriate professional guidelines relevant to the clinic's geographic area, and incorporating any requirements into practice.
- Surveying the location of cryopreservation storage units to evaluate for accessibility, safety, and security for maintaining tank integrity and temperature uniformity, which is necessary to protect cryopreserved material and staff.
- Ensuring that liquid or vapor nitrogen tanks are in good condition, operational, and stored properly in a well-ventilated area. Oxygen monitors are strongly recommended.
- Developing routine cryopreservation equipment and tank management processes to include regular equipment and tank inspection, as well as repair and replacement based on manufacturer's guidelines and standard industry usage.
- Installing locking and electronic monitoring systems on all cryopreservation storage tanks. This should include appropriate monitoring probe placement within the tanks, multiple alarm notification pathways, and backup energy supplies (i.e., generators or batteries).
- Maintaining executed cryopreservation agreements with depositors that address cryopreservation processes, location and duration of storage, storage fees, depositor's obligation to maintain contact, off-site transfer permission (if applicable), and clear final disposition instructions.
- Developing protocols to reduce specimen loss during inventory (e.g., consider automated identification) and contamination during process and storage (e.g., consider sterilization of liquid nitrogen and universal precautions).
- Addressing emergency and disaster responses, including staff safety, availability of first aid, cryostorage tank security, backup facilities, processes for closure and/or movement of cryopreserved gametes and embryos to alternative location(s) as needed.
- Initial and periodic mandatory training of all embryology and andrology personnel on cryopreservation and cryostorage processes, policies, and procedures.

TRANSPORTING GAMETES AND EMBRYOS

As the world economy becomes more global, so does reproductive care. Domestic and international movement of gametes and embryos are seen every day as patients relocate or move their care to different clinics both within and outside their home countries. Prompted by reasons from access to better care and more services to removing legal barriers and improving availability of donors or surrogates to lowering costs, a recent review of cross-border reproductive care showed an upward trend of people traveling outside their home countries for ART treatments (33). In addition, more fertility clinics are opting for off-site storage because of space constraints, cost factors, or avoidance of final disposition risks, and the minimal data available show little detriment to survival, implantation, and pregnancy outcomes (34). As reproductive care travels, so will cryopreserved gametes and embryos, and the regulations and best practices for getting cryopreserved material safely from point A to point B will be tested.

Current Legal and Professional Guidance

Transporting human tissue, including cryopreserved gametes and embryos, has become a growing business. Today, a quick internet search results in a long list of commercial businesses involved in the routine transport of gametes and embryos from state to state and across the world. However, the outcome of an early legal tussle over "I want to move my embryos to California" (35) stands to remind us that patients have a say in where their gametes and embryos will be stored or used. That does not necessarily mean that the transport is risk free or that the law of the intended transporting or receiving entity/country allows such transfer.

A serious consideration is the mode and method of gamete and embryo transport. Although commercial transport websites imply that moving embryos is relatively risk free (36, 37), recent studies report that methods of shipment and types of transportation matter. Liquid nitrogen vapor

containers or "dry shippers" (cryotanks filled with liquid nitrogen that is absorbed into porous interior packing material) are commonly preferred for air transport, whereas liquid nitrogen–filled tanks are more often seen in shorter, land-based travel because of the specific requirements and risks of each mode of transport (6). Damage to vitrified oocytes has been reported from factors such as vibration/movement, increased temperature, air pressure, and horizontal tank positioning during transport (38). Furthermore, loss of survival of vitrified oocytes was reportedly lessened with the use of a road courier as opposed to air transport (39). Moving embryos can be risky business for all parties, as was seen in a 2017 federal lawsuit when the embryos arrived at their destination in a nonviable state. The devastated intended parents sued for destruction of embryos resulting from improper shipping practices, including claims against the sending long-term storage facility (party who packed the shipper), the shipping company (employer of the worker who opened the container because he saw "gas" escaping), and the receiving fertility clinic (party who unpacked the shipping container) (40). But documented incidents are only one guiding force in how to move embryos.

As with cryostorage, regulations governing the transportation of gametes and embryos vary around the globe and are most easily divided into those that determine operational aspects of shipping and those that limit transport. An example of operational legislation is seen under the United Kingdom's Human Fertilisation and Embryology Authority (HFEA) which has clearly stated rules for importing and exporting gametes and embryos. These rules include packaging and labeling of cryoshipped specimens, restrictions on sending gametes or embryos to an unlicensed clinic, and even a requirement for written agreements if third-party carriers are used (41). EU transport is fairly easy among the EU countries, requiring, among specific packaging guidelines, a written confirmation of acceptance from the receiving clinic as well as documentation of infectious disease testing compliance. Gametes and embryos coming into the United States may need to meet US Food and Drug Administration tissue guidelines (42) and are subject to United States customs inspections (which has caused some problems in the past as a result of delays in processing) (43). A commercial invoice describing the contents and value of cryopreserved material is also required. Importing and exporting patient specimens in and out of the United States may also trigger compliance with some of the regulations of the International Air Transport Association and the Federal Department of Transportation (44). For example, under the Federal Aviation Association, airlines may allow the transport of cryopreserved material if it is contained in a dry shipper where the liquid nitrogen is completely absorbed in a porous lining, there is no liquid, and regardless of package position the liquid nitrogen cannot escape (45) Other countries may require the receiving clinic to have certain certification (import/export certificates that prove the authorization to receive the shipment) or the courier to be certified or approved. Finally, before moving gametes or embryos, it is important to ascertain whether the receiving jurisdiction has any restrictions on the importation/exportation of gametes or embryos or whether it even allows for cryostorage of specific reproductive material. For example, some Australian states must approve the import or export of donor gametes/embryos, and some centers refuse to accept commercially obtained donor gametes (46). As discussed in the section on disposition of gametes and embryos below, some countries ban cryostorage of certain reproductive material, and shipped specimens may be refused when they reach the intended destination.

Sources for direction in transporting gametes and embryos can also be found in guidelines published by various professional organizations. While specifically relevant to accredited tissue banks, the AATB provides general guidance that can be applied to frozen gamete and embryo transport (47). Other organizations such as the ASRM, for example, have developed online training material for the embryology laboratory that specifies appropriate measures for packaging, transporting, and receiving cryopreserved gametes and embryos (48). Although moving gametes and embryos does not fall under medical treatment, which would trigger traditional concepts of informed consent, full disclosure and acknowledgement of the risks involved must be conveyed to the gamete/embryo owners. Candid discussions of potential losses and the limitations of the fertility clinic's ability to control or predict such losses should be explained to the patient(s), and their understanding and acceptance of the risks should be well documented.

Practical Considerations for Fertility Clinics

Recommendations for the safe transport of gametes and embryos must include full compliance with all applicable state and national laws and regulations. It is also essential to consider the rules that may be applied by the receiving jurisdiction and any other jurisdiction that the material may pass through on the way to its final destination. In short, the process of transport starts with an understanding of what is being shipped and where is it coming from and going to.

This information gathering can sometimes be time-consuming and daunting for gamete and embryo owners and for clinic and embryology staff who assist in the process. Risk assessment, management, and liability reduction regarding transporting gametes and embryos requires developing current policies and procedures that include the following:

- Appropriate informed consent for the movement of cryopreserved material out of one facility and into the receiving facility (generally, seen in two documents), with full discussion of risks and benefits.
- Discussion and selection of the most efficient and safest method of transport, and by whom, including transport by road or air, using a commercial transport company by road or air, as determined by the clinic or by the patient.
- Appropriate packing policies and procedures that address, among other items, what materials and cryopreservants (dry shipper vs. liquid nitrogen) are allowed, labeling

requirements, and time constraints (how long is shipper tank safe for use while in transport).
- Clear understanding of shipping policies and requirements/limitations of shipping by road or by air, as well as the ability to discern any conditions or restrictions that the receiving country or facility may impose on transporting gametes or embryos.
- Essential training (initial and periodic) for all andrology, embryology, and administrative staff on packing and transport policies and procedures.

DISPOSITION OF GAMETES AND EMBRYOS

The gametes or embryos are frozen, and they are at the appropriate location as chosen by the gamete or embryo owners; now what? For most patients, the gametes or embryos will be used over a defined period of time for their own treatment cycles to create a pregnancy. However, there are many reasons why cryopreservation may continue for a longer period than initially intended. According to many experts, gametes and embryos can be retained in a cryopreserved state for decades and still be viable (49). This suggests a possible endless storage period that patients may assume for various reasons as they wait for the "right time" to have a child or grow their family (be it for medical or social reasons), navigate a split in their relationship, "forget" they have gametes or embryos in cryostorage, or find a final disposition decision so difficult that they choose passivity and allow the cryostorage to continue indefinitely (50). While disposing of sperm or eggs appears easier to accept, stopping cryopreservation for embryos becomes more problematic because of the overlay of ethical issues involving an embryo, discussed above.

Generally, there are five choices for embryo disposition: thaw and transfer for intended parent's pregnancy attempt; donate to another individual/couple for a pregnancy attempt; donate for research (or clinical training); thaw and discard; or what has sometimes been described as a nonchoice, maintain indefinitely in cryostorage (an option that is no longer typically offered but that may be done passively by patients avoiding contact with the clinic) (9). Studies show that given these disposition options, over 50% of patients were likely to choose to use cryopreserved embryos for their own family building, another roughly 20% would choose donation to research, and donating to others or thawing and discarding were less likely choices (51). Ending cryopreservation of gametes and embryos is clear when the gamete/embryo owners make their choice known in a written disposition agreement and the cryostorage facility/fertility clinic has specific written policies regarding gamete and embryo disposal. But that still leaves the disposition of excess gametes and embryos for which there is no disposition declaration, or the gamete owners are not available to make a disposition decision. Further, questions also arise as to whether disposition agreements (also deemed advanced directives) made at the time of embryo creation remain valid when storage limits are reached (52). The concern over the growing number of delinquent cryostorage accounts and "unclaimed" or "unused" gametes and embryos remaining in storage without any disposition decisions is a real dilemma for fertility clinics. This issue has led to increasing legislation and professional guidelines regarding how long embryos can remain in cryostorage and what will be done with them when the cryostorage period ends.

Current Legal and Professional Guidance

While patients wrestle with the decision to stop cryopreservation, some government authorities have limited the decision-making process by law, setting finite time frames for gamete or embryo storage and/or determining the method of disposition. Arguably an infringement of a patient's right over their reproductive tissue, these time frames provide a "hard stop" for cryopreservation and a clear disposition decision. Such clarity assists both fertility clinics in managing cryopreserved embryos and disposition policies, and patients in making decisions for treatment and final disposition.

Maximum storage times for frozen gametes exist in a few areas and are growing as egg freezing becomes more prevalent. In the Australian states of Victoria and Western Australia, gametes may be frozen for up to 10 years and 15 years, respectively (53). The United Kingdom allows cryostorage of eggs and sperm for up to 10 years with some extensions (i.e., eggs may be held longer if they were frozen because of a medical diagnosis, and some sperm freezing may be extended to 55 years in some cases) (54). However, as in Canada, Spain, and the United States, many countries do not currently have legislated time limits on egg and sperm cryostorage.

Embryos are another story. Entangled with ethical concerns and differing definitions of an embryo, legislative cryostorage limits often include policy considerations such as reducing the number of stored embryos and lifting the storage burden for clinics (53). This has led to numerous maximum embryo cryostorage limitations after which destruction is mandated. Denmark has a 5-year limit on cryopreservation storage of embryos. Switzerland, the United Kingdom, New Zealand, and some Australian states have enacted 10-year storage limits. Finland (55) and at least one Australian state allow for 15 years (53). Poland has a recently legislated 20-year storage limit; however, the embryos cannot be destroyed but must be donated to another infertile couple (56). Although the United States has no federal law on cryostorage limits or disposition, at least one state has banned embryo destruction (57), and others have limited disposition choices through judicial determinations. With the exception of Quebec, where disposal is at the clinic's discretion, Canada's limitations on embryo storage have also been mostly left to judicial action (58, 59).

Mandated storage limits and directed disposition laws are useful in reducing stored reproductive tissue, but jurisdictions without such laws can look to professional guidelines for some direction. The ASRM Ethics Committee guidelines for treating excess, and perhaps unclaimed, embryos emphasize the need for clinics to counsel patients on disposition options and to have written policies and procedures that address retention processes and also disposal processes if the depositors have not been in contact with the clinic for a reasonable

amount of time (60). In Australia, clinics can look to the Fertility Society of Australia and Reproductive Technology Accreditation Committee's *Code of Practice for Assisted Reproductive Technology Units* (RTAC Code) for further guidance. Incorporating ethical guidelines for the National Health and Medical Research Council, the RTAC Code as adopted by various Australian states sets forth guidelines regarding cryostorage and disposition (53).

Disposition procedures in jurisdictions where laws mandate disposal or donation at set times are easily transferred into compliant clinic policies. The more concerning problem arises when the depositors are unavailable to make a contemporaneous disposal determination (if legally required) and the clinic has no clear regulatory guidance to follow. Further, the burden becomes larger when clinics are hesitant to follow guidelines alone or their own internal policies regarding disposal of gametes and embryos because of fear of legal liability.

Practical Considerations for Fertility Clinics

Managing cryopreserved gametes and embryos and disposal decisions can be a complex process, especially for fertility clinics that are highly risk averse. Initially, a clinic must decide whether it is willing to provide long-term cryostorage (which will potentially trigger future decisions to discard unclaimed reproductive tissue) or whether it will use off-site long-term storage companies for gametes and embryos preserved in its laboratories (which shifts some of the risk to the off-site facility). Operational decisions may also vary based on whether the clinic is initiating its cryostorage program or whether it finds itself with an abundance of unclaimed gametes and embryos.

How and when to dispose of cryopreserved semen specimens and embryos where the facility does not have clear disposition direction from the gamete/embryo owners (also called the "depositor") remains a dilemma for many fertility clinics, particularly where there is no federal or state regulation that specifically addresses the issue. In fact, those who must make the decision on whether to stop cryopreservation may feel significant social and psychological pressure, which add to the controversy (9). Disposition then becomes an issue of how risk-averse a fertility clinic's owners are, the tenor of the clinic's home state regarding the legal status of sperm/embryos (as seen in state case law), and well-written cryopreservation policies and patient-signed documents. These three factors must be considered before any determination on disposition is made to assess the best approach for your center.

- How risk-averse are you? The risk in any disposition is that a depositor will return to claim their sperm, eggs, or embryos after the cryopreserved material has been disposed of and will either file a lawsuit against the fertility clinic for the loss or drag the clinic into a dispute between depositors. Depositor's claims that this property is irreplaceable are financially and emotionally draining. The most risk-averse fertility clinics are maintaining cryopreserved gametes and embryos if they do not have up-to-date disposition instructions (even if earlier instructions are on record). Others are expending resources on contacting patients again, and the least risk-averse centers are disposing of cryopreserved material on a routine basis in accordance with various written disposition policies and depositors' directions in consent forms and medical records.
- What do your home country/state laws say about gamete and embryo disposition? An initial search of current laws (they change all the time), pending regulations, or the outcomes of relevant lawsuits on disposal of gametes or embryos in the governing jurisdiction is advised. This may require the assistance of an attorney to determine any potential liability that is not easily apparent.
- What do your policies say? A well-written policy that is communicated to depositors and followed by the clinic is necessary to avoid future unclaimed property concerns, costs, and anxiety. In the absence of a written policy on cryopreserved gametes or embryos, or in cases where policies are unclear or not followed, observers (lawyers and judges) look to a fertility clinic's routine operational practices and the forms used for cryopreservation permission (often referred to as cryo consent forms or, more recently, cryopreservation disposition contracts or agreements) as documentation of the clinic policy. The danger in this is that practices and forms may change or evolve over time, leading to inconsistencies in handling depositors' accounts. Furthermore, policy language may not be embodied in documents. This creates confusion in how to handle storage accounts that are unpaid and gametes and embryos that are unclaimed over a long period of time.

To avoid increasing uncertainty, general considerations for developing a program for cryopreserved gametes and embryos disposition should include the following steps. Most importantly, once adopted, any disposal policies devised should be followed as written. Furthermore, a patient's valid disposal request, in a cryo consent form or otherwise, should be acted on and not deferred. These strategies will reduce future indecision and disposal questions, which lead to more accumulated gametes and embryos.

- Create detailed policies and procedures for cryopreserved sperm, eggs and embryos to include specific information on the following:
  - Conditions for cryopreservation (e.g., IUI, IVF, fertility preservation).
  - Maximum duration of storage in house.
  - Conditions requiring transfer to long-term storage, if applicable.
  - Definition of "unclaimed" gametes and embryos (i.e., account unpaid for x months, no contact after x period).
  - Reasonable efforts to contact after deemed unclaimed (e.g., number of attempts by telephone, e-mail, postal service).
  - Criteria for sending delinquent accounts to collections and/or using a skip-tracer service can be used to locate depositors.
  - Processes for immediate discard when the depositor specifically requested disposal after a certain time and that time has elapsed, contact attempts are futile over a

period of years (e.g., 5 years or more) and the depositors have a written determination on file, or contact attempts are futile over a period of years (e.g., 5 years or more) and the depositors do not have a written determination on file but are deceased or beyond reproductive age.
  - Immediate destruction if no response to reasonable, repeated contact attempts after the agreed-upon storage time elapses.
- Draft and use documents (i.e., cryo consent forms, disposition contracts) that clearly explain all disposition options, the storage limits, and final disposition if depositors become unavailable. These documents should include all policy and procedure considerations and specific depositor contact information, and should be fully completed and witnessed before cryopreservation is initiated.
- Consider using e-mail addresses and social media contact information as a method for tracking patients. Individuals tend to change these less frequently than telephone numbers and residence or workplace addresses.
- Provide initial counseling to patients on the available disposition options, their freedom to change disposition designations, and the process to do so, and the clinic's policies and procedures regarding embryo cryopreservation, retention, and final disposition. Offer patients adequate time to consider all options with appropriate legal advice.
- Provide training for all staff on how to explain disposition options correctly to depositors, the specifics of all relevant policies and procedures, and the importance of finalizing all disposition documents before cryopreservation is undertaken.

CONCLUSION

Cryopreservation of gametes and embryos in ART is here to stay and, by some accounts, is growing (61). Storage, transport, and disposition issues will continue to arise and become more complex as reproductive medicine develops more technology and treatments. The influence of genetic technology and changing generational attitudes toward cryopreserved material will also add significant challenges. Additional discussion and guidance are needed at legislative and organizational levels to assist fertility providers and clinics in determining the best approach to management of cryopreserved reproductive material. Global collaboration regarding the scientific, ethical, and social issues involved are key components necessary to providing consistent frameworks for determining the future of cryopreserved gametes and embryos.

REFERENCES

1. Ombelet W, Van Robays J. Artificial insemination history: hurdles and milestones. Facts Views Vis Obgyn 2015;7:137–43.
2. Trounson A, Mohr L. Human pregnancy following cryopreservation, thawing and transfer of an eight-cell embryo. Nature 1983;305:707–9.
3. Zeilmaker GH, Alberda AT, van Gent I, Rijkmans CM, Drogendijk AC. Two pregnancies following transfer of intact frozen-thawed embryos. Fertil Steril 1984;42:293–6.
4. Konc J, Kanyó K, Kriston R, Somoskői B, Cseh S. Cryopreservation of embryos and oocytes in human assisted reproduction. Biomed Res Int 2014;2014:307268.
5. Swain JE, Carrell D, Cobo A, Meseguer M, Rubio C, Smith GD. Optimizing the culture environment and embryo manipulation to help maintain embryo developmental potential. Fertil Steril 2016;105:571–87.
6. Alikani M, Parmegiani L. Human reproductive cell cryopreservation, storage, handling, and transport: risks and risk management. Semin Reprod Med 2018;36:265–72.
7. Bosch E, De Vos M, Humaidan P. The future of cryopreservation in assisted reproductive technologies. Front Endocrinol 2020;11:67.
8. Van Der Westerlaken L, Naaktgeboren N. Contribution of embryo cryopreservation to the pregnancy/delivery rates in an IVF/ICSI programme with the single embryo transfer. Presented at the 19th Annual Meeting of the European Society of Human Reproduction and Embryology, Madrid, Spain, June 2003.
9. Bankowski BJ, Lyerly AD, Faden RR, Wallach EE. The social implications of embryo cryopreservation. Fertil Steril 2005;84:823–32.
10. Burger WE. Reflections on law and experimental medicine. In: Smith GP, editor. Ethical, legal and social challenges to a brave new world. Tarrytown, NY: Associated Faculty Press; 1982.
11. Blake VK, McGowan ML, Levine AD. Conflicts of interest and effective oversight of assisted reproduction using donated oocytes. J Law Med Ethics 2015;43:410–24.
12. Prescott DE, Debele GA. Shifting ethical and social conundrums and stunningly anachronistic laws: what lawyers in adoption and assisted reproduction may want to consider. J Am Acad Matrim Law 2017;30:127.
13. Crockin SL, Debele GA. Ethical issues in assisted reproduction: a primer for family law attorneys. J Am Acad Matrim Law 2015;27:289–308.
14. Letterie G, Fox D, Lawsuit frequency and claims basis over lost, damaged, and destroyed frozen embryos over a 10-year period, Presented at the 75th Annual Meeting of the American Society Reproductive Medicine, Philadelphia, Pennsylvania, October 12–16, 2019.
15. Bahadur G. Ethical challenges in reproductive medicine: posthumous reproduction. Int Congr Ser 2004;1266:295–302.
16. Casolo J, Curry-Ledbetter C, Edmonds M, Field G, O'Neill K, Poncia, M (Eds.). Assisted reproductive technologies. Georgetown J Gender Law 2019;2:313–354.
17. Crockin SL, Gottschalk KC. Legal Issues in gamete and embryo cryopreservation: an overview. Semin Reprod Med 2018;36:299–310.
18. LA Rev Stat 9 §127, Responsibility.
19. Calhaz-Jorge C, De Geyter C, Kupka M, Wyns C, Mocanu E, Motrenko T, et al. Survey on ART and IUI: legislation, regulation, funding and registries in European countries: The European IVF-monitoring Consortium (EIM) for the European Society of Human Reproduction and Embryology (ESHRE). Hum Reprod Open 2020;1:hoz044.
20. European Society of Human Reproduction and Embryology. Europe moves towards complete statutory regulation of ART. Available at: https://www.eurekalert.org/pub_releases/2020-02/esoh-emt020320.php. Accessed September 24, 2020.
21. Trappe H. Assisted reproductive technologies in Germany: a review of the current situation. In: Kreyenfeld M, Konietzka D, editors. Childlessness in Europe: contexts, causes, and consequences. Demographic Research Monographs (A series of the Max Planck Institute for Demographic Research). Cham: Springer; 2017 https://doi.org/10.1007/978-3-319-44667-7_13.
22. Brennan B. Single woman in Poland? Your embryos could be given to another couple. Available at: https://mobile.abc.net.au/news/2019-11-24/single-women-in-poland-embryos-could-be-given-to-others/11706842. Accessed September 30, 2020.
23. Fox D. The legal limbo of lost embryos. Available at: https://blog.petrieflom.law.harvard.edu/2019/07/08/the-legal-limbo-of-lost-embryos/. Accessed September 24, 2020.
24. Ministry of Justice, Finland. Act on assisted fertility treatments (1237/2006), Section 24. Available at: https://www.finlex.fi/en/laki/kaannokset/2006/en20061237.pdf. Accessed October 1, 2020.
25. Human Fertilisation and Embryology Act 1990. Anyone who is involved in the procurement, testing, processing, preservation, storage and distribution

of gametes, embryos or provide in-vitro fertilisation or artificial insemination treatments must obtain a license from the HFEA.
26. New York State Department of Health. Executive summary of assisted reproductive technologies: analysis and recommendations for public policy. Available at: https://www.health.ny.gov/regulations/task_force/reports_publications/execsum.htm. Accessed November 5, 2020.
27. State of New Jersey. An act concerning the regulation and licensure of embryo storage facilities and supplementing Title 26 of the Revised Statutes. (S-3075). Available at: https://www.njleg.state.nj.us/2018/Bills/A5000/4605_I1.HTM. Accessed November 5, 2020.
28. College of American Pathologists. Accreditation checklists. Available at: https://www.cap.org/laboratory-improvement/accreditation/accreditation-checklists. Accessed November 5, 2020.
29. AATB Guidance. Current good tissue practices [No. 3, June 27, 2006]. Available at: https://www.aatb.org/sites/default/files/AATB%20Guidance%20Document%20No.%203%20%286.27.06%29.pdf. Accessed September 28, 2020.
30. Practice Committee of the American Society for Reproductive Medicine. Cryostorage of reproductive tissues in the in vitro fertilization laboratory: a committee opinion. Feril Steril 2020;114:486–91.
31. Ueno S, Uchiyama K, Kuroda T, Yabuuchi A, Ezoe K, Okimura T, et al. Cryostorage duration does not affect pregnancy and neonatal outcomes: a retrospective single-centre cohort study of vitrified-warmed blastocysts. Reprod BioMed Online 2018;36:614–9.
32. Schiewe MC, Freeman M, Whitney JB, VerMilyea MD, Jones A, Aguirre M, et al. Comprehensive assessment of cryogenic storage risk and quality management concerns: best practice guidelines for ART labs. J Assist Reprod Genetics 2019;36:5–14.
33. Salama M, Isachenko V, Isachenko E, Rahimi G, Mallmann P, Westphal LM, et al. Cross border reproductive care (CBRC): a growing global phenomenon with multidimensional implications (a systematic and critical review). J Assist Reprod Genetics 2018;35:1277–88.
34. Senn S, Nehchiri F, Artac R, Dangcil M, Rabara F, Dasig D, Shipping cryopreserved embryos to long-term storage. Abstract presented at the annual meeting of the American Society for Reproductive Medicine, October 19, 2009; Atlanta, Georgia.
35. York v. Jones. 717 F. Suppl. 421 (E.D. Va. 1989).
36. Made in the US Surrogacy. Can I transport frozen embryos?. Available at: https://madeintheusasurrogacy.com/can-i-transport-frozen-embryos-ivf/. Accessed November 5, 2020.
37. CryoStork. Frequently Asked Questions: What you need to know about transporting frozen embryos, sperm, and IVF samples safely & securely with CryoStork. Available at: https://mycryostork.com/faq-shipping-frozen-embryos-sperm-safely-cost-insurance/. Accessed November 5, 2020.
38. McDonald CA, Valluzo L, Chuang L, Poleshuk F, Copperman AB, Barritt J. Nitrogen vapor shipment of vitrified oocytes: time for caution. Fertil Steril 2011;95:2628–30.
39. Parmegiani L, Maccarini AM, Rastellini A, Bernardi S, Troilo E, Arnone A, et al. Oocyte vitrification/storage/handling/transportation/warming, effect on survival and clinical results in donation programmes. Curr Trends Clin Embryol 2017;4:34–40.
40. Lucio v. UPS Co. Case No. 9:16-CV-81703-RLR (S.D. Fla. Jan. 31, 2017).
41. Human Fertilisation and Embryology Authority. Code of Practice, 9th Ed. Guidance Note 15. Available at: https://portal.hfea.gov.uk/media/1527/2019-12-16-code-of-practice-9th-edition-december-2019.pdf. Accessed September 28, 2020.
42. FDA Compliance Program Guidance Manual. Imported human cells, tissues, and cellular and tissue-based products (HCT/Ps) 7342.007 Addendum, Section III B(4). Available at: https://www.fda.gov/media/73960/download. Accessed September 30, 2020.
43. U.S. Customs and Border Protection. What you need to know before importing biologic material into the U.S. Available at: https://www.cbp.gov/trade/basic-import-export/what-you-need-know-importing-biological-materials-united-states. Accessed September 24, 2020.
44. University of Pennsylvania Environmental Health & Radiation Safety. Shipping manual for infectious substances, biological materials, and dry ice. Available at: https://ehrs.upenn.edu/sites/default/files/2018-02/Shipping%20October%202017r_0.pdf. Accessed September 30, 2020.
45. 49 CFR 175.10(a)(24).
46. Jefford S. Importing and exporting embryos. Available at: https://sarahjefford.com/importing-and-exporting-embryos/. Accessed September 30, 2020.
47. AATB. Guidance document, qualification of packaging and validation of shipping/transport procedures [No. 9, October 23, 2017]. Available at: https://www.aatb.org/sites/default/files/sites/default/files/private/AATB%20Guidance%20Doucment%20No.%209%20final%2010.23.17%5B1%5D.pdf. Accessed November 5, 2020.
48. American Society for Reproductive Medicine. AirLearning Course, LAB126: Management of cryopreserved gametes and embryos. Available at: https://airlearning.asrm.org/pluginfile.php/3098/mod_resource/content/5/LAB126_Lesson.pdf. Accessed September 30, 2020.
49. Aflatoonian N, Pourmasumi S, Aflatoonian A, Eftekhar M. Duration of storage does not influence pregnancy outcome in cryopreserved human embryos. Iran J Reprod Med 2013;11:843–6.
50. Vaughn R. Uniform laws needed to regulate abandoned embryos. Available at: https://www.iflg.net/laws-needed-abandoned-embryos/. Accessed September 24, 2020.
51. Lyerly AD, Steinhauser K, Voils C, Namey E, Alexander C, Bankowski B, et al. Fertility patients' views about frozen embryo disposition: results of a multi-institutional U.S. survey. Fertil Steril 2010;93:499–509.
52. Pennington G. The validity of contracts to dispose of frozen embryos. J Med Ethics 2002;28:295–8.
53. Stuhmcke A, Chandler E. Storage limits of gametes and embryos: regulation in search of policy justification. J Law Med 2014;22:121–35.
54. Human Fertilisation and Embryology Authority. Code of Practice, Guidance Note 17. Available at: https://www.hfea.gov.uk/media/2565/hfea-draft-code-of-practice-9th-edition-consultation-version.pdf. Accessed September 29, 2020.
55. Act on Assisted Fertility Treatments (1237/2006). Available at https://www.finlex.fi/en/laki/kaannokset/2006/en20061237.pdf. Accessed January 5, 2021.
56. Sussman AL. When the government seizes your embryos. Available at: https://www.newyorker.com/tech/annals-of-technology/when-the-government-seizes-your-embryos?utm_source=onsite-share&utm_medium=email&utm_campaign=onsite-share&utm_brand=the-new-yorker. Accessed November 5, 2020.
57. LA Rev Stat §9:129.
58. Lam v. University of British Columbia. 2013 BCSC 2142.
59. Cattapan A, Baylis F. Frozen in perpetuity: 'abandoned embryos' in Canada. Reprod BioMed Online 2016;108:104–12.
60. Ethics Committee of the American Society for Reproductive Medicine. Disposition of abandoned embryos: a committee opinion. Fertil Steril 2013;99:1848–9.
61. Christianson MS, Stern JE, Sun F, Zhang H, Styer AK, Vitek W, et al. Embryo cryopreservation and utilization in the United States from 2004-2013. F&S Rep 2020;1:71–7.