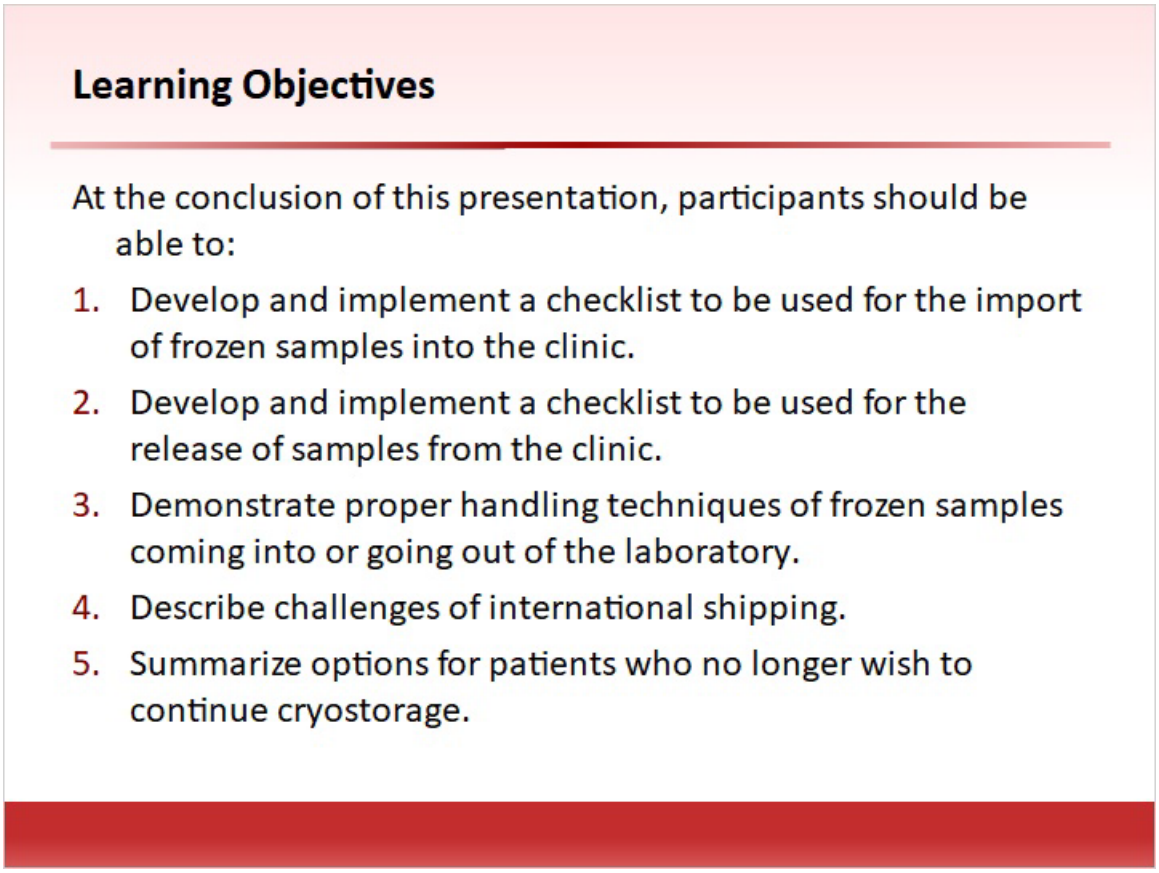
LABCC100 Lesson 26

1.1 Management of Cryopreserved Gametes and Embryos

Notes:

Welcome to the American Society for Reproductive Medicine's eLearning modules. This module discusses the Management of Cryopreserved Gametes and Embryos.

1.2 Learning Objectives

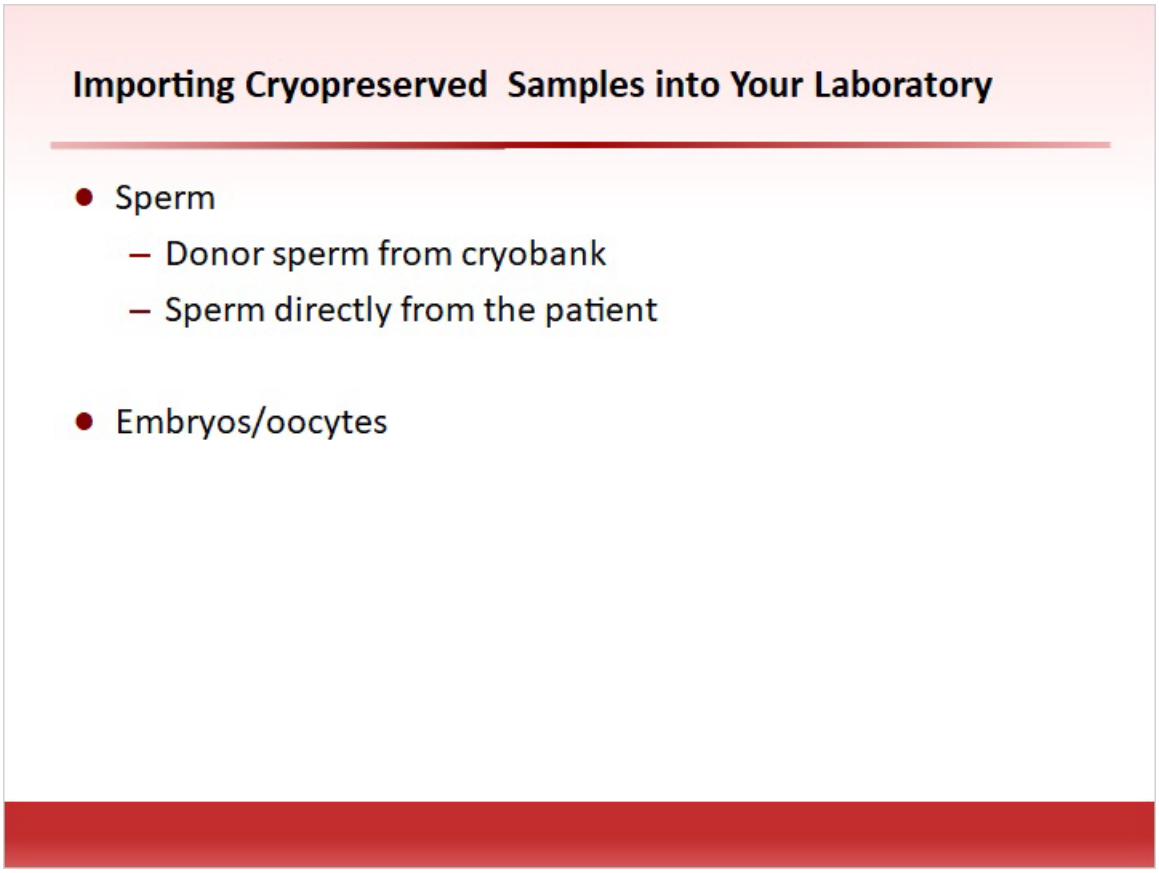


Notes:

At the conclusion of this presentation, participants should be able to:

1. Develop and implement a checklist to be used for the import of frozen samples into the clinic.
2. Develop and implement a checklist to be used for the release of samples from the clinic.
3. Demonstrate proper handling techniques of frozen samples coming into or going out of the laboratory.
4. Describe the challenges of international shipping.
5. Summarize options for patients who no longer wish to continue cryostorage at your facility.

1.3 Importing Cryopreserved Samples into Your Laboratory



Notes:

Several different types of reproductive tissues may come into the laboratory, including sperm, oocytes and/or embryos. Sperm may arrive in a dry shipper from a cryobank, or they may be delivered frozen by the patient himself on dry ice. It is extremely important that frozen samples be handled correctly for the best results.

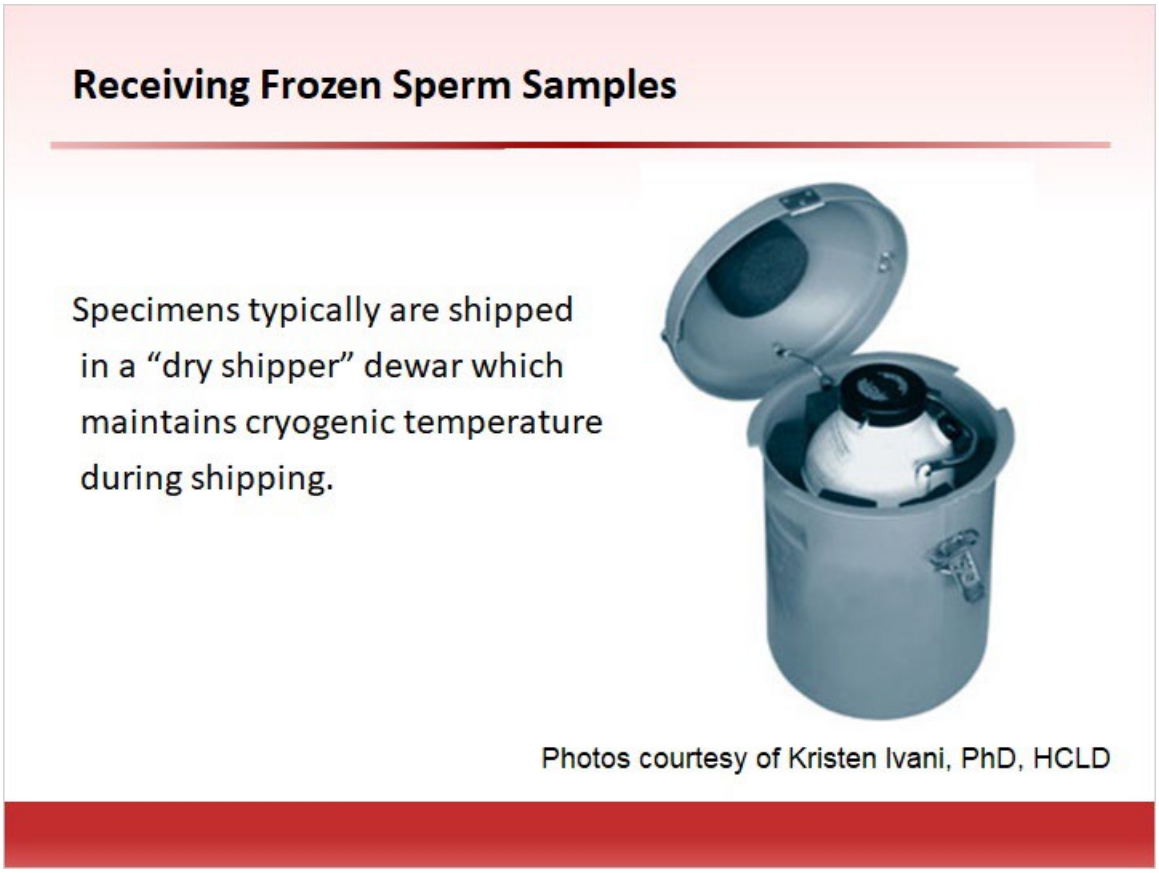
1.4 How Do Samples Arrive at Your Clinic?

Notes:

Frozen samples of any type generally arrive by one of 4 methods:

1. A national or international shipping company may deliver the dry shipper tank to the clinic.
2. A specialized courier or supply chain service may be used.
3. Larger metropolitan areas may have a local courier experienced in the handling of frozen biological materials.
4. Samples may be transported from one clinic to another by the patient or partner. These samples may be delivered in a dry shipper, on dry ice, or even at body temperature.

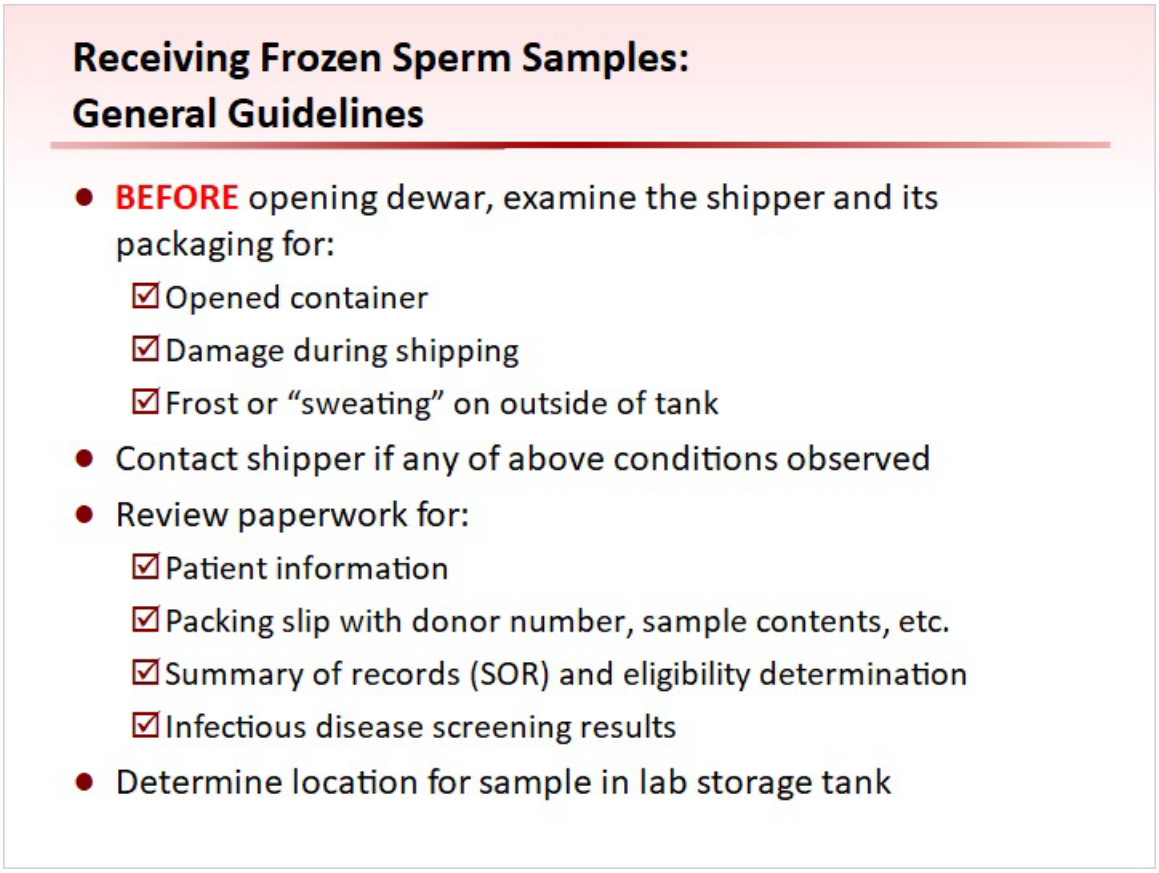
1.5 Receiving Frozen Sperm Samples



Notes:

Most frozen sperm samples are delivered to the lab in a "dry shipper" dewar. The dry shipper is used to maintain proper cryogenic temperature during shipping. Generally a dry shipper will maintain this temperature for up to 7 days. While not required, securing the dry shipper dewar in a hard plastic carrier, as shown here, or a designated dewar-sized cardboard box is recommended to prevent tipping of the dewar during shipping.

1.6 Receiving Frozen Sperm Samples:



Notes:

Laboratory personnel should be properly trained before being allowed to open any shipping dewars containing frozen biological materials! Before opening the dewar itself, it is important to examine the shipper and its container as damage may occur during the shipping process. The shipper and its packaging should be closed securely upon arrival to the clinic. Look closely for any signs of damage to the shipper, including the lid and the vacuum plug near the lid. Look for any frost or "sweating" on the outside of the tank—these may indicate vacuum failure and potential loss of the samples within.

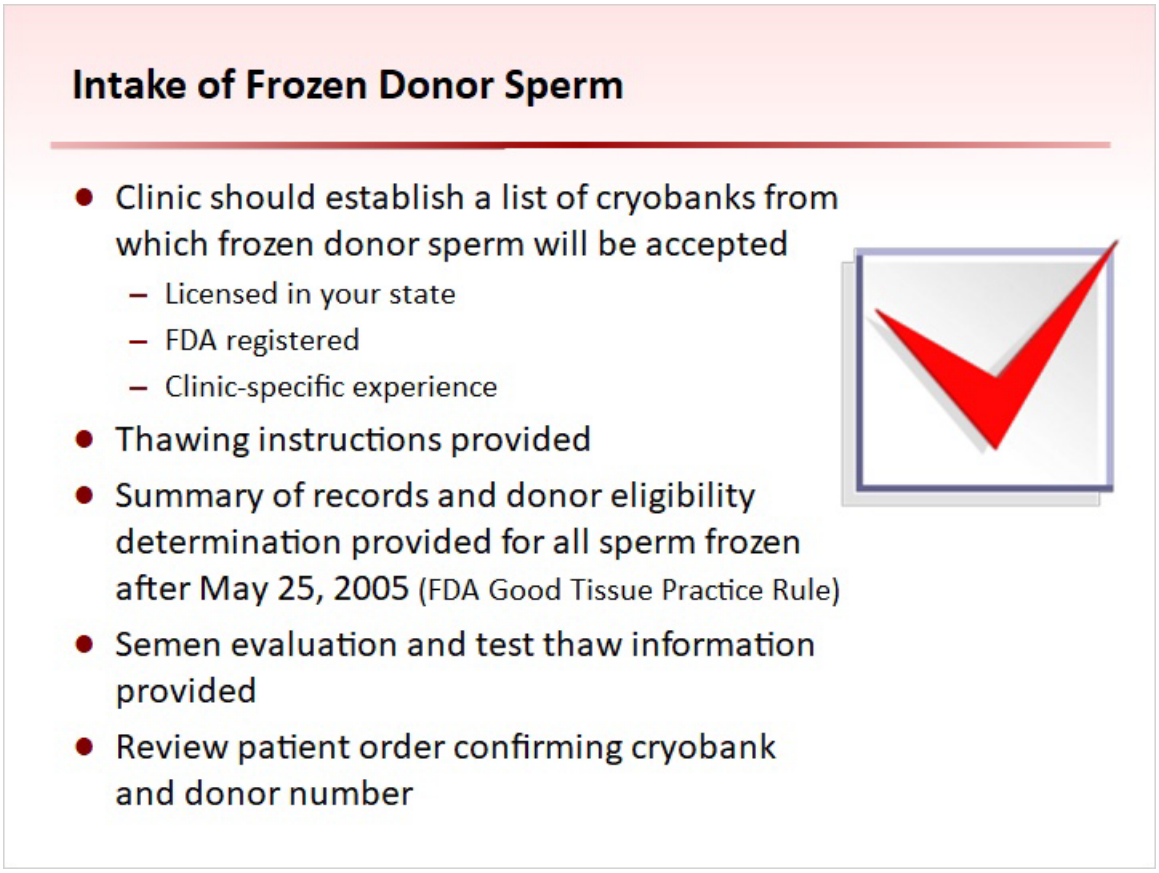
Contact the shipper immediately if any of these conditions are observed!

Next, remove the paperwork packet from the shipping container. The paperwork should contain the following information:

1. Patient name, contact information, and physician of record
2. The enclosed packing slip should list the number of vials, identifying information (such as donor number or patient name/cryo number and date of birth), sample contents ("washed" or "unwashed", ejaculate or testicular, etc.)
3. Summary of records and eligibility determination if donor sperm
4. Infectious disease screening results in compliance with state regulations

Determine a location for the sperm sample in the appropriate liquid nitrogen storage tank in the laboratory.

1.7 Intake of Frozen Donor Sperm

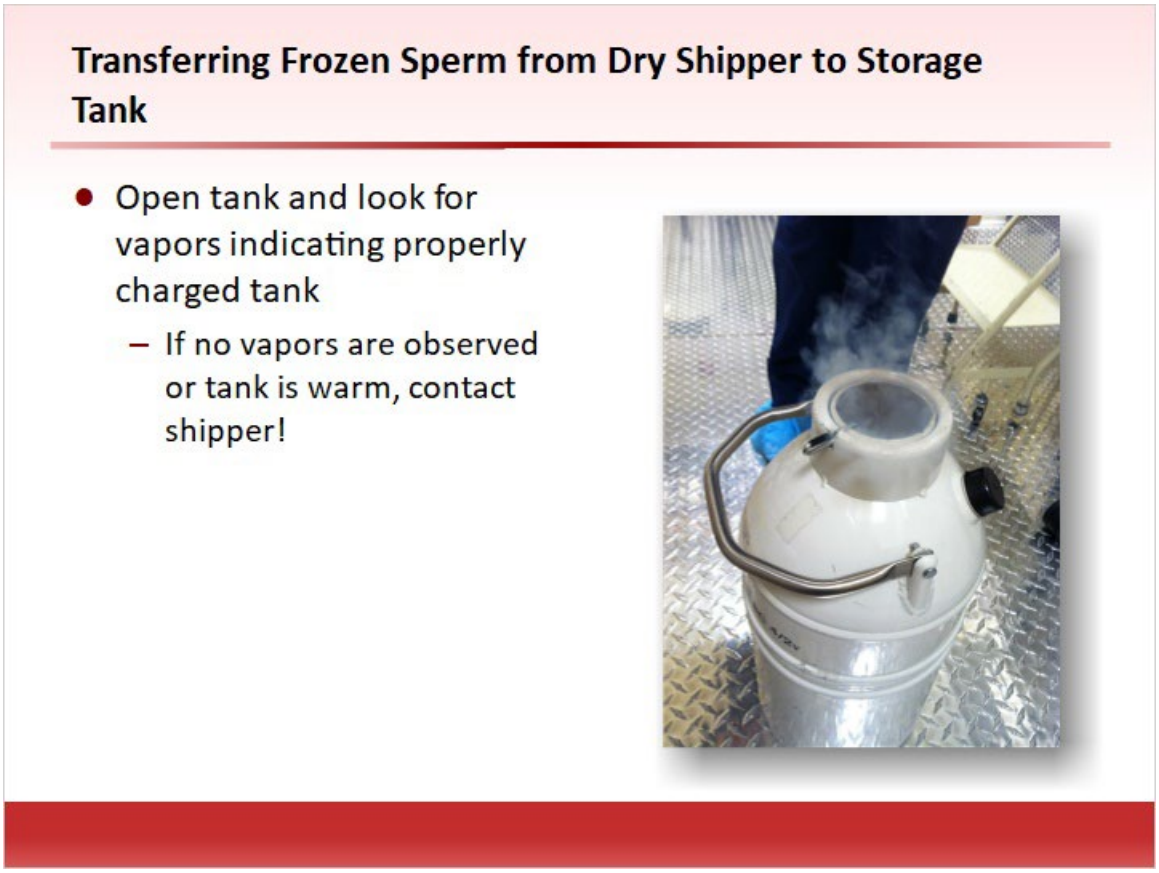


Notes:

Each clinic should establish a list of cryobanks from which frozen sperm samples will be accepted. Clinics should maintain appropriate state and local licenses and should be registered with the FDA. Previous experience with the specific cryobank may determine whether or not samples will be accepted. Clear thawing instructions should be provided, and special notation made on storage records if the thawing protocol is different from the clinic's standard. It is a good idea to develop a chart with thawing instructions from the various cryobanks from which your clinic accepts samples to be sure the appropriate instructions are followed. Donor sperm frozen after May 25, 2005 should be accompanied by a summary of records (SOR) and donor eligibility determination. This date is important because the FDA's good tissue practice rule was established and became effective at this time. Prior to this date, reproductive tissue was not regulated

by the FDA.
Pre-freeze semen evaluation and/or test thaw information should also be provided for each sample. The individual receiving the frozen samples should review the patient order or treatment plan and confirm the donor number and cryobank are correct.

1.8 Transferring Frozen Sperm from Dry Shipper to Storage Tank



Notes:

When the cap is removed from the dewar the presence of vapors indicates the dry shipper is still properly charged. If no vapors are observed and/or the dewar is warm, the shipper should be contacted immediately.

1.9 Transferring Frozen Sperm from Dry Shipper to Storage Tank

Notes:

A container such as a thermal polystyrene foam box should be filled with liquid nitrogen. Exposure to liquid nitrogen can cause frostbite or injury. Extreme caution should be exercised during handling. Protective safety attire including, but not limited to, cryogloves and eye/face protection should be worn when handling liquid nitrogen. Be sure not to overfill the transfer vessel.

1.10 Transferring Frozen Sperm from Dry Shipper to Storage Tank

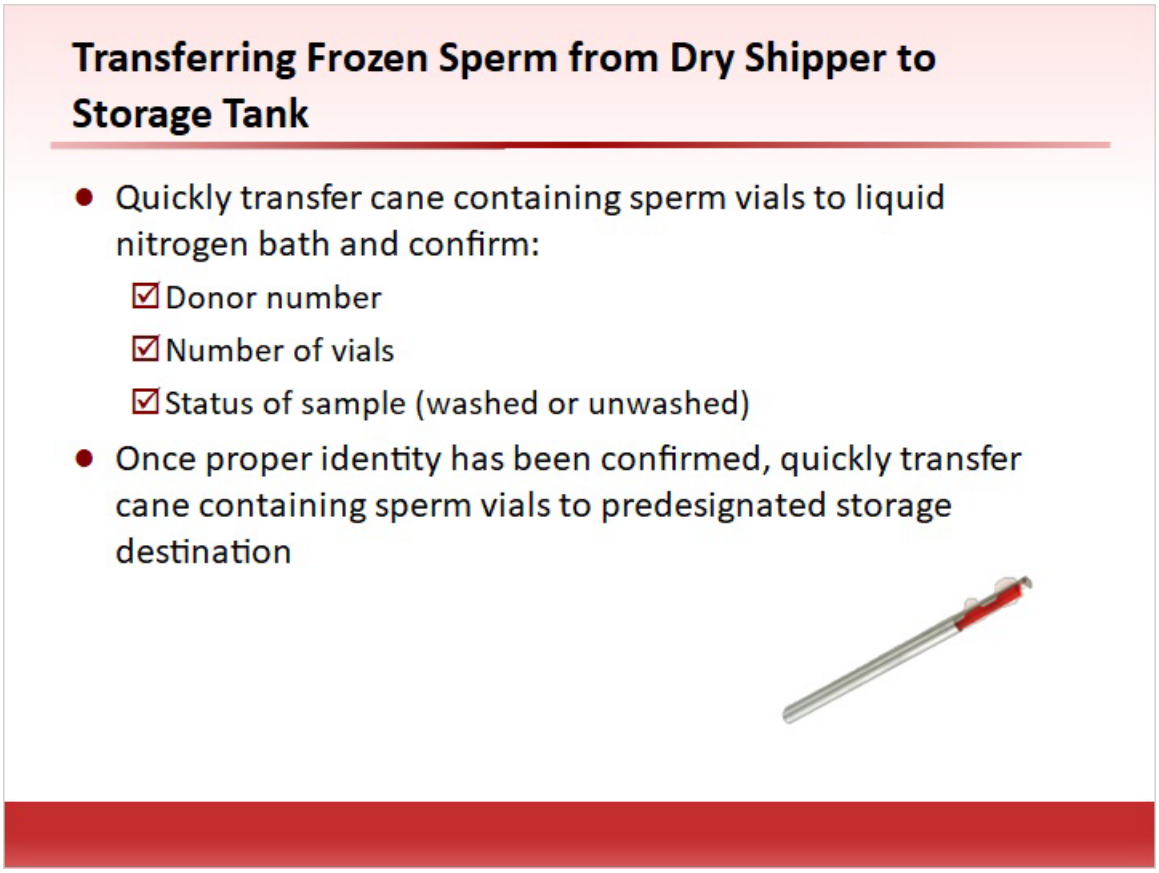
Transferring Frozen Sperm from Dry Shipper to Storage Tank

- The venting of liquid nitrogen will deplete available oxygen
- Liquid nitrogen should not be stored or handled in areas with poor ventilation.

Notes:

The venting of liquid nitrogen will deplete available room oxygen. Liquid nitrogen should not be handled or stored in areas with poor ventilation. An oxygen sensor should be used to alert users to low oxygen levels.

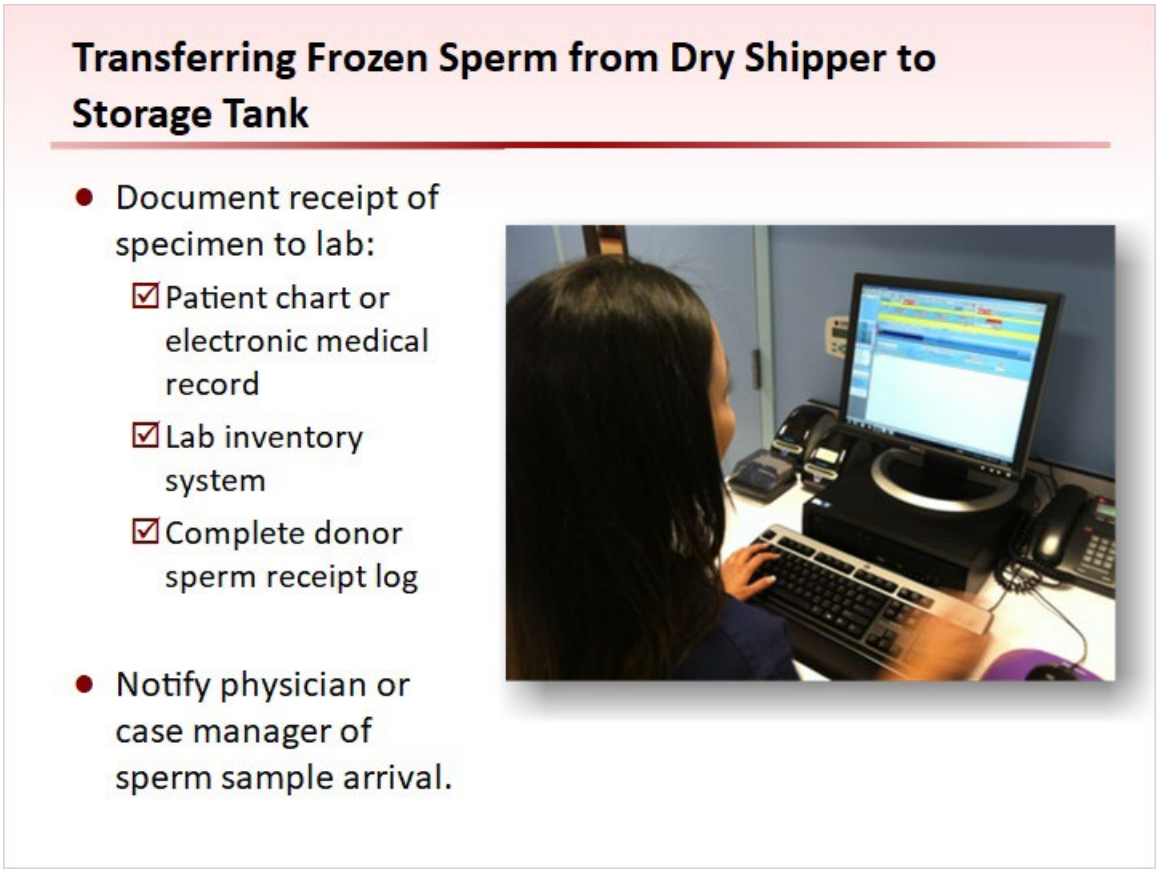
1.11 Transferring Frozen Sperm from Dry Shipper to Storage Tank



Notes:

The cane containing the frozen sperm vials or straws should be quickly transferred from the dry shipper to the liquid nitrogen bath. The donor number, number of vials, and the status of the sample (washed or unwashed) should be confirmed. Once confirmation has been made, the cane containing the sperm vial(s) is quickly transferred to the predesignated storage destination.

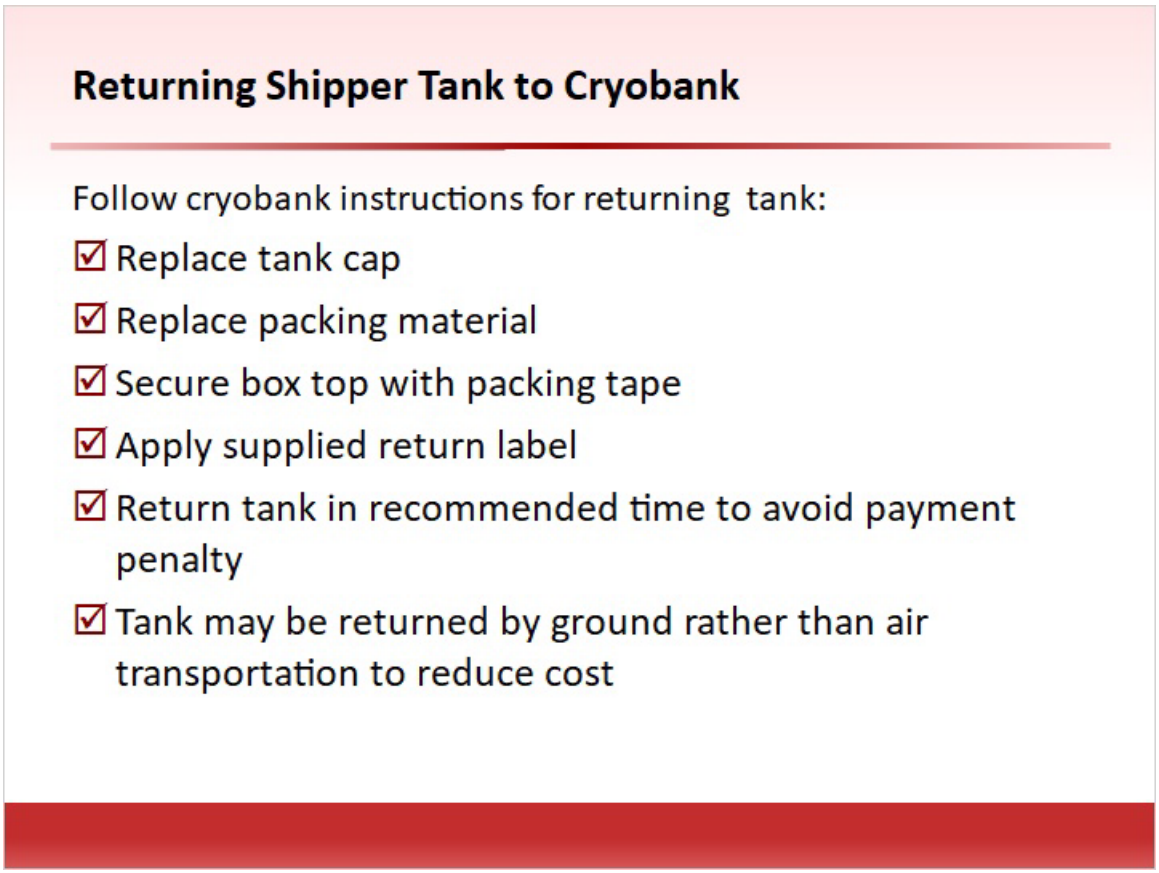
1.12 Transferring Frozen Sperm from Dry Shipper to Storage Tank



Notes:

Once the specimen has been transferred to the storage tank, receipt of the specimen should be documented in the patient's medical record. This may be documented in a paper chart or into an electronic medical record. Documentation into the lab's inventory system should be performed. The physician or case manager should be notified of the sperm sample arrival according to the lab's standard operating procedure. This may be documented in the form of a progress note or sent via email. It is important to record the number of the sperm donor in the patient's chart because some patients have more than one sperm donor. When a thaw request is received, the patient must be asked which donor is preferred so that the sperm from the preferred donor can be selected. Finally, receipt of the sperm sample should be documented in the donor sperm receipt log. This log is a chronological record of all samples received to the laboratory and should include the patient name, date of receipt, cryobank, and donor number, number of vials, wash status of sample, physician of record, FDA status, storage location, receipt technician identification, and an area for notes to record additional information/concerns. It is important that the donor sperm number and all of the accompanying documents be included in the patient's medical chart because some patients have more than one frozen sperm donor.

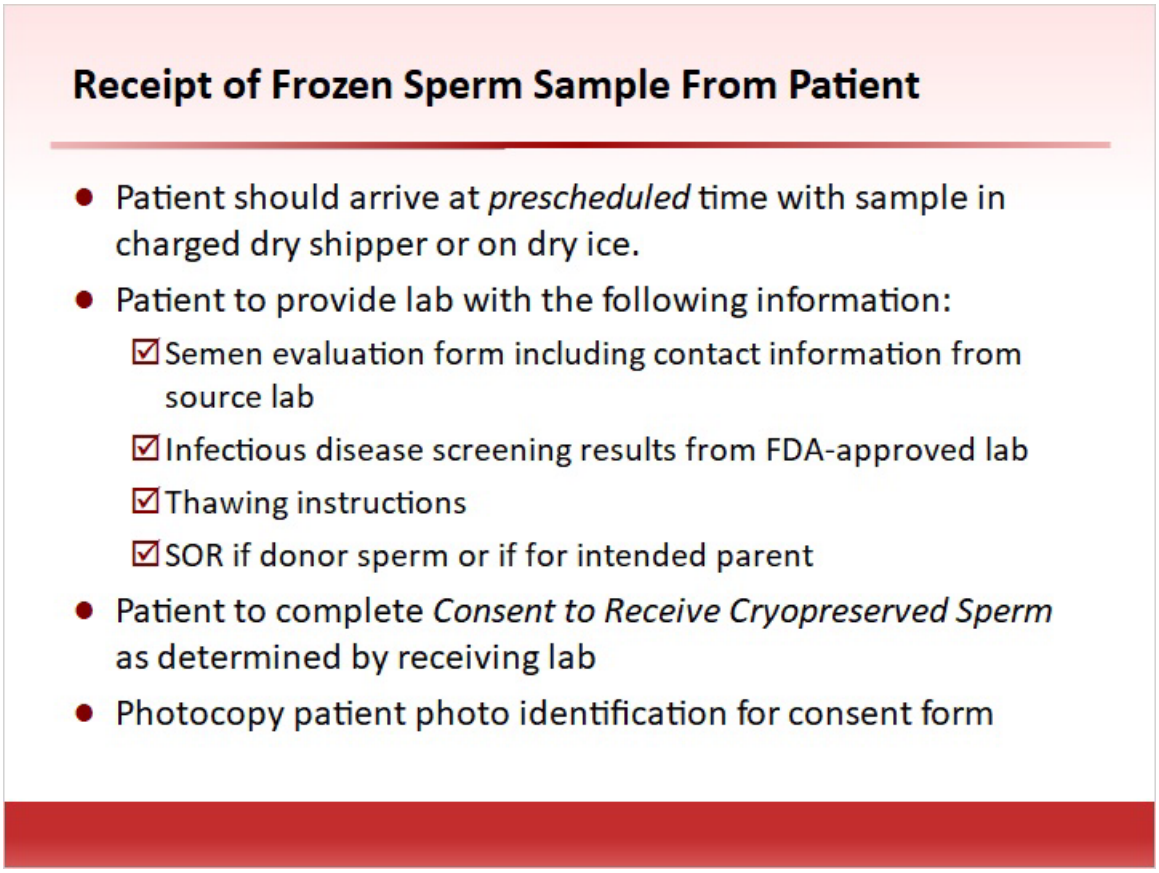
1.13 Returning Shipper Tank to Cryobank



Notes:

Always follow the cryobank's instructions for returning the dry shipper. Replace the tank cap and return the dewar to its shipping container if removed during specimen transfer. Replace any packing material that came with the tank. Secure the box top with packing tape, and apply the supplied return label. The tank should be returned within the recommended time to avoid any payment penalty. Some cryobanks may request the tank be returned by ground rather than by air transportation to reduce shipping costs. Be sure to check this before calling for tank pick up.

1.14 Receipt of Frozen Sperm Sample From Patient



Notes:

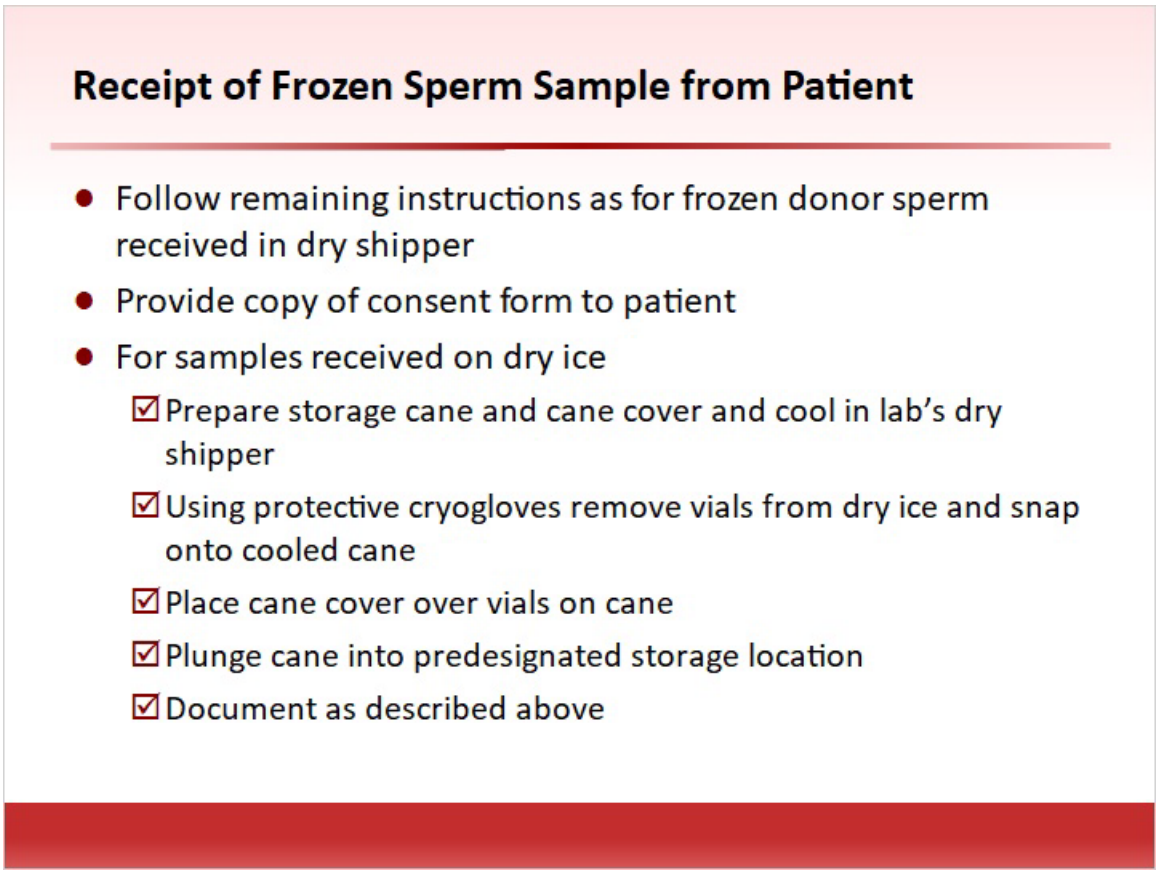
In some cases, a patient may hand carry frozen specimens from a cryobank or clinic to your laboratory. An appointment should be made with the lab so a staff person is able to meet the patient and receive the samples without interruption or distraction. Twenty to 30 minutes should be adequate for this appointment. The patient should provide the receiving lab with the following information:

- Semen evaluation form which should include the laboratory/cryobank's contact information, a sample evaluation form with quality, washing status, number of vials frozen, etc.
- Infectious disease screening results
- Thawing instructions
- Summary of records if the sample is from a sperm donor or is from the male partner planning to use a gestational carrier

The patient will be asked to complete a "Consent to Receive Cryopreserved Sperm" as determined by the receiving lab. This form may be provided to the patient prior to dropping off the sample; however, the receiving technician should verify the patient's photo identification and witness the signature on the consent form. A copy of the

patient's photo identification and the consent form should be retained by the receiving lab.

1.15 Receipt of Frozen Sperm Sample from Patient

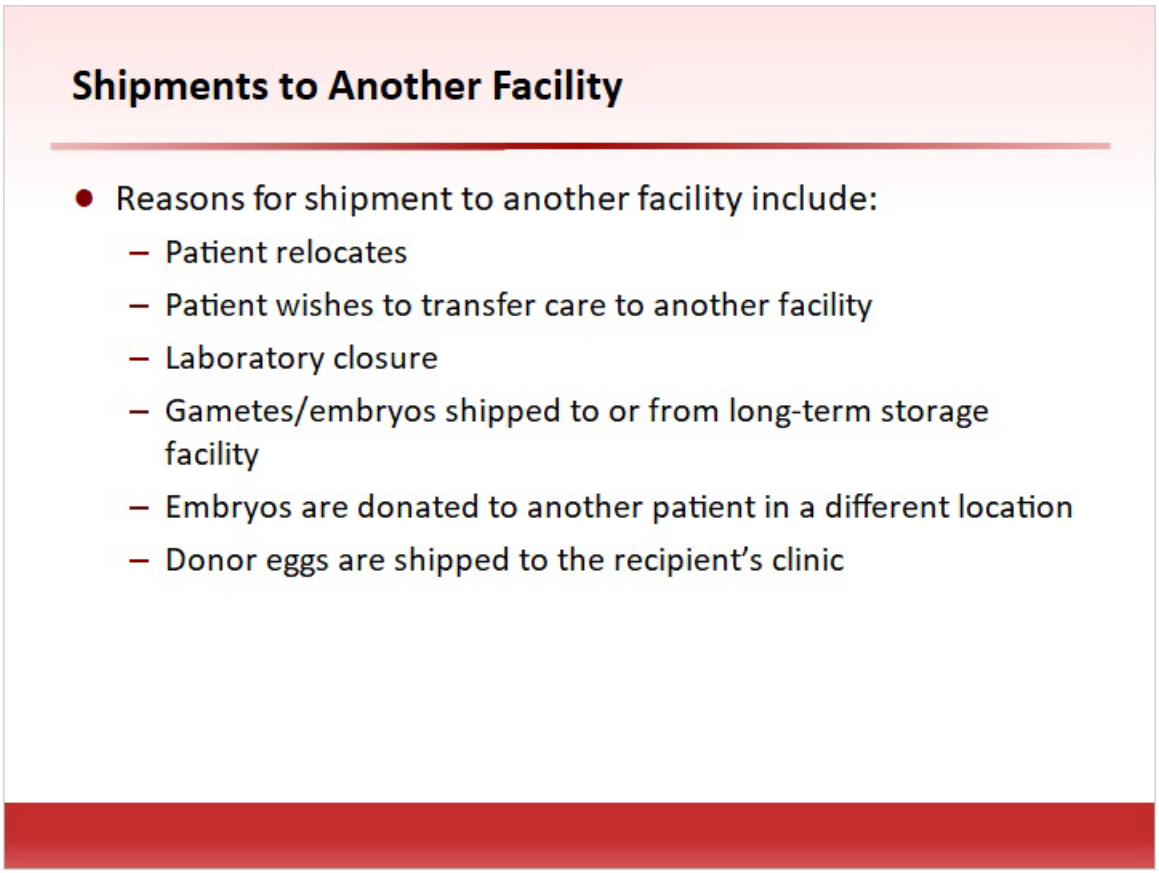


Notes:

The receiving tech should remove the sample from the tank to a liquid nitrogen bath as described earlier. The patient's unique identification number on the cane should match that on the vials. Some cryobanks or clinics will reuse cryo canes—do not assume the number on the cane top matches that on the vial!

For samples received on dry ice, prepare the storage cane and cane cover prior to the patient's arrival. The cane and cover can be cooled in a charged dry shipper. Using protective cryogloves, carefully remove the vials from the dry ice, verify the identification number on the vials, and quickly snap the vials onto the cooled cryocane. Slide the labeled cane cover over the vials to prevent them from falling off into the storage tank. Plunge the cane into the predesignated cryostorage location. Document receipt of the samples as described above.

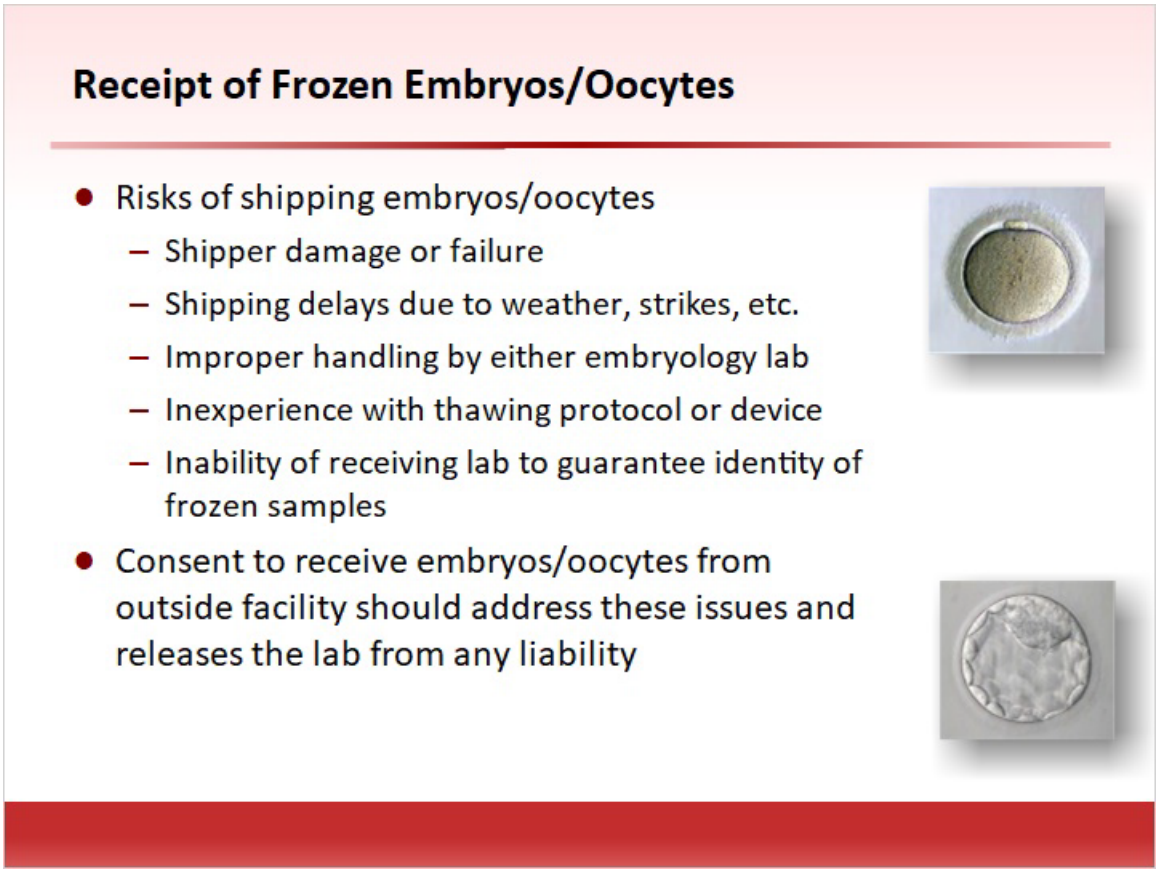
1.16 Shipments to Another Facility



Notes:

Sperm, oocytes, and embryos may be shipped to another facility for various reasons including, but not limited to: the patient relocates, the patient wishes to transfer care to another facility, a laboratory closure, gametes or embryos are shipped to or from a long-term storage facility, embryos are donated to another patient in a different location, or donor eggs are shipped to the recipient's clinic. Individual laboratories must establish a policy outlining conditions under which they will accept frozen embryos or oocytes from an outside facility. Some clinics may opt *not* to accept frozen materials from any facility.

1.17 Receipt of Frozen Embryos/Oocytes



Notes:

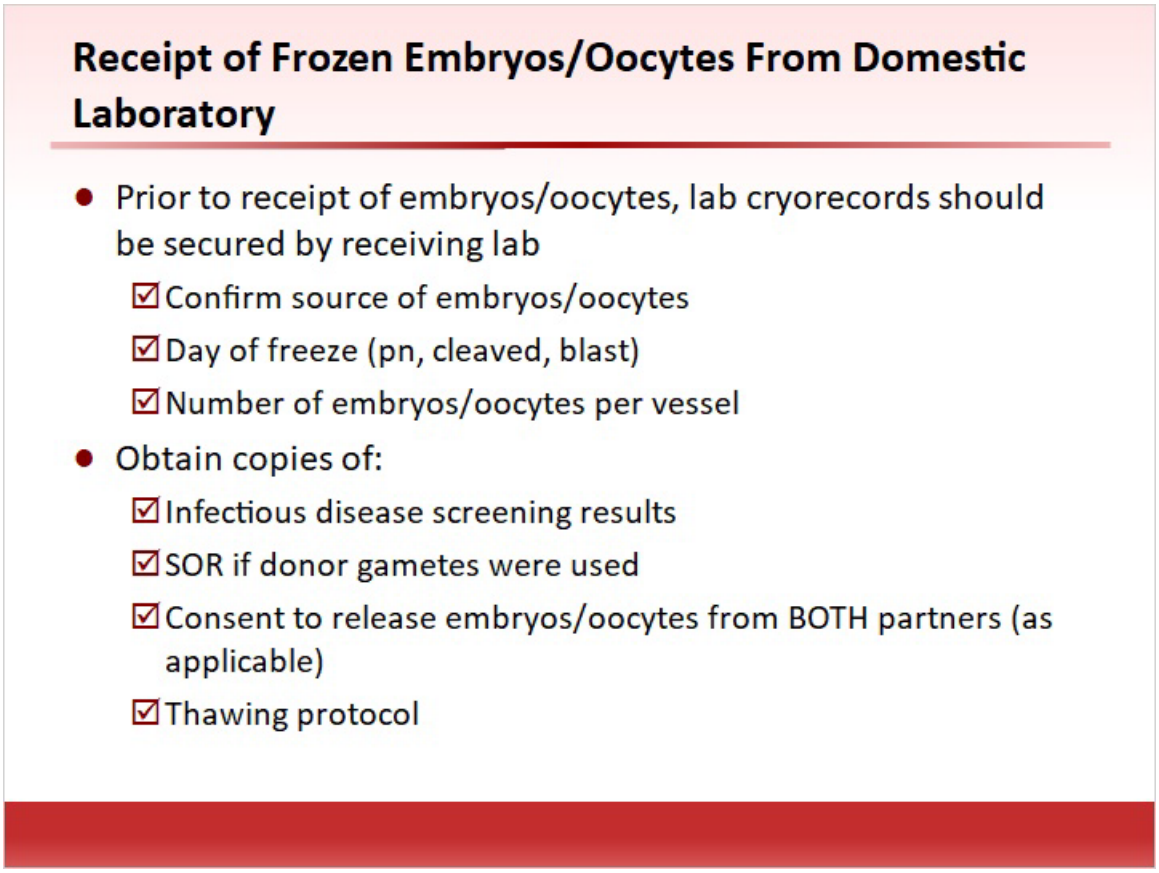
While the practical aspects of receiving frozen embryos and oocytes to the lab are similar to those for sperm, frozen embryos and oocytes are more susceptible to improper handling and temperature changes due in part to the small volume of cryoprotectant used. Shippers can be damaged by improper handling during transport. This can result in vacuum failure and warming of the shipper tank. Shipments can be delayed due to inclement weather, strikes, customs, etc. Improper handling by the embryology staff during loading or unloading the tank can result in damage to or even loss of the embryos/oocytes.

In the days of slow freezing, there were few thawing protocols and cryodevices (typically straws or vials). Today, however, with the majority of labs using vitrification as the cryopreservation method of choice, freezing protocols and cryovessels abound. It would not be uncommon to receive embryos or oocytes vitrified on a cryodevice a lab has not used before. Inexperience with a particular warming protocol or cryodevice can have devastating consequences. For this reason, the warming protocol and an empty cryodevice should be requested in advance of shipping the embryos. This allows the receiving lab to become familiar with the protocol, to practice using the cryodevice, and to order or make the required warming kit solutions. It also allows the lab staff to contact the source lab with any questions about the protocol or the cryodevice. The receiving lab is not able to guarantee the identity of the frozen samples. These

risks, however small, must be disclosed to the patient.

It is recommended that the receiving lab provide the patient a consent form that addresses each of these risks and releases the lab from any liability. Both the releasing and receiving clinic have no control over the handling of the shipper tank once it leaves the releasing facility.

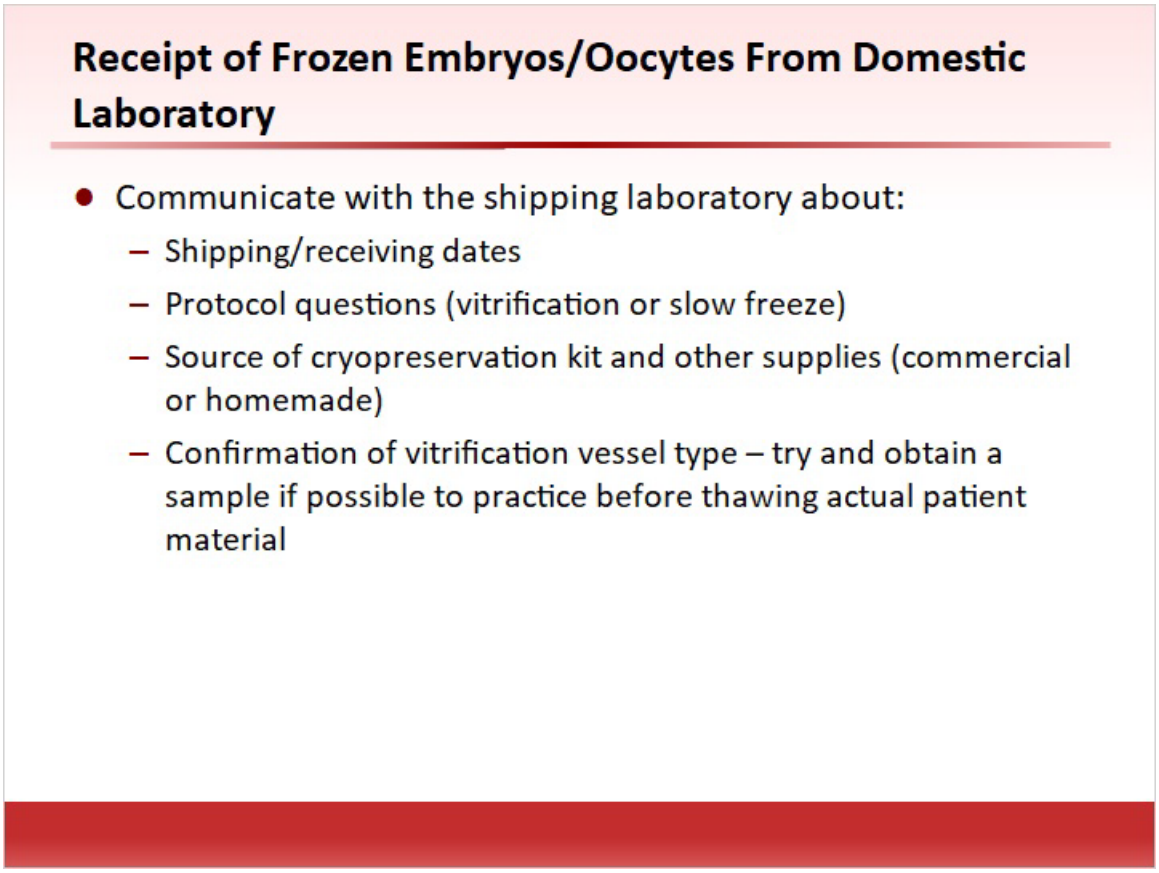
1.18 Receipt of Frozen Embryos/Oocytes From Domestic Laboratory



Notes:

Prior to receiving the embryos/oocytes, the receiving lab should secure freezing records from the source lab. The source of the embryos/oocytes, day of freeze, and number of embryos/oocytes per cryodevice are noted.

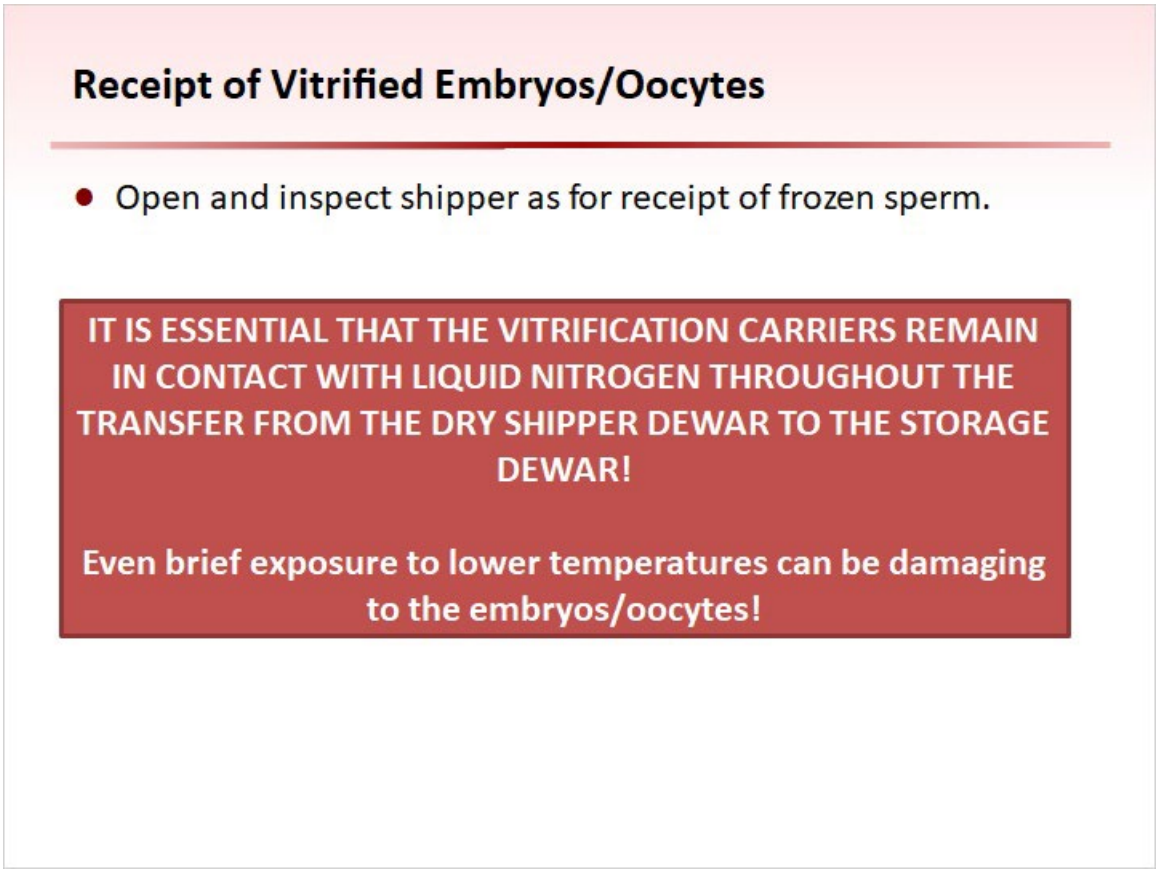
1.19 Receipt of Frozen Embryos/Oocytes From Domestic Laboratory



Notes:

Do not hesitate to contact the shipping lab with any questions about protocol, warming solutions, supplies, and the cryodevice. The shipping date should be mutually agreed upon. If neither lab has a shipping dewar, the patient should be referred to a reputable vendor who can supply the appropriate dewar. The receiving lab should have a clear understanding of the thaw protocol as well as any supplies needed for thawing.

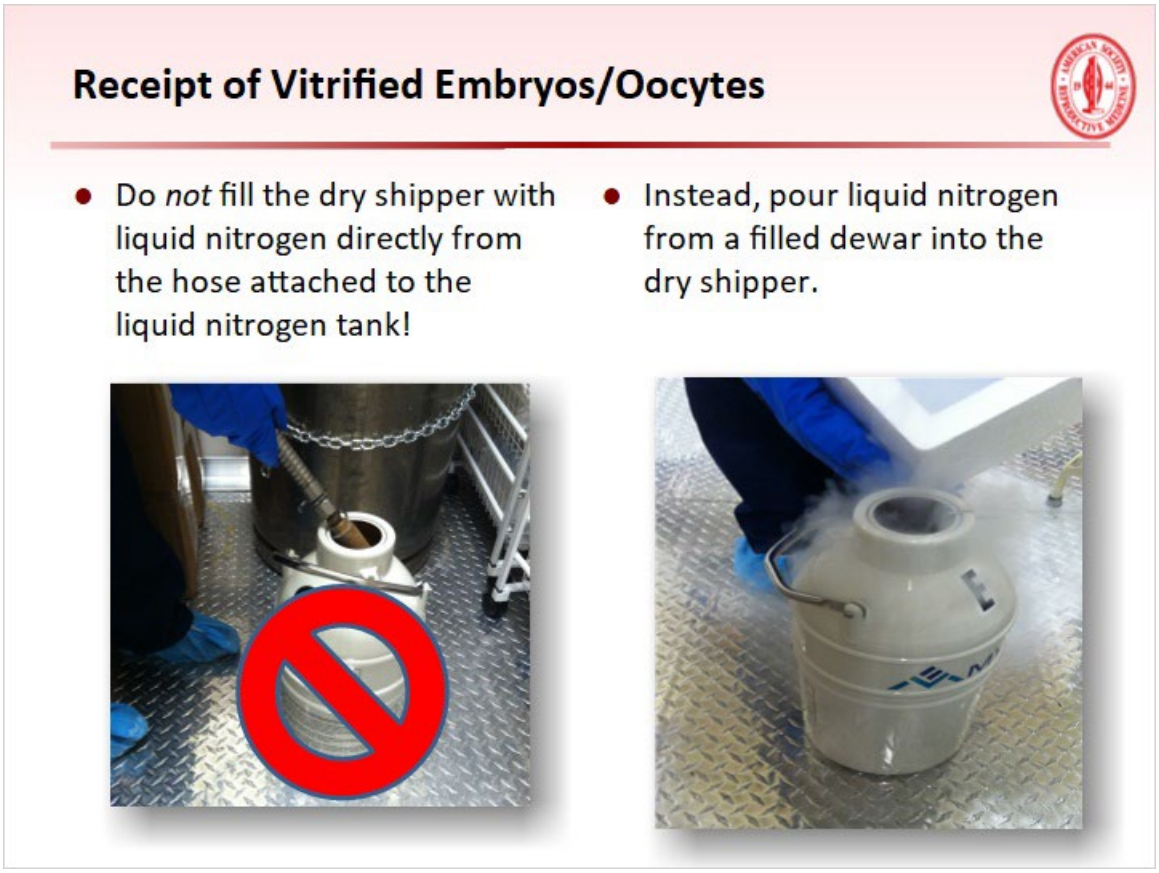
1.20 Receipt of Vitrified Embryos/Oocytes



Notes:

When a shipper tank containing frozen embryos or oocytes is received into the lab, the shipper should be inspected for damage as well as the presence of vapors. As with the receipt of frozen sperm samples, if the tank is damaged or it is warm, the shipper and the source lab should be notified immediately. It is absolutely essential that vitrification vessels remain in direct contact with liquid nitrogen throughout the transfer from the dry shipper dewar to the storage tank. Even brief exposure to lower temperatures can be damaging to the embryos/oocytes!

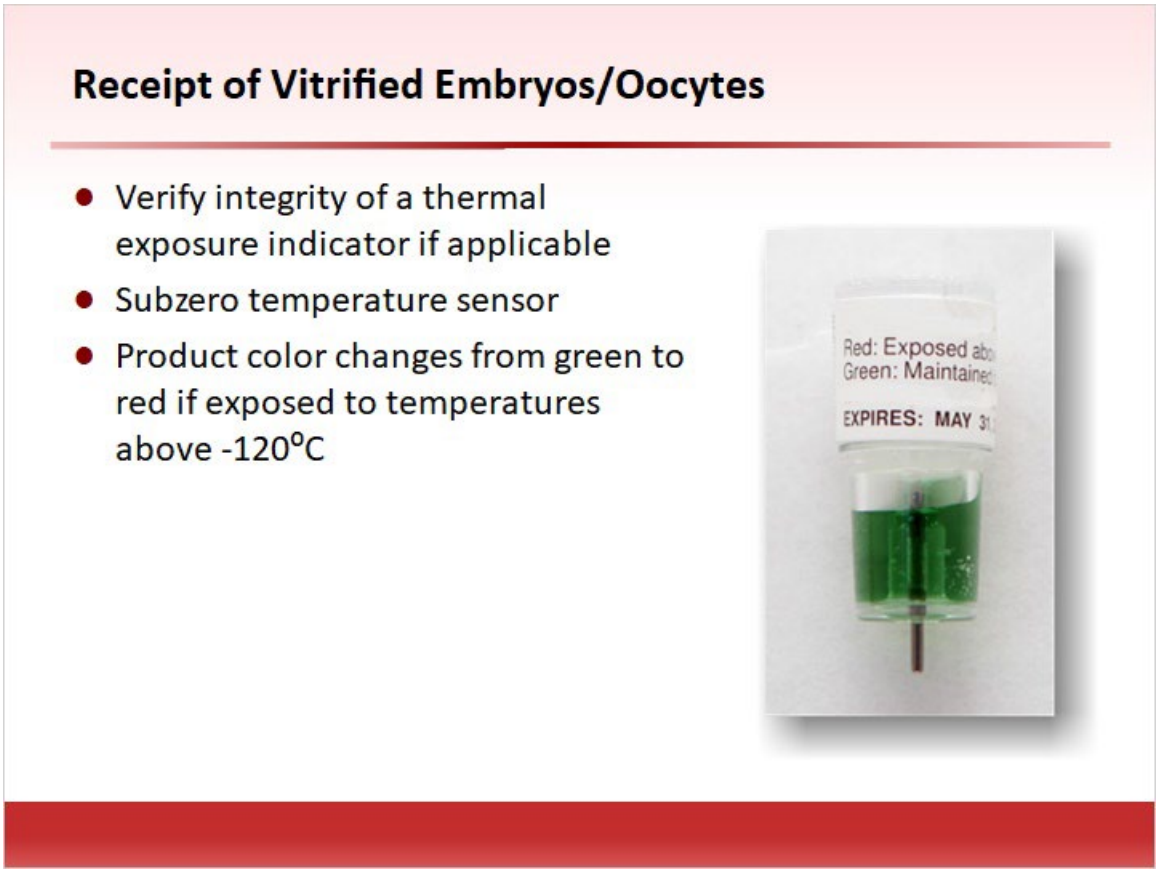
1.21 Receipt of Vitrified Embryos/Oocytes



Notes:

Prior to removing the cane containing the vitrified embryos/oocytes, the shipper tank should be filled with liquid nitrogen. Do *not* fill the dry shipper with liquid nitrogen directly from the hose attached to the liquid nitrogen tank. For the first 5-10 seconds after turning on the tank, warm air, not liquid nitrogen, blows out of the hose. This exposure to warm air will raise the temperature of the vitrified embryos/oocytes enough to render them nonviable. Fill a dewar or other container with liquid nitrogen and carefully pour it into the dry shipper. Fill a polystyrene foam box or other bath with liquid nitrogen.

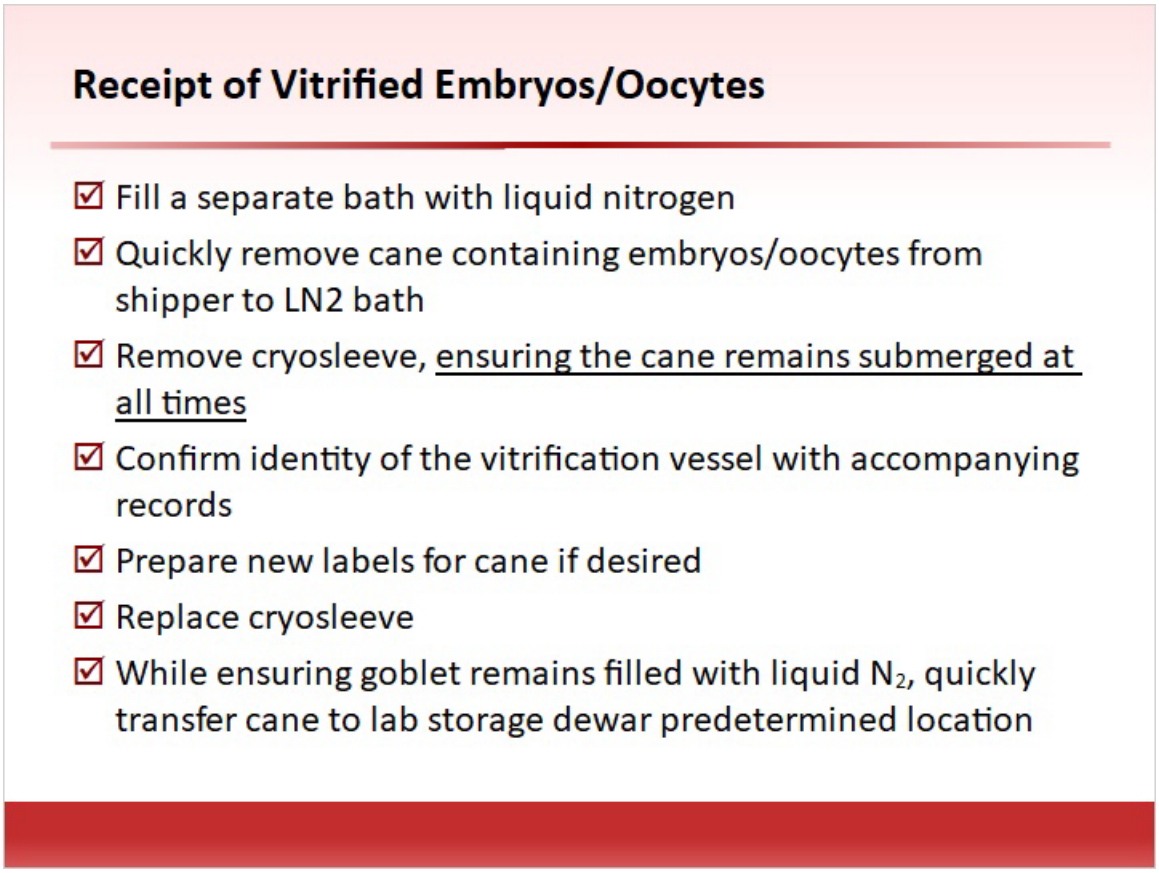
1.22 Receipt of Vitrified Embryos/Oocytes



Notes:

Vitrified samples should be sent with a thermal exposure indicator and are used to monitor subzero temperatures in products shipped or stored in dry shippers or liquid nitrogen. In one type of device as that shown here, the activated product will change from green to red if exposed to temperatures above –120°C and is recommended for monitoring environments at or below –145°C. The color change is not reversible even upon refreezing, so if the monitor is red, the temperature of the dry shipper was compromised.

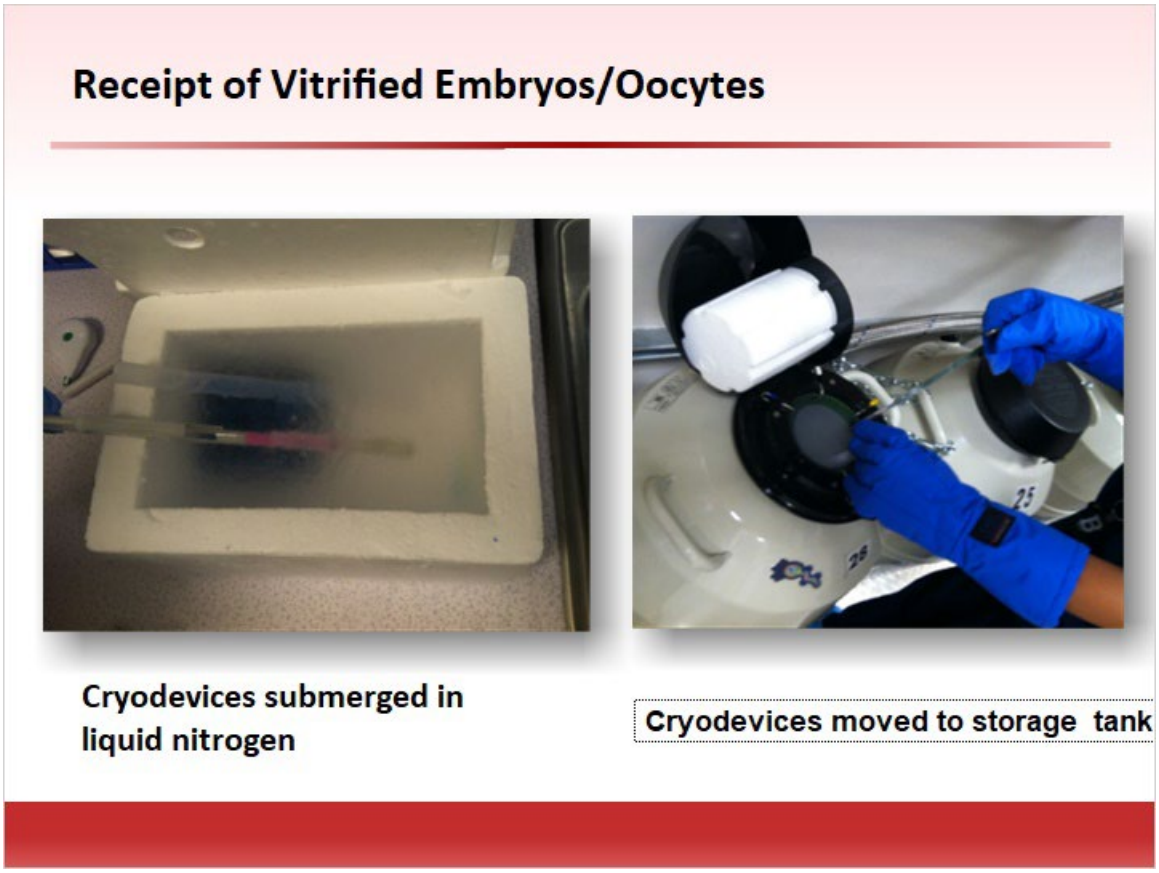
1.23 Receipt of Vitrified Embryos/Oocytes



Notes:

Once it has been determined that the temperature integrity was maintained, quickly remove the cane containing the embryos/oocytes from the shipper tank to the liquid nitrogen bath. Filling the shipper tank with liquid nitrogen will ensure that the goblet containing the cryodevices remains full during the move from the shipper to the liquid nitrogen bath. Remove the cryosleeve, ensuring the cryodevices remain submerged at all times! Confirm the identity of the vitrification vessel with the accompanying paperwork. In some cases, it may be necessary to remove the cryodevice from the goblet to read the identification label. Once identification of each cryodevice has been verified, return the cryodevices to the goblet. If desired, prepare new labels for the cane and cane sleeve. Replace the cooled cryosleeve. While ensuring the goblet remains filled with liquid nitrogen, quickly transfer the cane to the predesignated storage tank location.

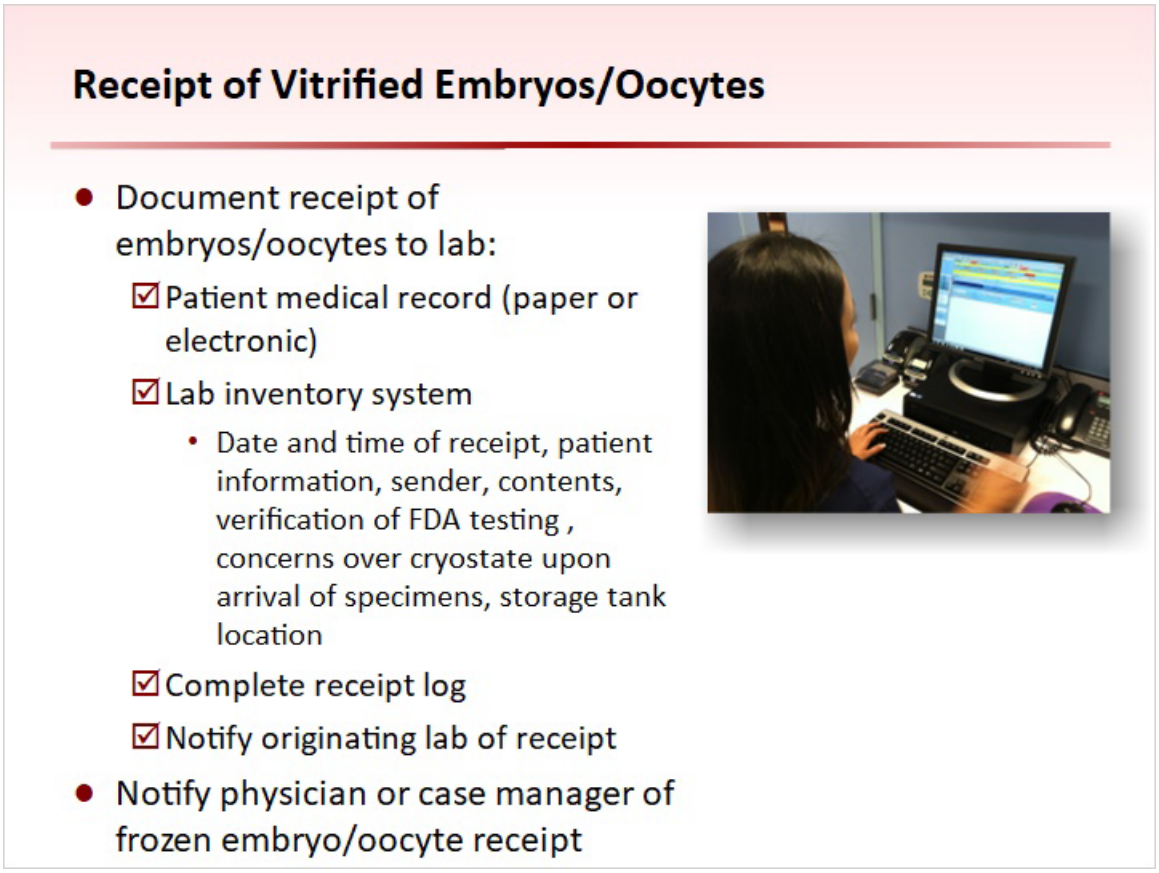
1.24 Receipt of Vitrified Embryos/Oocytes



Notes:

The figure on the left depicts one way to verify identification of the cryodevice. The cryosleeve is removed and the labels are visible under the surface of the liquid nitrogen. Note that the cryodevices remain submerged. The cryosleeve is replaced, and the cane containing the goblet full of liquid nitrogen is quickly moved to the storage tank.

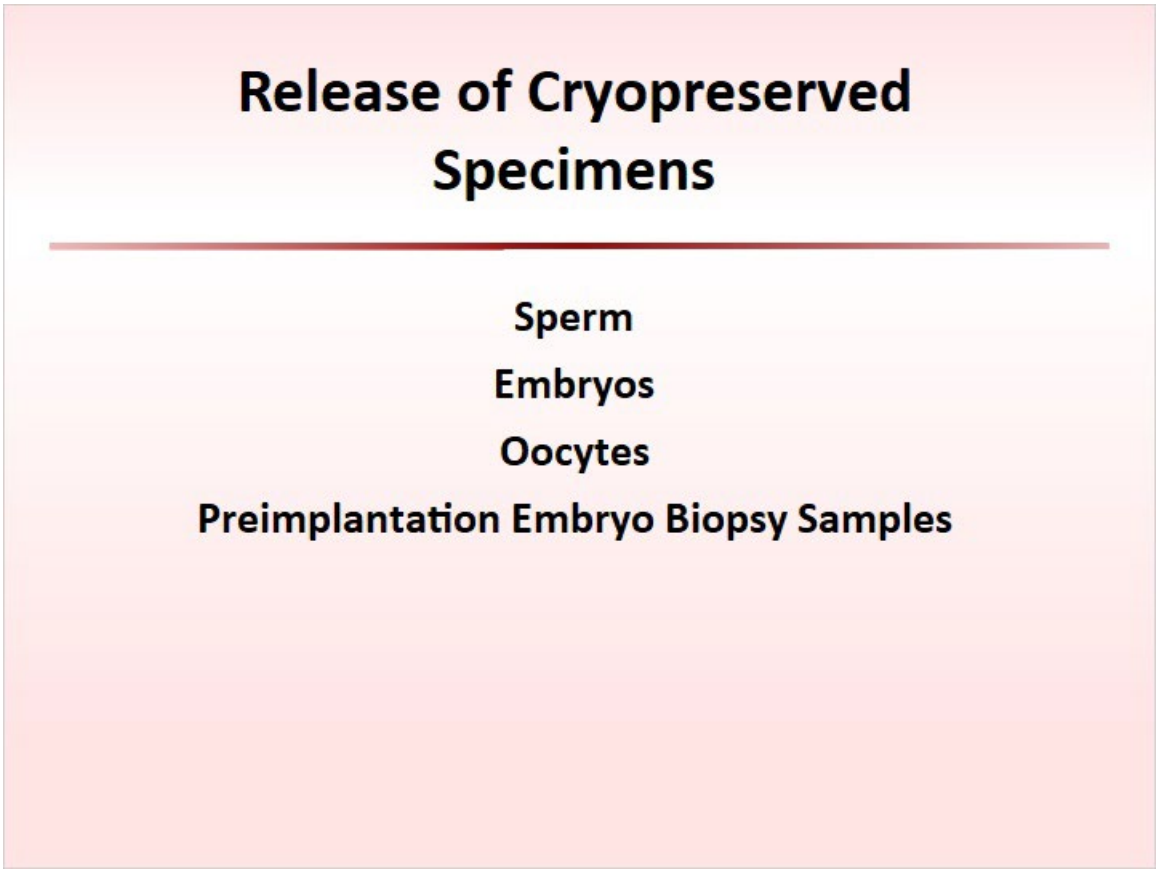
1.25 Receipt of Vitrified Embryos/Oocytes



Notes:

Receipt of frozen embryos or oocytes to the laboratory should be clearly documented in the patient's medical record (paper or electronic) and into the laboratory's cryostorage inventory system. The following information should be entered into the laboratory's biological specimen receipt and release log: date and time of receipt, patient information, sender, contents, verification of FDA testing as required, concerns over cryostate upon arrival of the specimens, and the storage tank location. The source lab should be notified of the embryo/oocyte receipt via email or telephone call. Finally, the physician of record and/or the case manager should be notified of the frozen embryo/oocyte receipt.

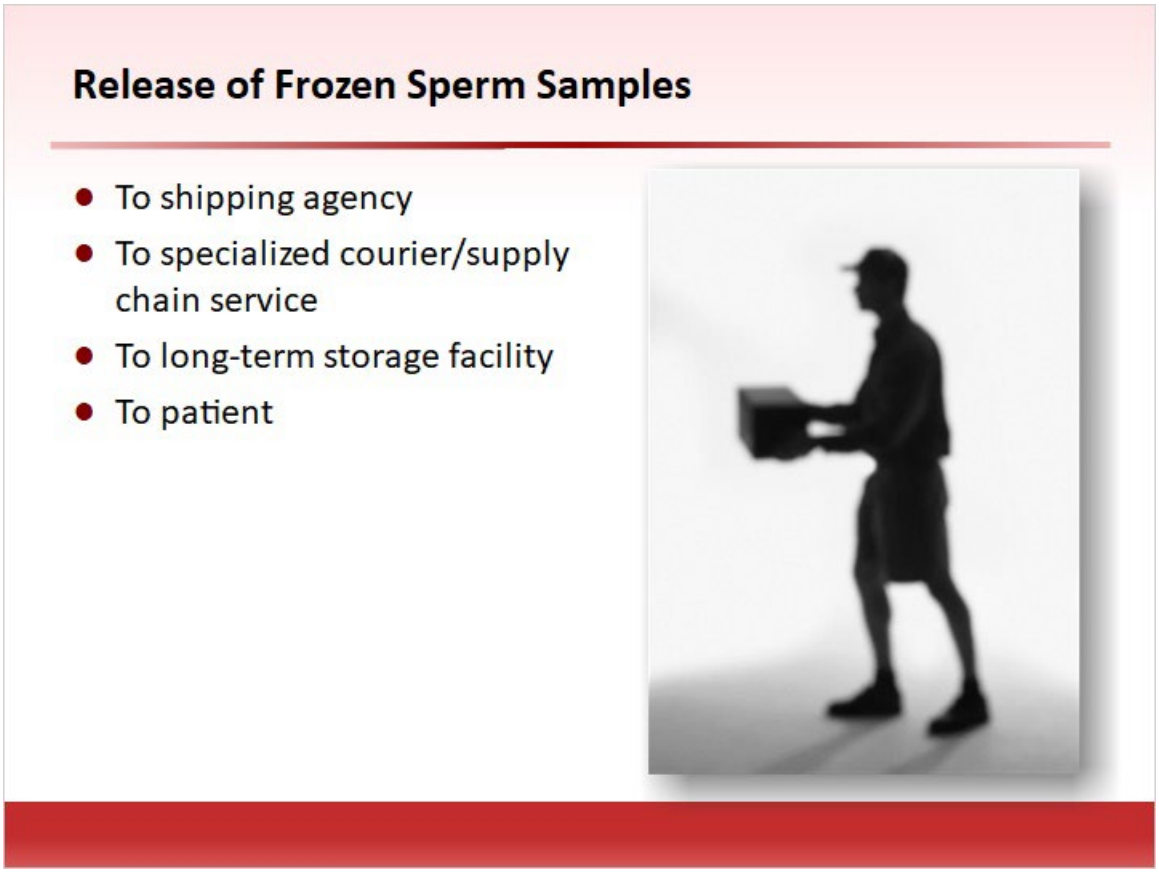
1.26 Release of Cryopreserved Specimens



Notes:

Different types of biological materials may be released from the IVF Lab, including sperm, embryos, oocytes, and embryo biopsy samples. In some cases, depending on the center, ovarian tissue samples also may be released. We will be reviewing methods for the more common specimens released from the lab.

1.27 Release of Frozen Sperm Samples



Notes:

Frozen specimens may be shipped using a variety of different couriers. Most often, a commercial shipping agent such as FedEx® or UPS is used. However other specialized courier/supply chain services may be used, especially for biopsy tissue samples. Some areas have a local courier that is experienced in handling biological tissues and will provide that service to local patients moving specimens from one area clinic to another. Specimens may be released to a long-term storage facility via a shipping agency, local courier, or even hand carried depending on the distance from the lab to the storage facility. Finally, specimens may be released directly to the patient who may drive or fly to the new destination.

1.28 Release of Frozen Sperm Samples

Notes:

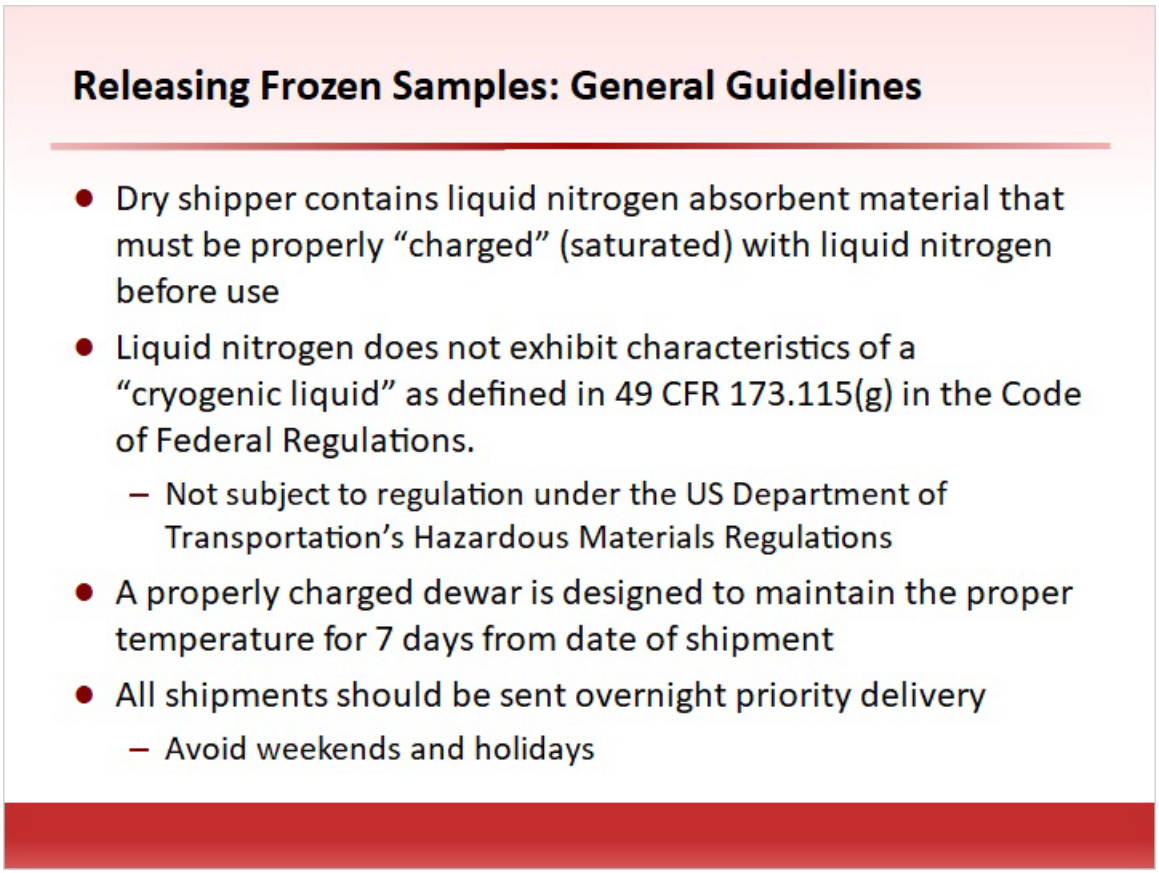
One of the first and most important steps in releasing frozen specimens is to confirm that the receiving laboratory will, in fact, accept specimens from outside their own lab. Most labs will accept frozen sperm specimens from outside labs. Some programs will make all of the shipping arrangements for the patient. Other programs may not have shippers available to loan so a third-party vendor may provide a rental tank to be used for the shipment.

Sperm specimens are most commonly shipped in a dry shipper dewar as discussed previously. A warm dry shipper must be "charged" before using with patient specimens. The dewar is filled from either the source tank hose or a dewar filled with liquid nitrogen. The dewar is filled and allowed to sit for 2 hours to allow the liquid nitrogen to be absorbed into the tank lining. The tank is refilled until the lining is saturated. Never overfill the dewar with liquid nitrogen. It is optimal to allow the tank to sit overnight. If the liquid nitrogen level is maintained, the tank is ready for use.

After 24 hours, the excess liquid nitrogen is poured off into a wide mouth container. A partially charged shipper will take less time to prepare, but the tank should be allowed

to sit for 2 hours to completely cool down before use. As before, pour off the excess liquid nitrogen, and the tank is ready for use.

1.29 Releasing Frozen Samples: General Guidelines



Notes:

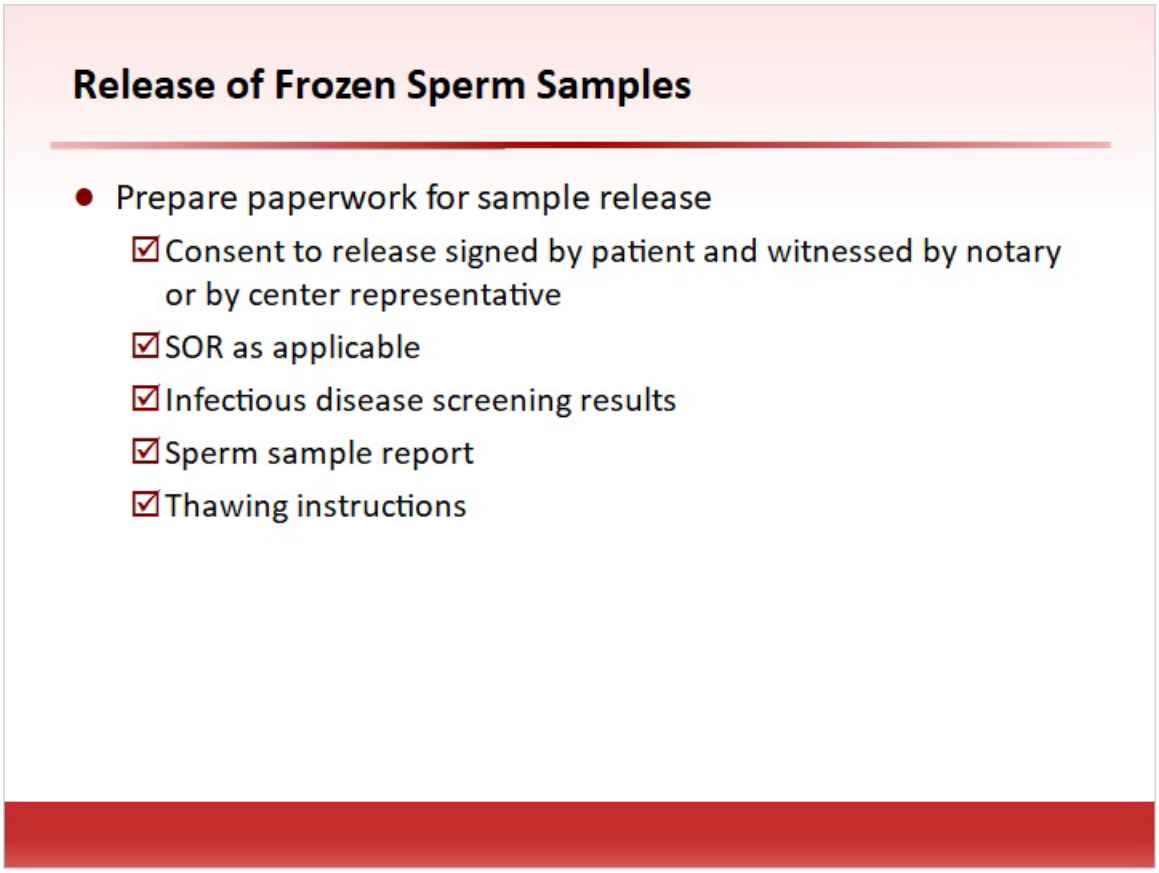
A dry shipper dewar is made of an outer container that is lined with an absorbent material. The container is filled with liquid nitrogen, which is absorbed into the container lining. The charged tank serves as a refrigerated container for the shipment of samples.

Because of the manner in which it is absorbed and because there is no free liquid present in the packaging, the liquid nitrogen does not exhibit the characteristics of a "cryogenic liquid" as defined in 49 CFR 173.115 (g) of the Federal Code of Regulations and does not pose a hazard in transportation. Therefore, it is not subject to regulation under the US Department of Transportation's Hazardous Materials Regulations.

All shipments should be arranged using overnight priority delivery. Weekend and

holiday shipments should be avoided whenever possible. The laboratory may elect to ship samples only on Monday, Tuesday, and Wednesday.

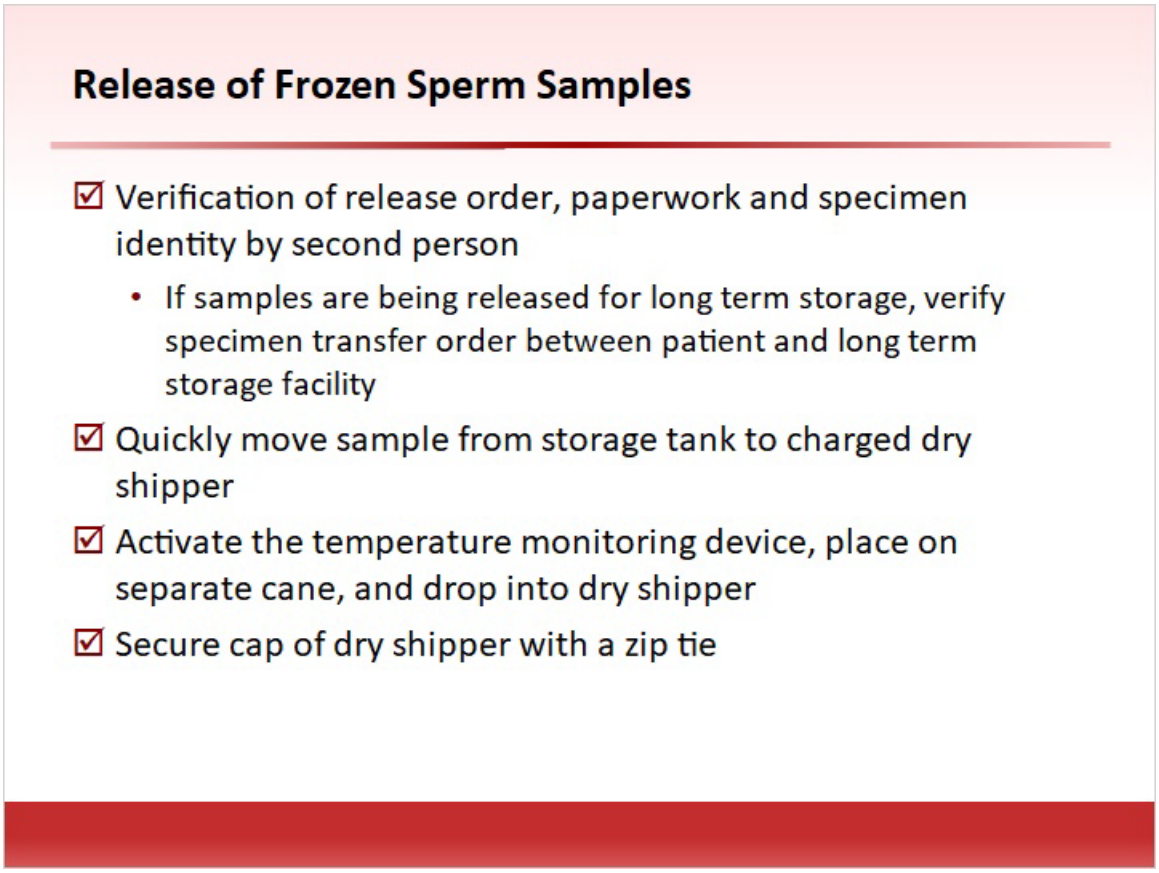
1.30 Release of Frozen Sperm Samples



Notes:

While waiting for the dry shipper to cool down, prepare the paperwork for releasing the samples. The patient must complete a "Consent to Release Cryopreserved Sperm." The consent form will be signed by the "owner" of the sperm and will be witnessed either by a notary public or by a center representative depending on the clinic's operating procedure. The summary of records as well as infectious disease screening results will be included as applicable. Finally, the specimen report and thawing instructions will be included in the paperwork packet.

1.31 Release of Frozen Sperm Samples

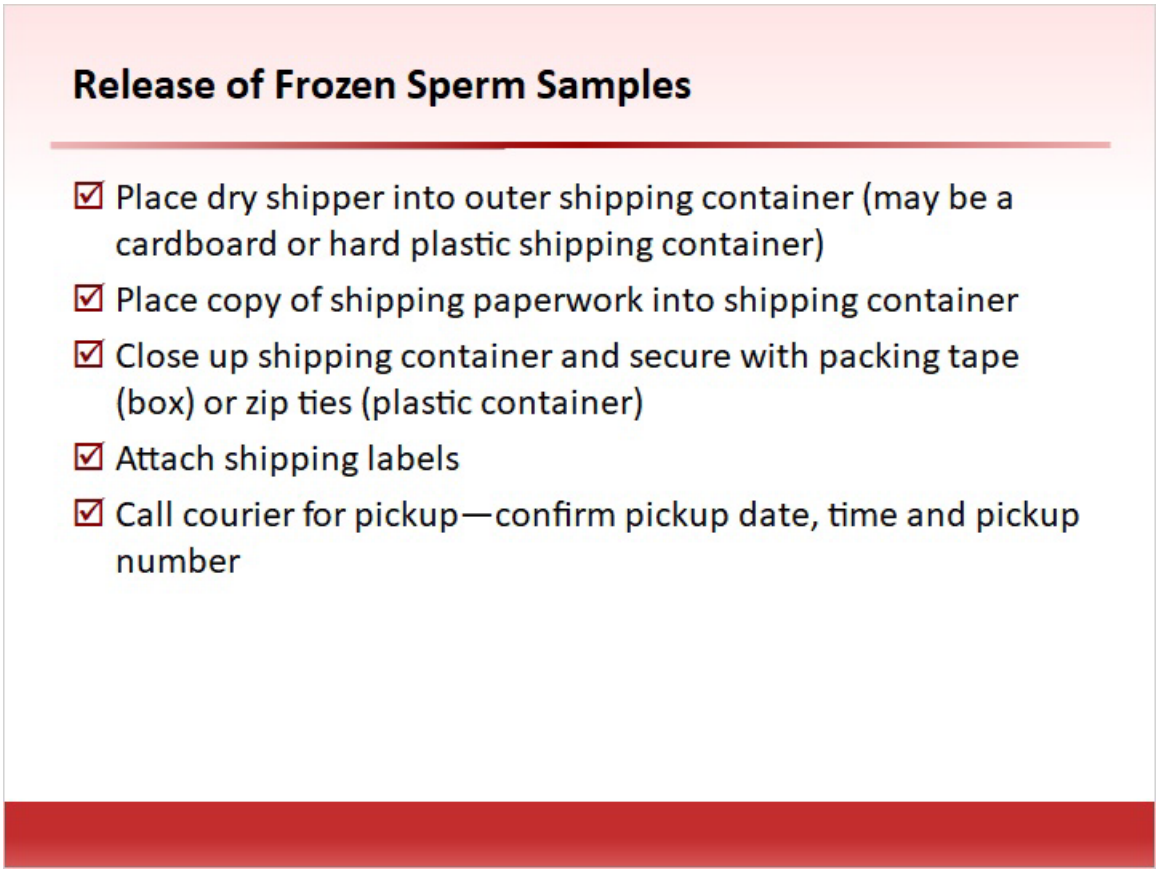


Notes:

A second staff person should always be used to verify the release order paperwork and the identity of the specimen to be released. If the specimens are being released to a long-term storage facility, the specimen transfer order between the patient and the long-term storage facility should be verified by 2 individuals. The lab should maintain a copy of the agreement with the release paperwork.

The cane containing the specimens should be removed from the storage tank to a dewar filled with liquid nitrogen to facilitate identity of the sperm vials. Once properly identified, the cane should be quickly transferred from the dewar to the charged dry shipper. If a temperature monitoring device is being used, the activated monitor can be snapped onto the same cane or onto its own cane and dropped into the dry shipper. The cap of the dry shipper is secured with a zip tie.

1.32 Release of Frozen Sperm Samples



Notes:

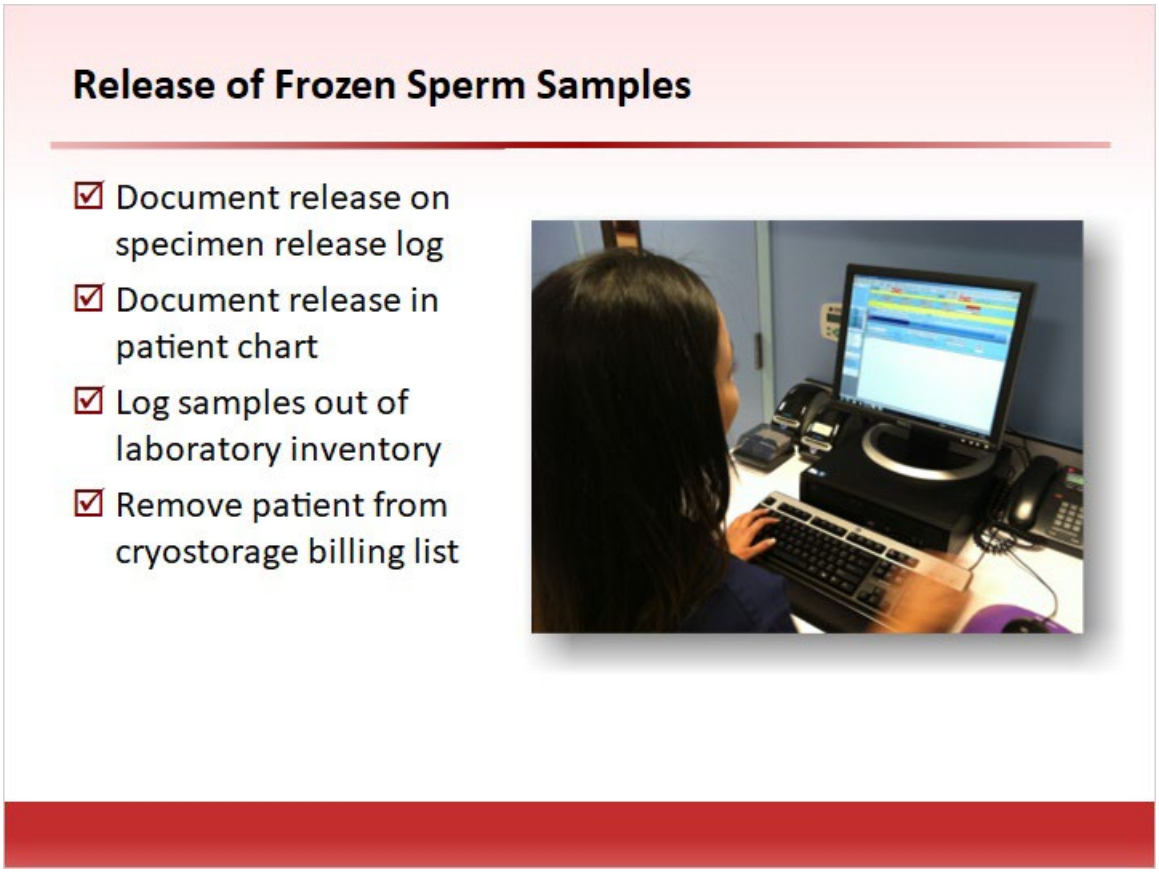
The dry shipper is placed into an outer shipping container. This may be a cardboard box or a hard plastic shipping container specially designed to hold and protect the dry shipper and maintain it in an upright position. Place the specimen paperwork into an envelope and then into the shipping container. Close the shipping container and secure with packing tape (box) or zip ties (plastic container). Attach shipping labels. Call the courier for pick up and confirm pickup date, time, and pickup order number.

1.33 Release of Frozen Sperm Samples: Shipper Options

Notes:

Examples of external shipping containers designed to protect the dry shipper dewar en route to its new location are shown here.

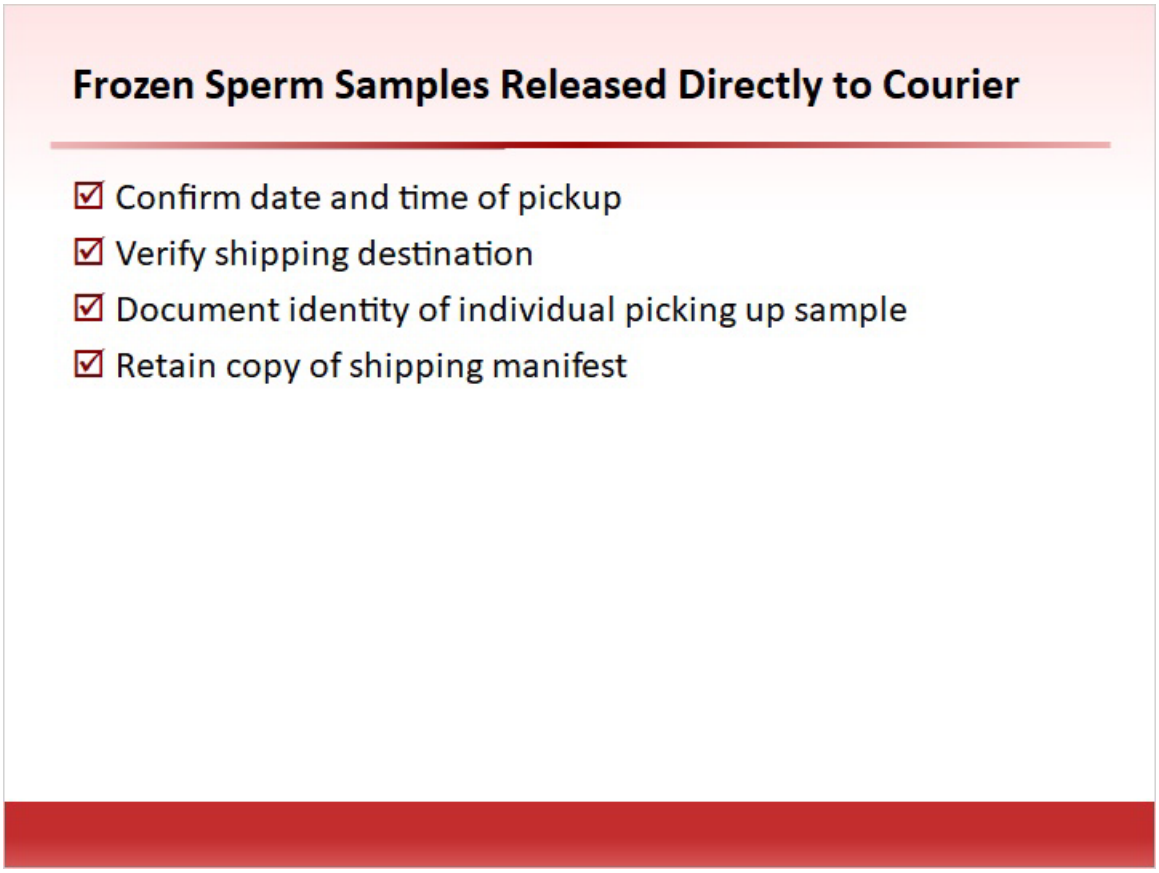
1.34 Release of Frozen Sperm Samples



Notes:

Samples released from the laboratory should be logged out on the biological specimen release log and the laboratory's cryoinventory, and the patient should be removed from the cryostorage billing list. Release of the specimens should be clearly documented in the patient's medical record. Confirmation of receipt of the shipped frozen specimens should be confirmed via email or telephone and documented as such in the medical record.

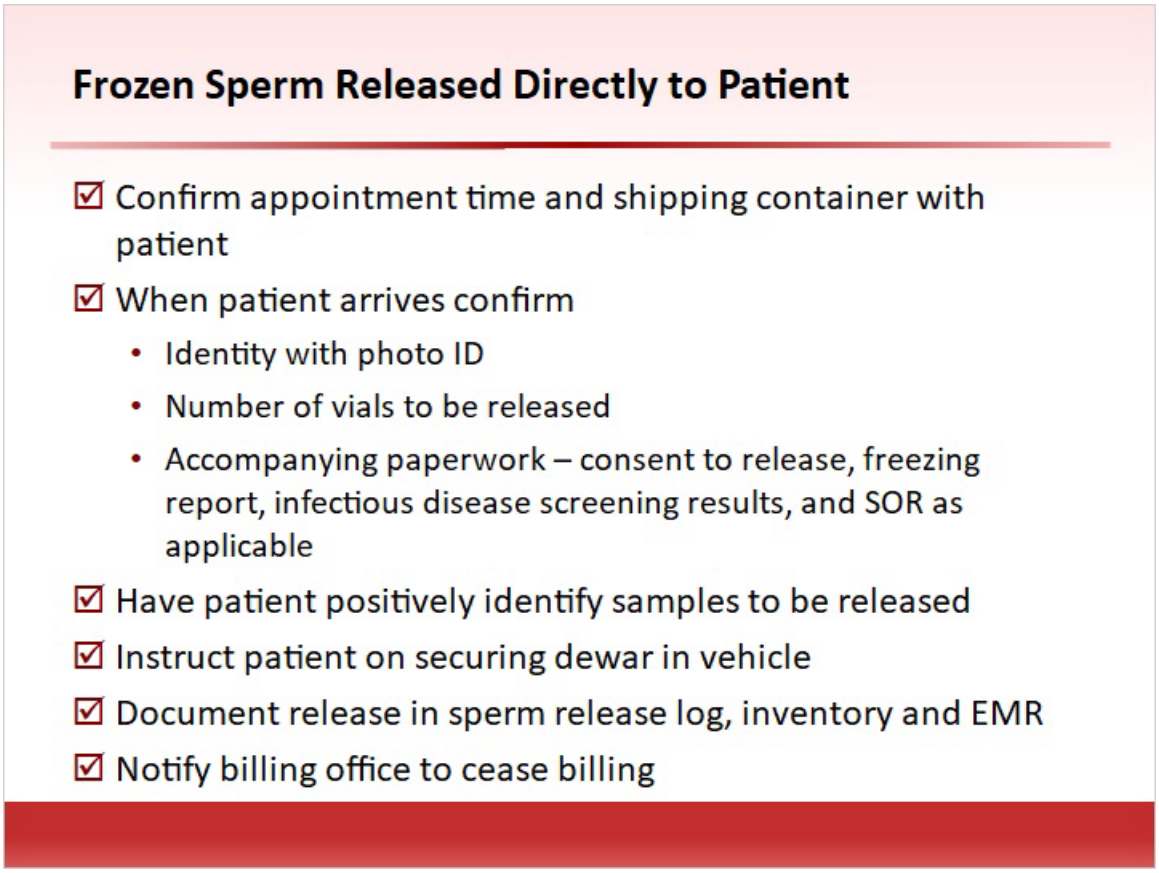
1.35 Frozen Sperm Samples Released Directly to Courier



Notes:

If a sample is being released directly to a courier, the sample is identified and packaged as described previously. In some cases, the courier will also require verification of the samples, so final securing of the dry shipper cap and outer shipping container should be delayed until the courier confirms the sample identity. The date and time of pickup as well as the destination should be confirmed with the courier. This allows the laboratory to provide a dedicated staff person to the release of the sample, thus minimizing interruption of the daily lab workflow. When the courier arrives, the laboratory staff should document the identity of the individual picking up the sample and should retain a copy of the shipping manifest.

1.36 Frozen Sperm Released Directly to Patient



Notes:

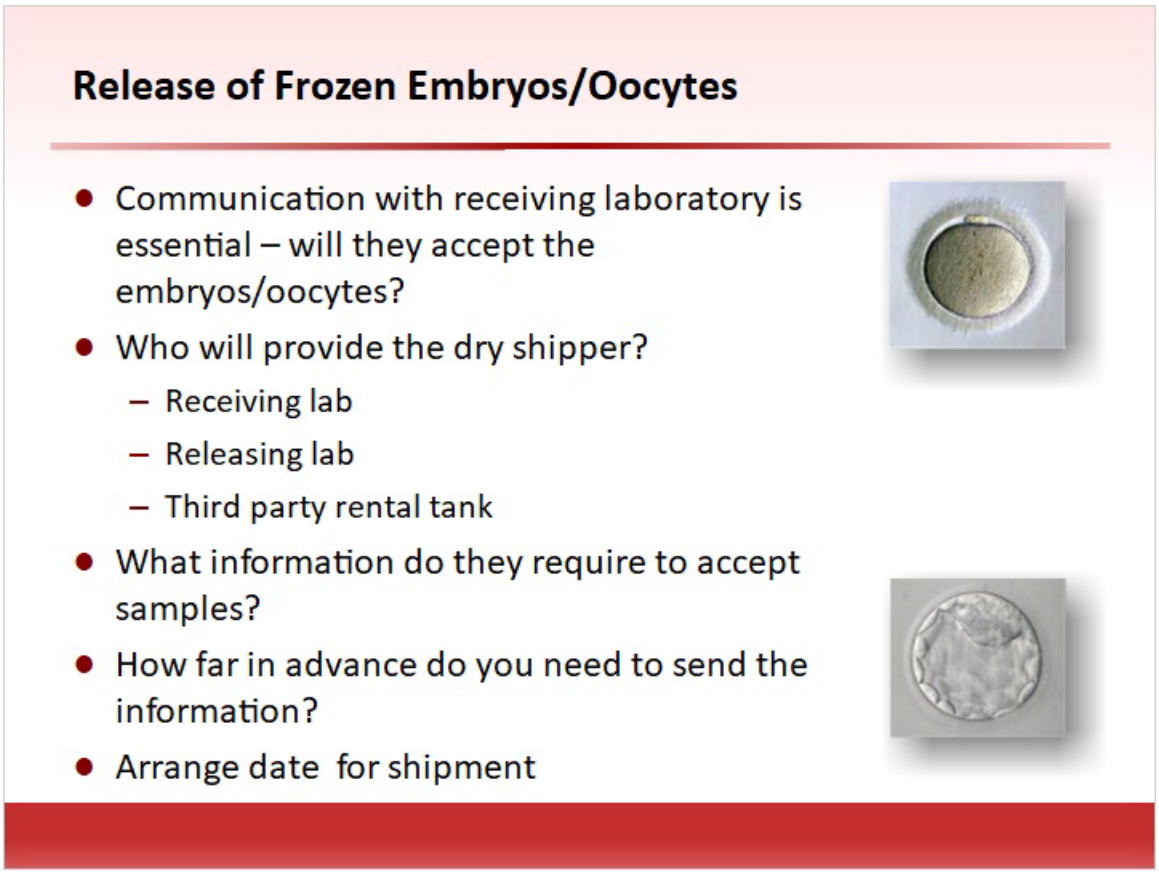
If a patient wishes to hand carry the frozen specimens to another facility, he/she should speak directly with a laboratory staff person prior to the pickup appointment time. It is important that the patient understands the lab's release procedure, including the paperwork required and who is responsible for providing the shipping container. The patient is responsible for making an appointment with the receiving lab so that the staff is expecting the specimen to be delivered. Confirm the appointment date and time with the patient, and plan to allow approximately 20–30 minutes for the specimen release.

When the patient arrives, confirm the patient's photo identification and the reason for the visit. Review the accompanying paperwork with the patient: including the consent to release, freezing report, infectious disease screening results, and summary of records as applicable. Have the patient positively identify the samples to be released. Instruct the patient on how to safely transport the dry shipper in an automobile. The dry shipper should be secured either on the seat with a seatbelt, or on the floor of the vehicle propped so that the risk of tipping is minimized.

After the patient leaves the lab, document the specimen release in the biological

materials release log, medical record, and cryoinventory as previously described. Notify the business office to cease cryostorage billing.

1.37 Release of Frozen Embryos/Oocytes



Notes:

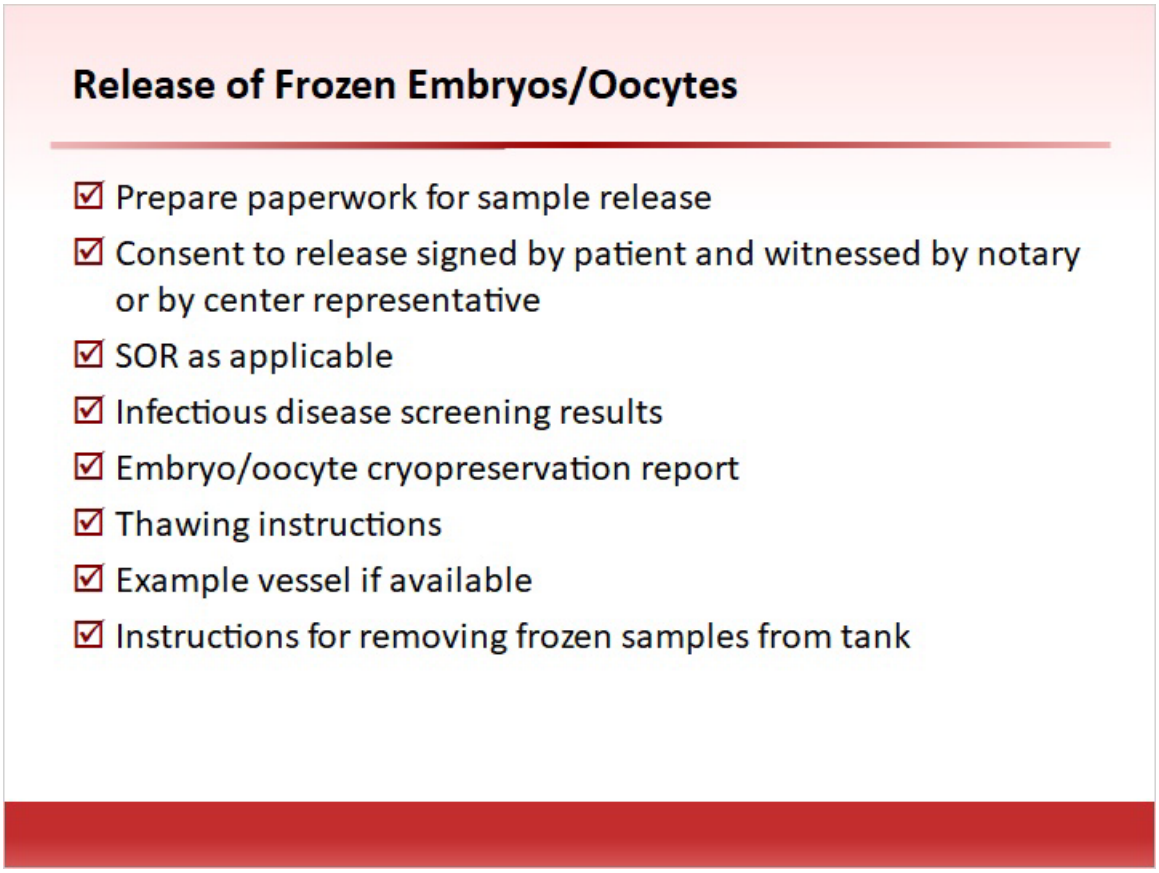
Communication is one of the most important elements for successfully releasing frozen embryos or oocytes to another facility. The most important question to ask is whether or not the destination lab will accept specimens frozen outside their facility. With the vast number of embryo thawing/warming protocols and cryodevices available today, some labs may choose not to accept embryos/oocytes frozen using a protocol or device they are not familiar with. The patient should understand that protocols and experience levels vary between laboratories, and that moving the embryos/oocytes to another lab might possibly compromise their chance of success.

Another important item to discuss is who will provide the dry shipper. As mentioned earlier, some labs do not maintain dry shippers to be used outside of their facility for economical or liability reasons. If this is the case, a third-party vendor may be used who

will provide a loaner tank for a fee. Generally, the tank is shipped warm to the lab releasing the embryos. The lab will charge the dry shipper and, using a prepaid shipping label provided by the vendor (and paid for by the patient), ship the embryos/oocytes to the receiving lab. The receiving lab will use the vendor-supplied prepaid shipping label to return the empty tank to the third-party vendor. This may be the preferred method as the third-party vendor bears the liability for the maintenance and integrity of the dry shipper tanks.

Different states have different requirements for infectious disease screening. This information should be confirmed ahead of time so that all of the necessary paperwork is available in time for the shipping date. Some labs may require this information far in advance of the shipment. Finally, confirm the date of the shipment, avoiding weekends and holidays.

1.38 Release of Frozen Embryos/Oocytes

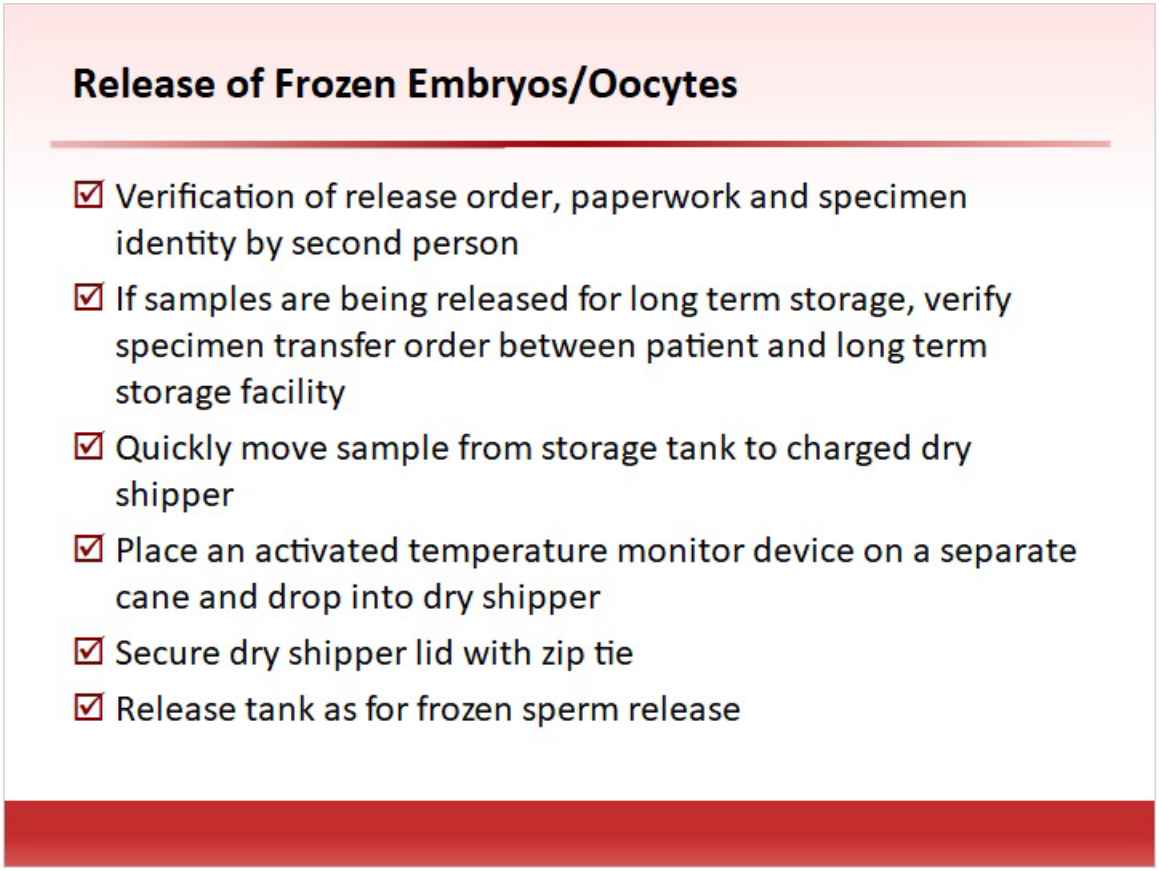


Notes:

A complete set of paperwork should be sent with the embryos/oocytes. The packet

should include a consent to release the frozen embryos/oocytes, signed by both parties (as applicable) and witnessed either by a notary public or by a center representative. The summary of records and infectious disease screening results, embryo/oocyte cryopreservation report and thawing instructions should be included. As a professional courtesy, an example cryodevice should be sent. This could be one saved and washed after thawing a previously frozen embryo/oocyte. This gives the receiving lab a chance to look at the device and practice handling it before thawing the actual patient sample. The releasing lab should provide instructions for the proper transfer of the frozen samples from the dry shipper to the storage tank. As mentioned earlier, the dry shipper should be filled with liquid nitrogen poured from a dewar, *not* from a hose attached to a liquid nitrogen source tank.

1.39 Release of Frozen Embryos/Oocytes

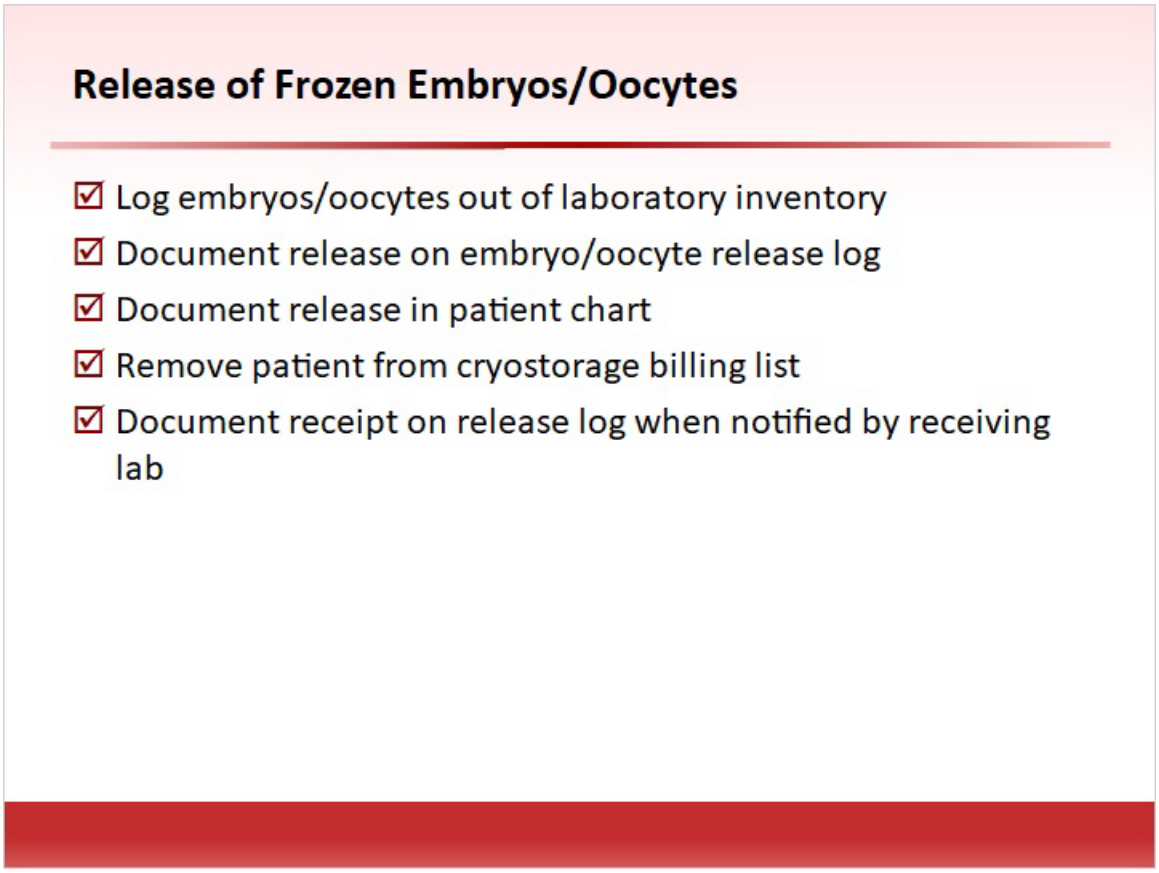


Notes:

A second person will verify the identity of the embryos/oocytes to be released and will compare the specimen identification to the accompanying paperwork. If samples are being released to long-term storage, the specimen transfer order between the patient

and the long-term storage facility will be verified as well. The cane containing the embryos/oocytes will be moved quickly to the charged dry shipper. The importance of maintaining submerged cryodevices cannot be emphasized enough, and only properly trained staff members should be handling frozen samples for release or receipt. An activated temperature monitor device is snapped onto a second cane, and that cane is dropped into the dry shipper. The lid is secured with a zip tie, and the dry shipper is placed into an outer shipping container and released as described previously for sperm samples.

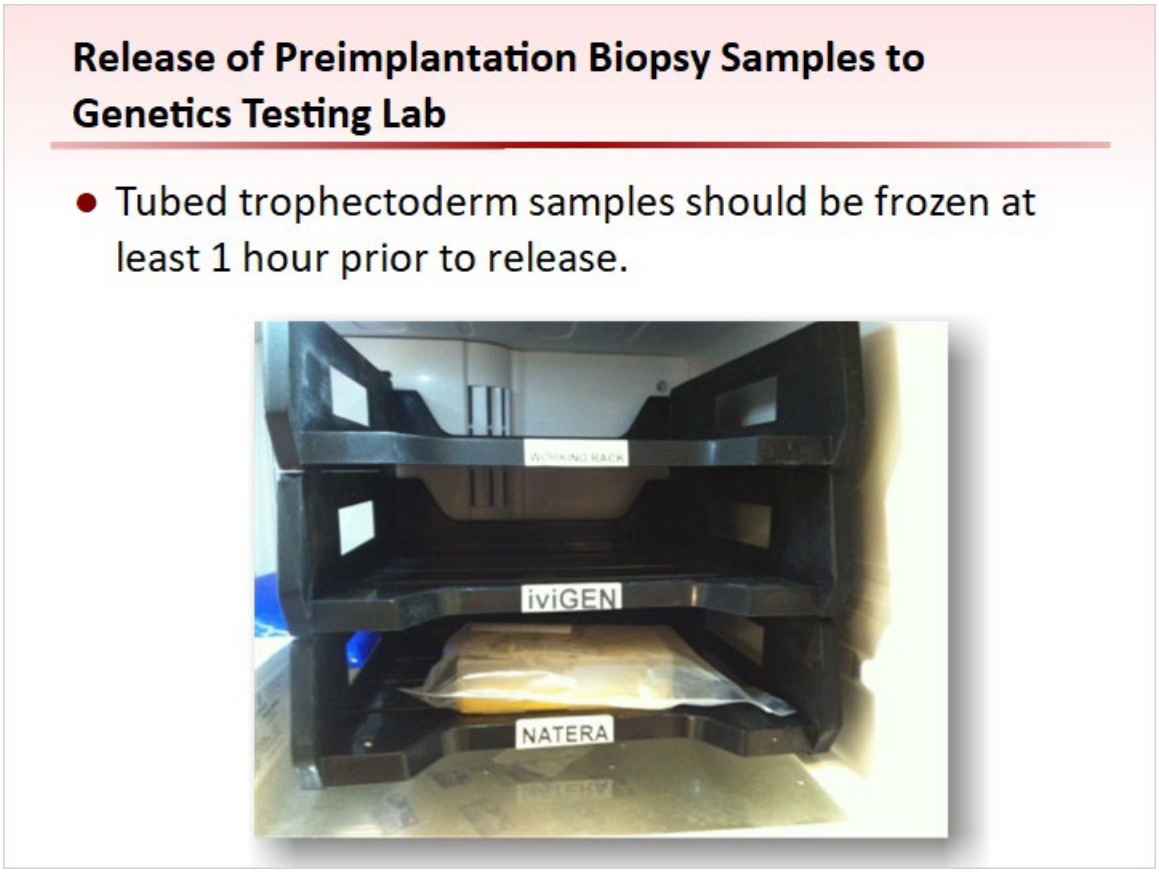
1.40 Release of Frozen Embryos/Oocytes



Notes:

Release of the embryos/oocytes will be documented in the patient record, cryostorage inventory, and the biological release log as described previously for sperm. Confirm receipt of the frozen embryos/oocytes by the receiving laboratory via email or telephone.

1.41 Release of Preimplantation Biopsy Samples to Genetics Testing Lab



Notes:

Embryo biopsy sample cells should be frozen for at least 1 hour prior to releasing the samples to the courier. This photograph shows how a simple paper file tray can be placed into the freezer to hold sample tube racks for multiple genetic testing labs.

1.42 Release of Preimplantation Biopsy Samples to Genetics Testing Lab

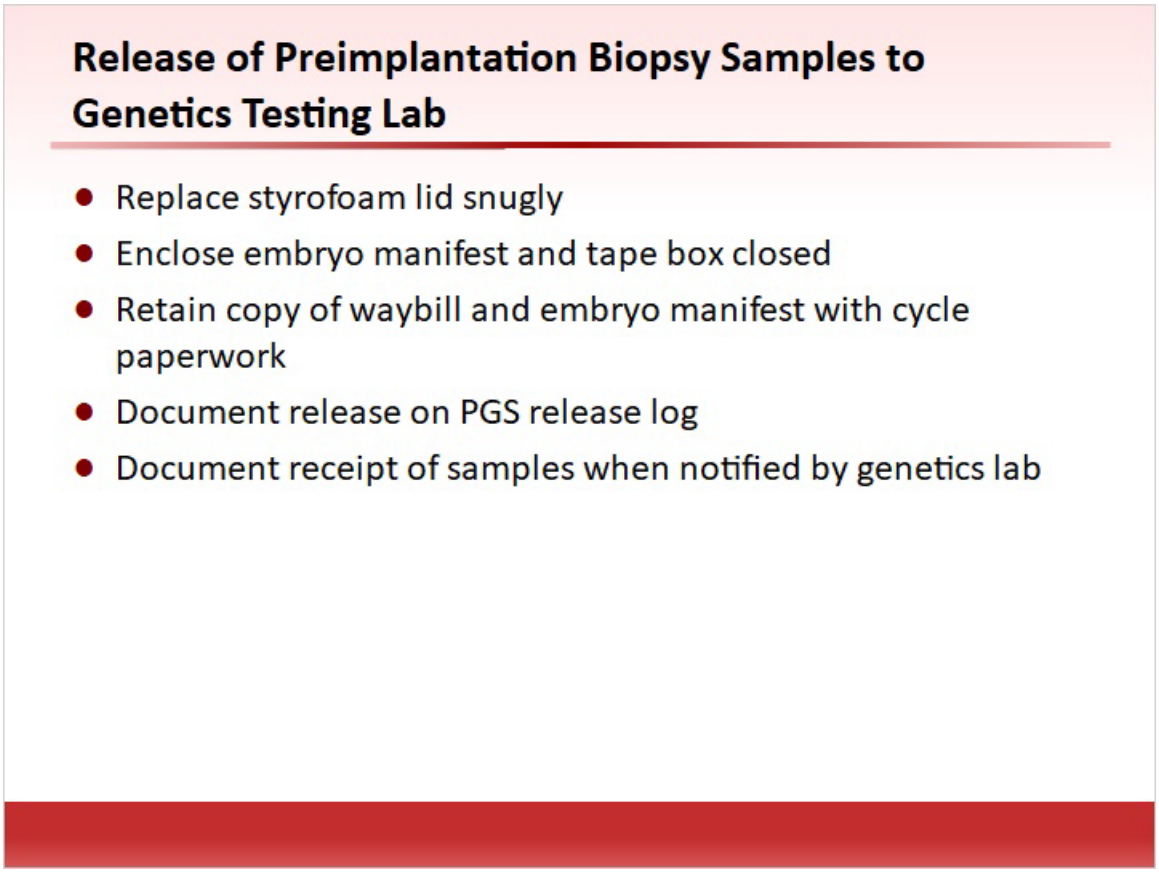
Release of Preimplantation Biopsy Samples to Genetics Testing Lab

- ☑ Courier should arrive with styrofoam packing box of dry ice.
- ☑ Fill shipping box half way with dry ice.
- ☑ Remove labeled rack (closed in zip loc bag) from lab freezer and place directly on top of dry ice.
- ☑ Pour dry ice on top of rack to cover.

Notes:

Unless a lab has access to dry ice, the courier will bring approximately 5 lbs of dry ice pellets (preferable to blocks or chunks). The styrofoam shipping box is filled approximately half way with dry ice, and the bagged biopsy kit is placed inside the shipper box on top of the dry ice. Dry ice pellets are poured carefully over the top of and around the sides of the biopsy kit box until the box is surrounded and secured by the dry ice.

1.43 Release of Preimplantation Biopsy Samples to Genetics Testing Lab



Notes:

The lid to the styrofoam shipping box should be replaced snugly. The embryo manifest is placed on top of the styrofoam lid, and the outer cardboard shipping box is securely taped closed. A copy of the embryo manifest and the waybill will be retained with the cycle paperwork. Release of the samples, including the tracking number, will be recorded on the preimplantation genetic testing release log.

1.44 International Shipping of Biological Materials

Notes:

It is no longer uncommon for patients to seek infertility treatment across the world. Intended parents may have embryos created in one country that will be transferred to a gestational carrier on another continent. However, there are unique challenges associated with shipping human biological specimens internationally. US clinics may be reluctant to accept embryos created outside the United States due to concerns over shipping, differences in infectious disease screening requirements, and unfamiliar protocols. It is an individual clinic's choice whether or not to accept international shipments.

1.45 International Shipping – Unique Challenges

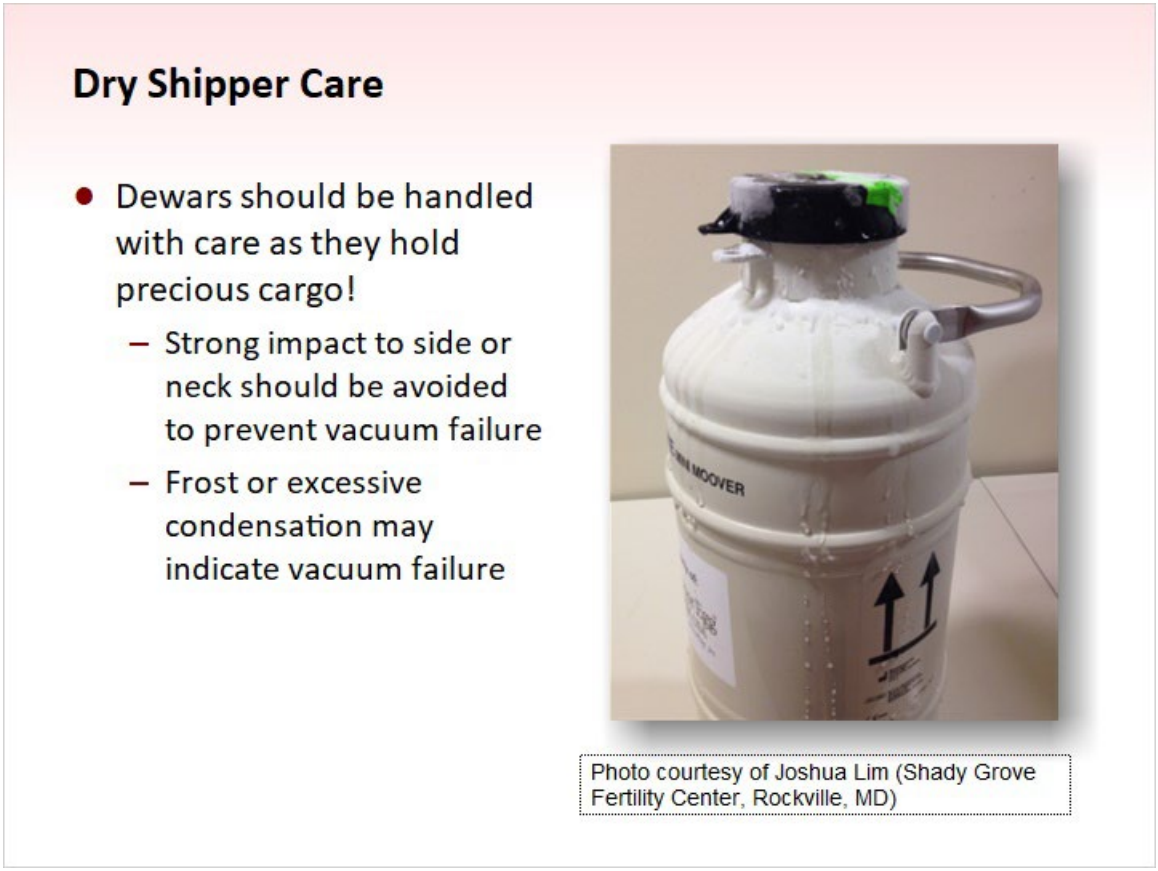
Notes:

When a patient inquires about shipping frozen sperm, embryos, or oocytes outside of the United States, the following recommendations should be made:

1. The chosen courier should provide a written service plan that will include a shipment timeline, precise tracking ability, and a communication team that is available 24 hours a day, 7 days a week.
2. The courier should be familiar with the current customs requirements. These requirements must be reviewed and verified prior to each shipment as the requirements often change.
3. A timeline should be provided along with a contingency plan should a delay be encountered. A shipment that takes 24 hours or less in the United States may take up to 10 days when sent internationally.
4. Plan for unexpected delays. Shipments can be delayed due to weather, strikes, local holidays, and customs. Verify that the receiving clinic has an import/export certificate. This certificate is an authorization from their government that they are allowed to accept and release international shipments. Without the import/export certificate, the shipment may not be allowed to enter the country. A commercial invoice is required for customs officials as it describes the contents and value of the shipment. It is critical

to secure this documentation prior to initiating the shipment to avoid delays that could have potentially devastating consequences.

1.46 Dry Shipper Care



Notes:

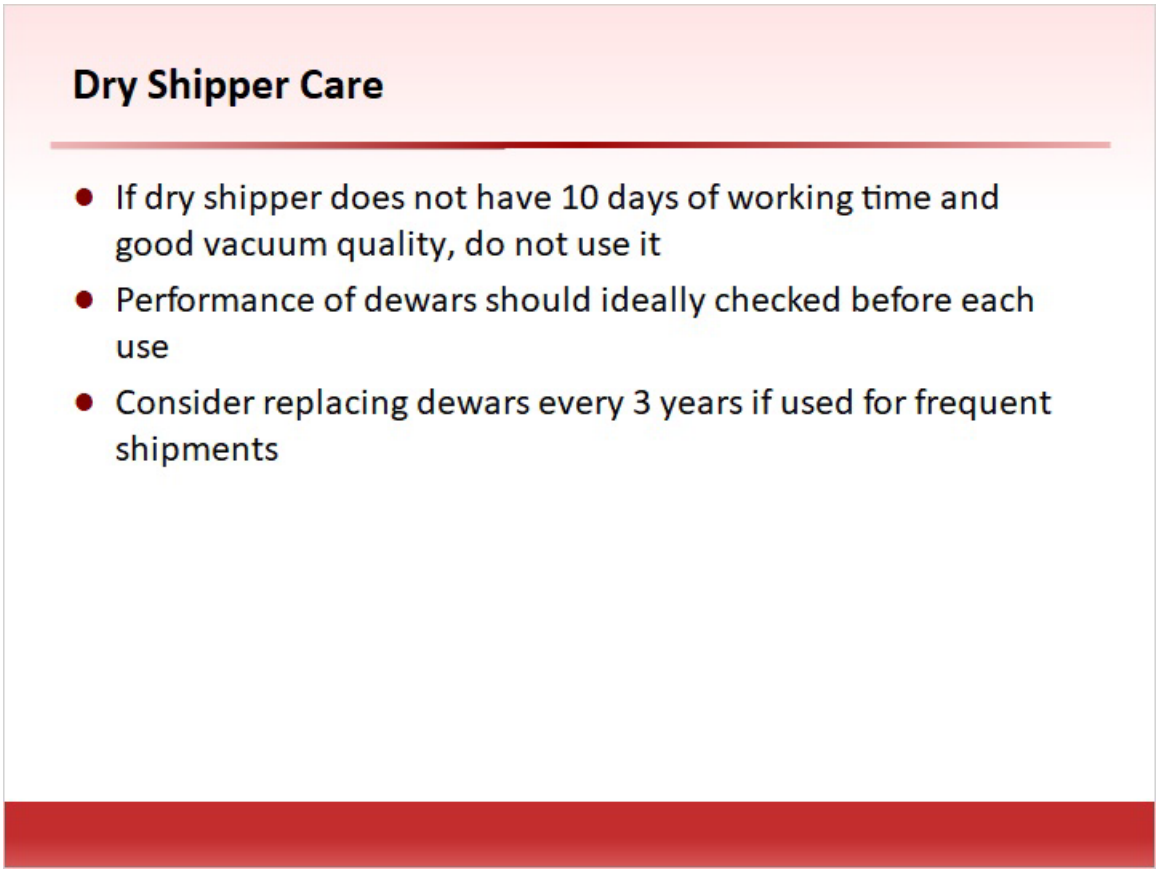
Dry shipper dewars should be handled with care as they hold precious cargo! Impact to the side or neck of the dewar should be avoided to prevent vacuum failure which may result in loss of the shipper's ability to maintain proper temperature.

1.47 Dry Shipper Care

Notes:

The vacuum plug near the neck of the shipper should be protected from liquid nitrogen spills. Exposure of the vacuum plug to liquid nitrogen can shrink the seal, causing air to leak into the insulating vacuum space. This can result in diminished performance of the dry shipper tank. A protective cap can be made of polystyrene foam or other material. Dewars should always be stored upright, never on their side. The lid of any vessel containing liquid nitrogen should never be airtight. Liquid nitrogen is constantly off-gassing nitrogen gas, and excessive buildup of nitrogen gas could result in an explosion. This is the reason the polystyrene foam caps fit loosely into the neck of shipper and cryostorage tanks.

1.48 Dry Shipper Care



Notes:

A dry shipper that does not have 10 days working time with good vacuum quality should not be used to ship samples. Ideally, performance of the shipping dewars should be checked before each use. Shippers that are used frequently should be replaced every 3 years.

1.49 Disposition of Frozen Embryos/Oocytes

Disposition of Frozen Embryos/Oocytes

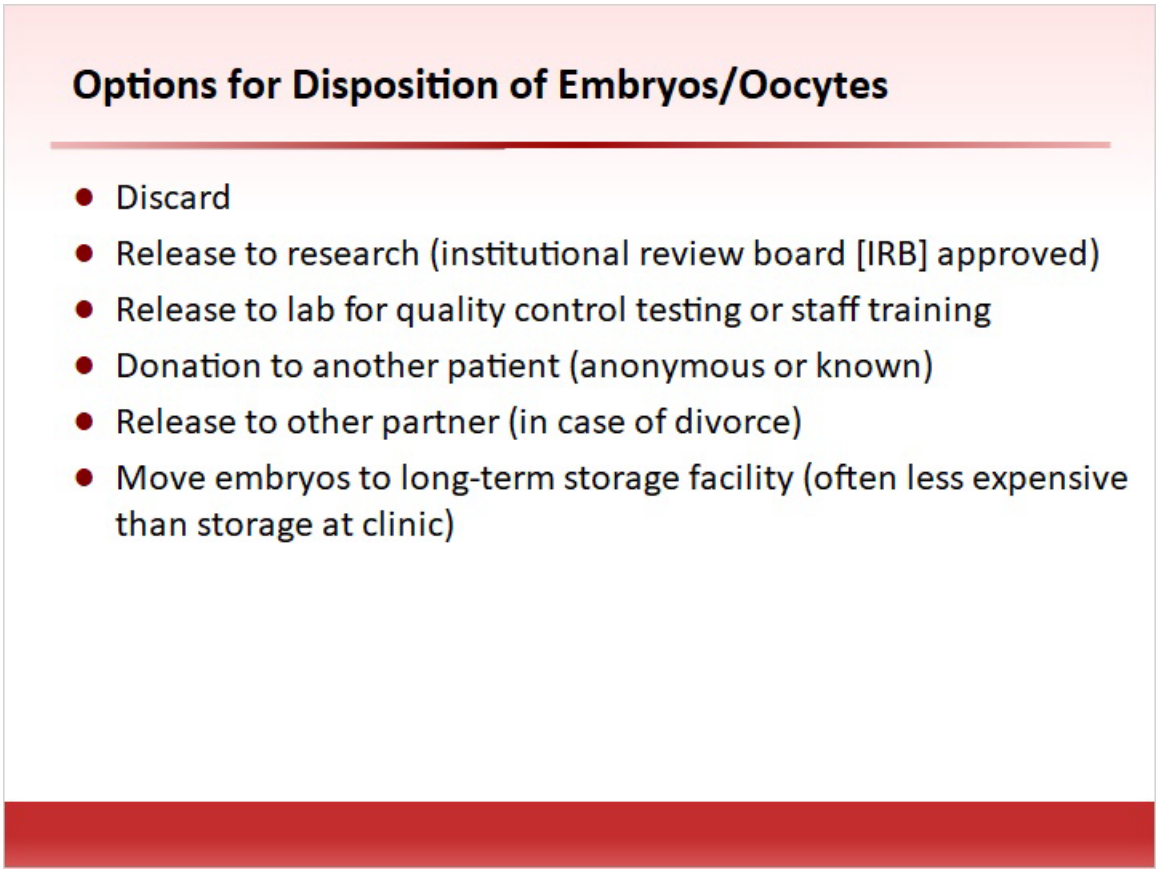
Reasons for disposition consideration

- Family is complete
- No further fertility treatments desired
- Death of one or both partners
- Divorce
- Reached the end of clinic's storage time limit

Notes:

Eventually many patients will face the difficult decision of what to do with their remaining frozen sperm, embryos and/or oocytes. They may have decided their family is complete or they no longer desire to pursue further fertility treatments. The death of one or both partners, as well as divorce, may force patients to make the decision. Some clinics impose time limitations on cryostorage, and once that time limit is reached, patients may be required to discard their embryos or move them to a long-term storage facility.

1.50 Options for Disposition of Embryos/Oocytes



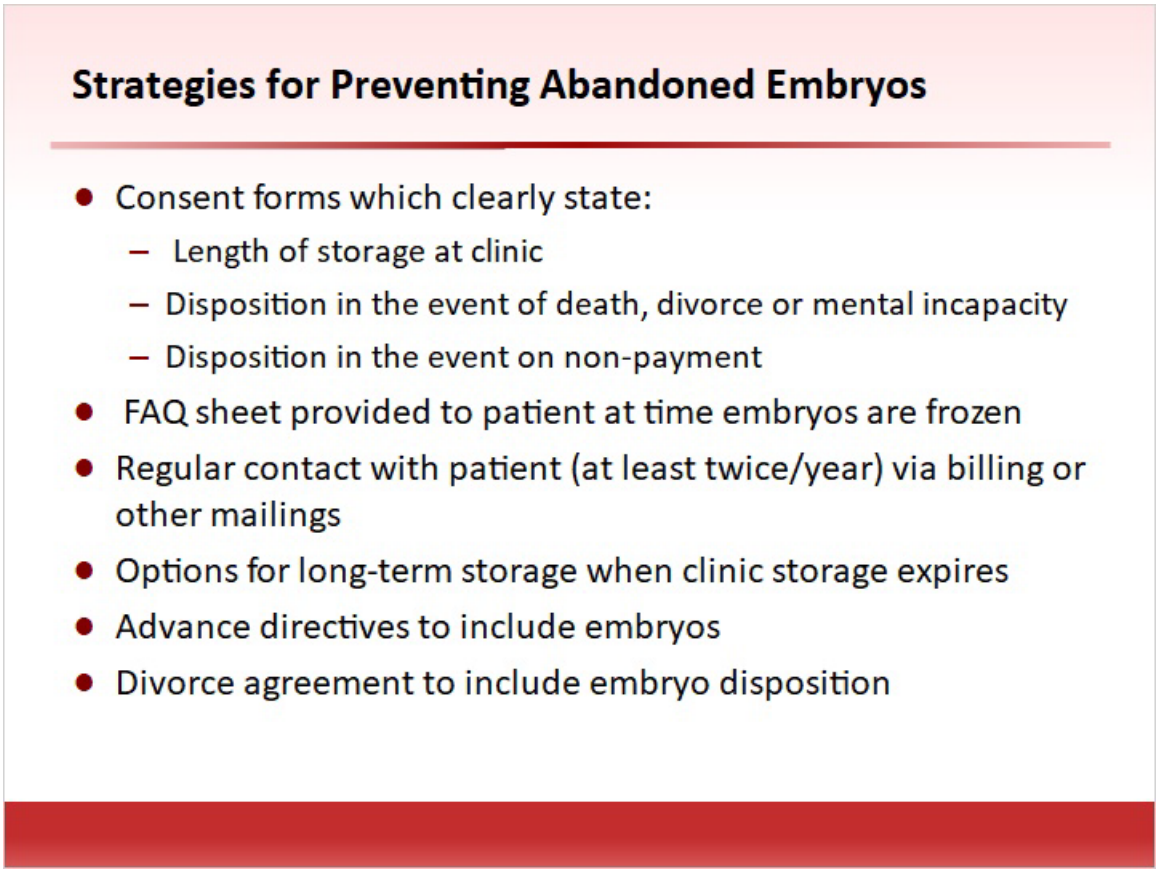
Notes:

There are many options for the disposition of frozen embryos/oocytes. While it is difficult for a new patient to ever imagine a situation described previously, a well-composed embryo cryopreservation consent form that covers each scenario is necessary to prevent future issues with cryostorage.

1. Patients have the option to discard their biological materials. The samples are removed from the cryostorage tank, the identity is verified by 2 embryology staff members, and the samples are placed into the biohazard waste container. In some cases the patient may want to come to the center and witness the discard. Some patients may want to come and pick up the samples and discard them privately. These wishes should be honored when possible, respecting how difficult this decision is for some patients.
2. Samples may be released to an institutional review board (IRB)-approved research program. This program may be in-house, or the samples may be shipped to an outside research laboratory.
3. The samples may be released to the lab for quality control or staff training purposes. This option provides excellent opportunities to train staff on warming, embryo biopsy, assisted hatching, embryo freezing, and general embryo handling. These embryos would be discarded afterwards.

4.Frozen samples may be donated to another patient. This may be done in-house or in conjunction with a donation agency.
5.Samples may be released to the other partner, such as when dictated by terms of a divorce. It is important to clarify responsibility for future storage, treatment, and childrearing costs.
6.Frozen samples may be released to a long-term storage facility, which may be at a significant cost savings to the patient.

1.51 Strategies for Preventing Abandoned Embryos



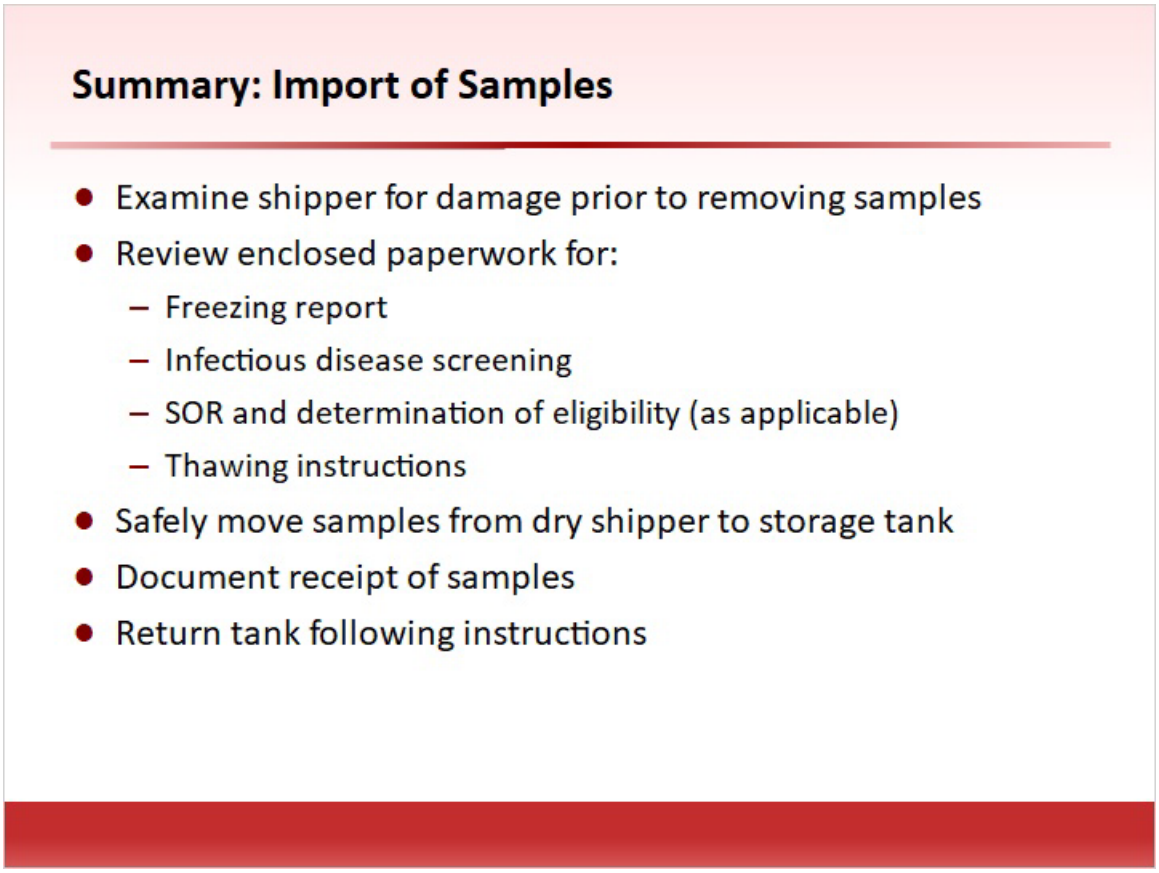
Notes:

There may be as many as 500,000 “abandoned” embryos stored in IVF clinics around the United States. Abandoned embryos include those belonging to patients who can no longer be located, patients who have stopped paying their cryostorage bills, and patients who no longer wish to use them but refuse to make a decision about what to do with them. These patients know that most clinics will not discard abandoned embryos without patient consent. Here are some useful strategies for limiting and/or reducing the number of abandoned samples.
1.While there is no way to guarantee a clinic will be free of abandoned embryos, having a well-constructed consent form signed by both partners (as applicable) will go a long

way in minimizing the volume of frozen samples left behind. The consent form should cover the length of storage provided by the clinic. Choices regarding disposition of the samples in the event of death, divorce, mental incapacity, and nonpayment should also be covered. As difficult as these scenarios are to consider when starting fertility treatment, these are real discussions that need to be brought up. Patients should be reassured that they may change their options at any time by updating their consent forms.

2. Provide a "frequently asked questions" handout to patients at the time their embryos are frozen. Questions can range from "how are my embryos frozen" to "what do I do if I no longer wish to store my embryos." Similarly, this information can be included on the clinic website so it is accessible to patients at all times.
3. Regular contact with patients is critical to maintaining current cryostorage accounts. Patients should be billed at least twice each year. Monthly billing is not uncommon, and credit card autopay saves time and money for both the clinic and the patient.
4. Patients should be provided with current and reliable long-term storage options as they approach the end of their storage period at the clinic. Some clinics opt for "auto-transfer" of all frozen samples in a specified time period after cryopreservation. The length of storage time may vary from immediate release to over 1 year or longer before being automatically transferred to a long-term storage facility.
5. Advanced directives are recommended for most medical procedures. Patients may want to consider completing an advanced directive form which would include their frozen biological materials.
6. Frozen sperm/embryos/oocytes may become part of the divorce agreement, simplifying the path to be taken once the divorce is finalized.

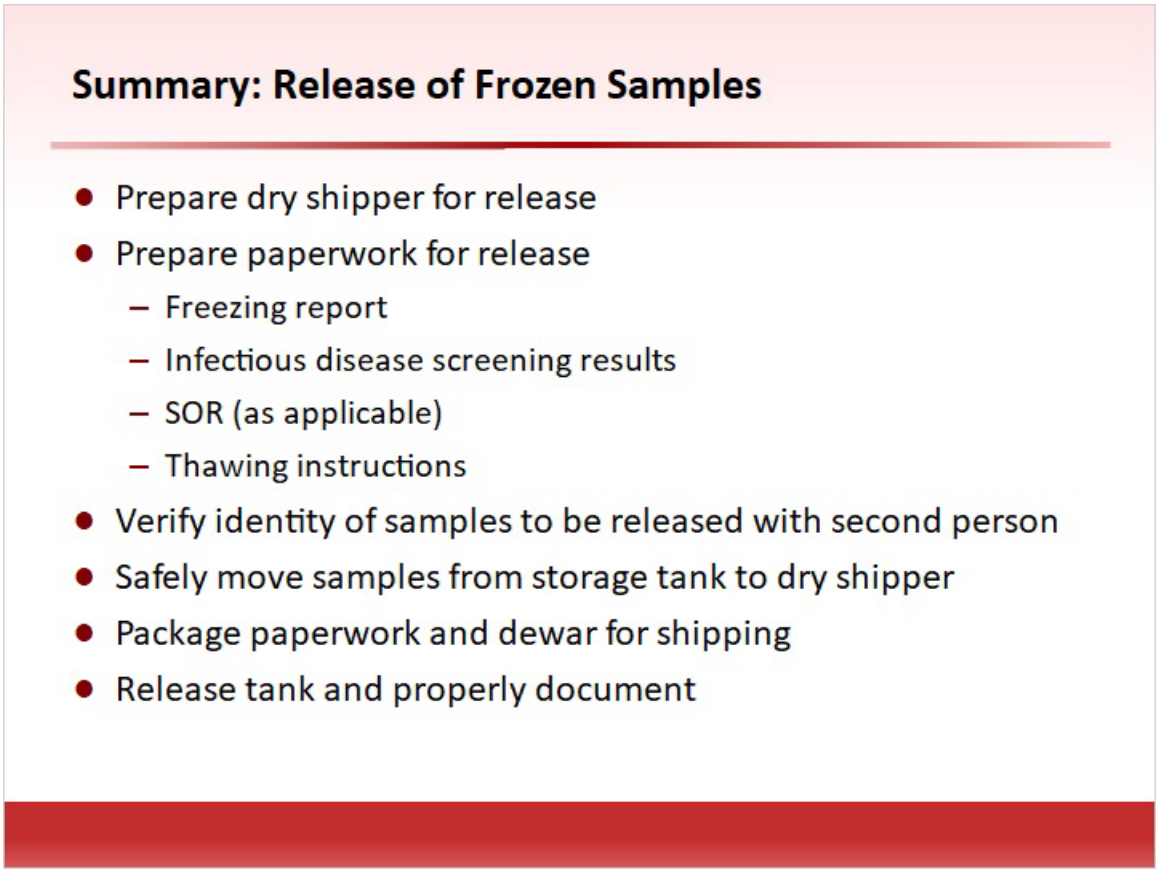
1.52 Summary: Import of Samples



Notes:

In summary, when importing frozen samples into your laboratory, the first step is to carefully examine the shipper for damage or vacuum loss *before* removing samples from the tank. Review the enclosed paperwork to be sure you have received a freezing report, infectious disease screening results, SOR, determination of eligibility (as applicable) and thawing instructions. Unpacking of imported cryopreserved samples should only be performed by trained personnel. Thoroughly document receipt of the frozen samples, and communicate receipt to the relevant parties. Finally, return the tank within the appropriate timeframe following the vendor's instructions.

1.53 Summary: Release of Frozen Samples



Notes:

When releasing samples from your laboratory, be sure to use a fully charged dry shipper known to be in good condition. Prepare release paperwork including the freezing report, infectious disease screening results, summary of records (as applicable), and thawing instructions. Two staff members should confirm identity of the frozen samples before release. Only trained lab personnel should be allowed to move the frozen samples from the cryostorage tank to the shipper tank. Package the paperwork and dewar for shipping and arrange for pickup. After the tank has been released, document release of the samples.

1.54 Summary: Challenges of International Shipping

Notes:

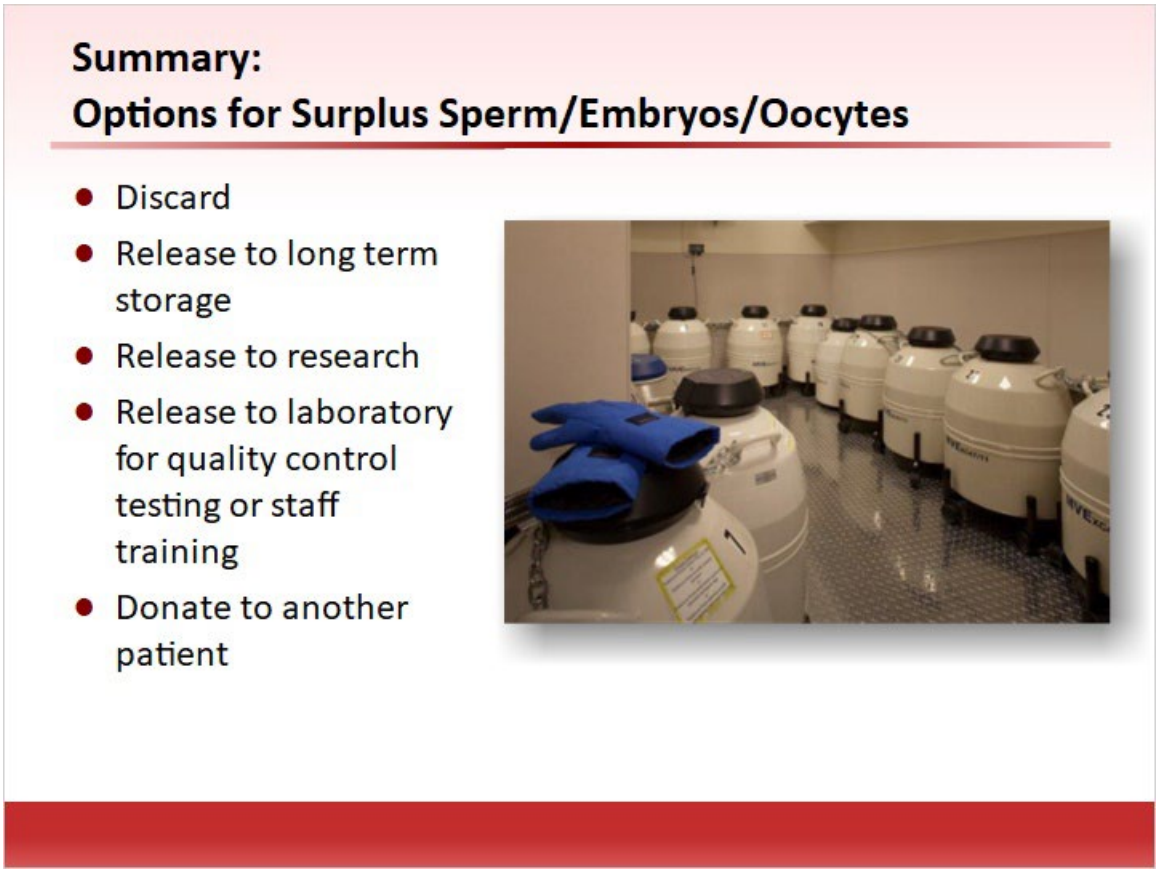
Frozen patient samples are being sent around the world with increasing frequency. International shipping presents unique challenges including changing customs requirements, unpredictable and unavoidable delays and proper equipment to accommodate longer travel times. A clear plan of communication is essential for safe transport.

1.55 Summary: Care of Dry Shippers

Notes:

Dewars are used to ship precious cargo and should be handled carefully, avoiding impact, tipping and overfilling. Dewars should be inspected regularly for signs of damage and loss of vacuum. Frequently used shippers should be replaced on a regular basis.

1.56 Summary:



Notes:

Provide multiple options to patients who no longer wish to continue storage of their frozen samples. Surplus sperm, embryos, and oocytes can be discarded, donated to research or to another patient, released to the lab for quality control testing and staff training, or released to an offsite facility for long-term storage.

1.57 Thank you!

Notes:

Thank you for participating in this educational activity.