

Revised guidelines for human embryology and andrology laboratories

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

Birmingham, Alabama

These guidelines provide clinicians with specific guidance on laboratory procedures to ensure that their programs' practice reflects current recommendations. (Fertil Steril® 2008;90:S45–59. ©2008 by American Society for Reproductive Medicine.)

GUIDELINES FOR HUMAN EMBRYOLOGY LABORATORIES

I. Organization of the Laboratory and Definition of Services

A. General Laboratory

1. The institutional affiliation, where appropriate, plus the history and definition of services and markets served, should be clearly defined for each embryology laboratory.
2. The laboratory must undergo certification and accreditation by an appropriate agency, e.g., College of American Pathologists/American Society for Reproductive Medicine, Joint Commission on Accreditation of Healthcare Organizations, or New York State Tissue Bank and must be in compliance with any local, state, or federal licensing requirements and/or regulations. Any current licenses, permits, and certification by any other groups or agencies should be listed.
3. The laboratory must satisfy Institutional Review Board (or equivalent Human Investigation Committee) requirements for any investigative procedures, if applicable.
4. Laboratory animals should be maintained humanely according to local, state, or federal requirements and/or regulations, if applicable.
5. Embryology laboratories are considered manufacturers of transplantation products (gametes and embryos) according to the FDA's Cell/Tissue Transplantation regulations (1). All embryology laboratories must be in compliance with these FDA regulations.

B. Specific Laboratory Procedures

Embryology laboratories are an integral part of In Vitro Fertilization (IVF), Gamete Intrafallopian Transfer (GIFT), Zygote Intrafallopian Transfer (ZIFT), Embryo Cryopreservation, Oocyte or Embryo Donation, and Gestational Surrogacy Programs. These are collectively known as Assisted Reproductive Technologies (ART). Embryology

laboratories are not referral laboratories but maintain specific affiliation with a physician group(s). Embryology laboratories perform some or all of the following steps:

1. Culture medium preparation and quality control testing
2. Examination of follicular aspirates with oocyte identification
3. Oocyte quality and maturity grading
4. Sperm preparation: semen collection and analysis, sperm washing
5. Insemination of oocytes
6. Evaluation of fertilization and zygote quality
7. Embryo culture and embryo grading
8. Embryo transfer (either uterine or tubal)
9. Oocyte/embryo/sperm cryopreservation, storage and thawing
10. Micromanipulation of human oocytes and/or embryos (e.g. Intracytoplasmic Sperm Injection [ICSI], Assisted Hatching [AH], polar body or embryo biopsy for Preimplantation Genetic Diagnosis [PGD]).

C. The laboratory must have evidence of informed consent for all procedures prior to performing said procedures.

II. Laboratory Personnel

A. Personnel Qualifications and Responsibilities

There should be sufficient personnel to provide embryology services as needed in a timely manner with a mechanism in place to provide back up for the laboratory personnel. There are several categories of personnel. Staffing levels should be appropriate for the size and volume of the program; a minimum of two qualified persons is required who are capable of performing all technical services.

1. Embryology Laboratory Director

a. Qualifications: The individual must fulfill *both* of the following requirements:

- 1) An earned doctorate degree (Ph.D.) from an accredited institution in a chemical, physical, or biological science as the major subject or a medical degree (M.D. or D.O.) from an accredited institution or have

Guideline

Revised August 2008.

Received and accepted July 28, 2006.

Reprints will not be available.

qualified as a laboratory director prior to July 20, 1999. Effective January 1, 2006, all new laboratory directors should hold High Complexity Laboratory Director (HCLD) or American Board of Bioanalysis Embryology Laboratory Director (ABB-ELD) certification or its equivalent. Laboratory directors grandfathered in are strongly encouraged to seek HCLD or ELD certification. The laboratory director should have the expertise and/or specialized training in biochemistry, cell biology, and physiology of reproduction with experience in experimental design, statistics, and problem solving. The laboratory director should be responsible for formulating laboratory policies and protocols and communicating with the medical director regarding patient progress and protocols as they affect the laboratory aspects of treatment.

- 2) Two years documented experience in a program performing IVF-related procedures. This experience should include:
 - a) Familiarity with laboratory quality control, inspection, and accreditation procedures.
 - b) Detailed knowledge of cell culture and ART and andrology procedures performed in mammalian systems.
- 3) The embryology laboratory director should have had a period of training of at least six months (may be concurrent with documented experience) and completed at least 60 ART procedures under supervision. A procedure is defined as a combination of the examination of follicular aspirates, insemination, documentation of fertilization, and preparation for embryo transfer. Satisfactory completion of this period of training should be documented by a signed letter from the laboratory director of the training practice. In addition to these qualification requirements, the embryology laboratory director should:
 - a) Obtain at least 12 hours of accredited continuing education annually in assisted reproductive technology or clinical laboratory practice.
 - b) Demonstrate technical competency in the embryology laboratory by documenting performance of specific procedures and results that are within acceptable standards for that program.
- b. Responsibilities: These include:
 - 1) Providing accessibility for on-site, telephone or electronic consultations as needed.

- 2) Ensuring that the physical plant (space, facilities and equipment) and environmental conditions of the laboratory are appropriate and safe.
- 3) Maintaining aseptic conditions in the laboratory.
- 4) Ensuring that patient confidentiality is maintained throughout the laboratory ART process.
- 5) Providing an approved procedural manual to all laboratory personnel, establishing and maintaining a laboratory quality assurance program.
- 6) Providing consultation to physicians and others, as appropriate, regarding laboratory aspects of treatment.
- 7) Employing a sufficient number of qualified laboratory personnel to perform the work of the laboratory. At a minimum, there should be two (2) qualified embryologists. **Table 1** provides minimum staff sizes for the volume of cycles (retrievals and cryopreservation cycles). Additional laboratory staff may be required if andrological and/or endocrinological duties are also assigned.
- c. The embryology laboratory director should ensure that all personnel receive appropriate training for the ART laboratory procedures to be performed, obtain the required number of annual continuing education hours, and demonstrate continued competency for the ART laboratory procedures performed.
- d. An “off-site” laboratory director is one whose primary directorship is at another physical facility, which has a separate identification number (SART number) and a separate medical director. An off-site director has the same responsibilities as an on-site director. While the laboratory is actively treating patients, the off-site director is required to physically visit the laboratory at a frequency that will ensure the proper functioning of the laboratory and assure appropriate patient care. Minimum

TABLE 1

Recommended staff according to volume.

Number of laboratory cycles	Minimum number of embryologists
1–150	2
151–300	3
301–600	4
>600	1 additional embryologist per additional 200 cycles

ASRM Practice Committee. Revised guidelines. Fertil Steril 2008.

standards would require a frequency of no less than 1 visit per month, while the lab is active. The lab director should also be available at all times by fax, phone, or email to address any issues that may arise. The off-site director must be present on site for any accreditation or certification procedures. A laboratory director shall direct no more than five separate laboratories of any type.

2. Embryology Laboratory Supervisor

The embryology laboratory may have one or more qualified laboratory supervisors who, under the direction of the laboratory director, provide day-to-day supervision of laboratory personnel performing ART procedures. If the medical director is also the laboratory director, there should be a designated laboratory supervisor. If the embryology laboratory director is primarily located off-site, there should be a designated laboratory supervisor.

a. **Qualifications:** The embryology laboratory supervisor should either meet the qualification requirements designated for laboratory director or fulfill **both** of the following requirements:

- 1) Have an earned bachelor's or master's degree in chemical, physical, biological, medical technology, clinical or reproductive laboratory science from an accredited institution;
- 2) Have documented training, which includes performing, at a minimum, at least 60 ART procedures under supervision.

b. In addition to meeting these requirements, the embryology laboratory supervisor should:

- 1) Obtain at least 12 hours of accredited continuing education annually in assisted reproductive technology or clinical laboratory practice
- 2) Perform at least 20 ART procedures per year.

c. **Responsibilities:** These include day-to-day supervision and oversight of the embryo laboratory and laboratory director responsibilities as authorized in writing by the embryology laboratory director.

3. Embryology Laboratory Technologist

a. **Qualifications:** Embryology laboratory technologists who perform ART laboratory procedures should either meet the qualification requirements for laboratory supervisor, or fulfill *both* of the following requirements:

- 1) Have an earned bachelor's or master's degree in chemical, physical, biological, medical technology, clinical, or reproductive laboratory science from an accredited institution;
- 2) Have documented training, which includes performing, at a minimum, at least 30 ART

procedures under continuous supervision of the laboratory director or supervisor.

b. In addition to meeting these requirements, the embryology laboratory technologist should:

- 1) Obtain at least 12 hours of accredited continuing education annually in ART or clinical laboratory practice;
- 2) Perform at least 20 ART procedures per year.

c. Experience and documented training in tissue culture, sperm-egg interaction, or related areas of animal reproduction is desirable. The embryology laboratory technologist works under the supervision of a laboratory director or supervisor. Programs for the appropriate training of embryology laboratory technologists should be in place with documentation of completion for each employee.

d. **Responsibilities:** These include processing specimens, being able to independently perform all the routine technical procedures carried out in the embryology laboratory under the supervision of a laboratory director or supervisor, and reporting results.

B. Personnel Records

There must be written documentation of compliance with the section described above. This should include the following items:

1. An itemized list of all personnel, their capacity (full-time versus part-time), and their shifts, if applicable. Include the total full-time equivalents filled by full-time and part-time personnel.
2. A list delineating the education, training, and job qualifications of all laboratory personnel.
3. An organizational chart documenting the chain of command so that a responsible individual can always be identified.
4. An itemization of the training of personnel for each specific laboratory test offered; definitive training programs for all procedures should be established.
5. An itemization of personnel participation in training courses, educational programs, and/or technical meetings and maintain a record of such participation.
6. Documentation delineating the continuing laboratory experience necessary to maintain technical competency.
7. Documentation of the health status, physical examinations, or laboratory tests on personnel whenever required.
8. Annual performance reviews for personnel.

III. Laboratory Space and Design

The embryology laboratory should have adequate space to ensure safe and comfortable working conditions and be of a design that is appropriate for the volume of procedures performed.

- A. The laboratory should be in a low-traffic, secure area; it should be physically isolated from other laboratory activities (e.g., designating a corner of another lab is not adequate unless it is walled off). Use of toxic chemicals or radioisotopes, including toxic cleaning materials, in the laboratory is not permitted. Use of aerosols and pest control substances should not be permitted in the laboratory.
 - B. The laboratory should be in proximity to the procedure room. If not in proximity to each other, then the laboratory must ensure that necessary conditions for embryo viability are not compromised. Intercom communication is recommended where direct communication is not possible.
 - C. The incubators and their chamber space should be of sufficient volume and configuration to ensure positive specimen identification and minimize the potential for errors.
 - D. Separate office space should be provided for record keeping, data entry, and related administrative functions. Computer equipment should be available for data collection compliance. Appropriate reference books, journals, and other publications should be available for use by laboratory staff.
 - E. A general “wet area” (i.e., media preparation, equipment, sterilization, etc.) should be separate from the area in which oocytes and embryos are handled.
 - F. Material for laboratory construction, ventilation of the area, and cleanliness should be appropriate to laboratory work. Walls and floors should be composed of materials easily washed and disinfected. Carpeting is not acceptable.
- 5. General laboratory supplies, such as glassware, dish-washing equipment, etc., as appropriate to the size of the laboratory.
 - 6. A pH meter and osmometer for regular monitoring of media.
 - 7. It is the responsibility of laboratory personnel to ensure that any material that comes into contact with sperm, eggs or embryos is not toxic, using an appropriate bioassay or animal model system. This includes, but is not limited to aspiration needles, transfer catheters, plastic ware, glassware, culture media, and protein source.
 - 8. All laboratory chemicals and reagents must be labeled to indicate date received, date opened, and shelf life, where applicable.

B. Procedure Manuals

- 1. Procedure manuals detailing all aspects of the assisted reproductive technologies should be available in each laboratory. The purpose of this manual should be to describe the laboratory procedures in sufficient detail to assure reproducibility and competence in handling of human gametes, including specimen identification and labeling. The National Committee for Clinical Laboratory Standards (NCCLS) has a specific format for procedure manuals described in NCCLS publication GP-2A.
- 2. These manuals should be reviewed and revised annually by the laboratory director and auxiliary personnel should be updated and trained on revised procedures.
- 3. These procedure manuals should include, but not be limited to, all laboratory procedures. Laboratory procedures should include detailed protocols, equipment and material lists, sources of materials, and competency level required to perform each procedure.
- 4. Maintenance manuals for all laboratory equipment should be maintained in the laboratory. These should include daily, weekly, monthly, or annual maintenance to be performed on each piece of equipment, documentation of maintenance completed, and corrective action taken, if any.
- 5. Policy manuals should be maintained in the laboratory. These policies might include, but should not be limited to, procedures for record keeping, result reporting, laboratory communication, and disposition of business/billing procedures.

C. Specific Aspects of Assisted Reproductive Technologies

- 1. Culture media preparation and quality control testing
 - a. Culture media formulated de novo should utilize dedicated reagents, glassware, and tissue-culture-grade water (or its equivalent) in its preparation. Quality control testing utilizing

IV. Equipment and Procedure Manuals

These are minimum standards for each category.

- A. All laboratories should maintain the following:
 - 1. Incubator(s) with remote alarm system and emergency power back-up. The incubator should be monitored daily for appropriate temperature and gas content before first opening when used for patient procedures. Incubators should be monitored using calibrated thermometers and independent methods of gas analysis, not by digital display alone.
 - 2. Microscopes suitable for oocyte recovery, determination of fertilization, semen analysis, manipulation of oocytes or embryos, and/or micromanipulation of oocytes or embryos should be used.
 - 3. Devices to maintain temperature and pH of media, eggs, and embryos during various phases of the procedure (slide warmers, incubators, water baths, heating block, isolettes, etc.).
 - 4. Disposable materials (tissue culture grade plastic) are recommended for steps that involve exposure to tissue and body fluids.

- an appropriate bioassay system to evaluate the media is required.
- b. Quality control testing is recommended when commercial media is purchased and used within its labeled expiration period if pretesting by the manufacturer does not reflect media suitability when in actual use in the laboratory. Documentation of quality control testing using an appropriate bioassay system must always be supplied by the manufacturer. Laboratories should also establish tolerance limits for acceptable receiving conditions for transported commercial media.
 - c. Procedures and documentation for preparation of media.
 - 1) The sources of ultrapure (tissue culture grade) water should comply with College of American Pathologists (CAP) standards for reagent grade water. If water is produced on site, a comprehensive program of quality control for the water system must be in place. This must include, but should not be limited to, system sanitization, cartridge exchange, part replacement, endotoxin tests and bacterial contamination (colony) testing, and chlorine and/or formaldehyde testing (if applicable). If ultrapure water is purchased, the source, shelf life, and storage conditions must be strictly defined. While there are no set standards for levels of endotoxins in embryo culture media, endotoxin testing of purchased water is recommended if it is not certified endotoxin-free.
 - 2) All lots of chemicals, prepackaged media, and other media components should be recorded and specific sources and product numbers identified as part of the procedure manual and quality control sheets. Separate, designated chemicals should be maintained specifically for ART.
 - 3) Glassware washing protocols, including detergent type and source, type of water used, number of rinses, and exact procedure to be followed, should be strictly defined. Heat sterilization should be used whenever possible.
 - 4) All media preparation should be performed using sterile technique including location and appropriate environment.
 - 5) Appropriate refrigerated facilities should be available for media. It is suggested that periodic checks of media be made using an acceptable bioassay system.
 - 6) The protein source for medical use should be strictly defined. While the use of blood-based media or a blood-based media supplement (e.g., human fetal cord serum, maternal or donor serum) prepared in-house is not recommended, if such media or supplements are prepared, the laboratory must test blood from the donor(s) with an FDA-licensed, approved or cleared test and show that the donor(s) is negative or non-reactive for the following: HIV-1 and HIV-2, hepatitis B, hepatitis C, syphilis, HTLV-I and HTLV-II. Each batch of blood-based media supplement should also be tested using an appropriate method before its use to ensure that it is not embryotoxic.
 - 7) Each batch of culture media should be tested before use for osmolarity. Media pH testing should be performed following equilibration with CO₂ at concentrations used for ART procedures. All lots of media and media components should be recorded and traceable to each patient procedure (e.g. lot numbers recorded on oocyte/embryo data sheets in case of recalls, adverse events, etc.).
2. Examination of follicular aspirates with egg identification
 - a. All procedures should be performed using sterile technique in an area that has appropriate communication with and proximity to the egg retrieval area. If the egg retrieval room is separated from the embryology laboratory, then a mobile laboratory unit, modified infant isolette, or other appropriate method must be in place for maintaining follicular fluid temperature and pH.
 - b. Written procedures for the egg search and identification including media used for aspiration, temperature, pH requirements of fluid, and rapidity with which each sample must be evaluated should be available.
 3. Egg quality and maturity grading
 - a. Written protocols should include description of stages of oocyte quality and maturity, magnification used, maximum time of observation, media for observation, and remedial steps to be used for immature oocytes.
 - b. The morphological condition of all eggs should be documented.
 4. Sperm preparation (including sample collection, analysis and sperm washing)
 - a. The protocol for sample collection should include abstinence period, type of container used, facilities for collection, and/or time period and conditions for sample collection outside the laboratory, procedure and conditions for sample collection with seminal pouches and intercourse, and the acceptable time

- period for sample collection and provision of frozen back-up sample, if any, in relation to egg retrieval.
- b. Written procedures for sperm washing should include medium type and protein supplementation, if any; semen to medium ratio; relative centrifugal force if centrifugation is used; sperm isolation technique and incubation, if any; techniques for determination of sample parameters of concentration, motility, and morphology.
 - c. Laboratories should establish their own internal standards for minimal recovery of total motile sperm cells for both male factor and non-male factor patients. This can be used as an internal quality assurance measure; while individual samples may occasionally deviate from the expected range (this norm), competency in recovery of motile sperm should be maintained.
 - d. The prepared sample should be used in a timely fashion.
 - e. Sterile technique and universal precautions should be observed in all procedures.
 - f. When donor sperm is used for insemination, complete documentation of its use should include source (either internal or external bank) and donor number. Programs should use only donor sperm banks that are accredited in the state where the sperm will be used. Accredited sperm banks should provide documentation that the bank selects and screens donors in accordance with FDA, state, and ASRM Guidelines (2).
5. Insemination of oocytes
- a. Written procedures for insemination should include such details as types of pipettes used, maximum volume to be added to oocytes, number of motile sperm to be used for insemination on a per oocyte, per dish, or per unit volume basis. Criteria for altering insemination concentrations for varying degrees of male factor should be specified. The maximum number of oocytes per dish or unit volume should be stated.
 - b. Procedure sheets for each sample, time of insemination, and relevant observation at time of insemination should be kept as part of the lab file.
 - c. Sperm sample volume added to oocytes should be based on a determination of sample concentration and motility performed before oocyte insemination.
 - d. During insemination of each dish, temperature, humidity, and pH of the media should be controlled using appropriate (e.g., infant isolette, oil overlay) measures.
6. Determination of fertilization
- a. All oocytes that have been inseminated should be examined for signs of fertilization by a single sperm (i.e., two pronuclei [2PN] should be documented).
 - b. The time interval from oocyte insemination to examination for fertilization should be specified.
 - c. If oocytes require removal of blood or cumulus cells prior to examination, this may be performed using a needle or narrow bore glass pipette (pulled over a low flame), or another suitable method.
 - d. If cleaning and examination of an individual oocyte takes longer than 60 seconds, a temperature and pH controlled chamber or oil overlay should be provided to protect the egg/embryo.
 - e. Each fertilized oocyte with two PN may be transferred to fresh pre-equilibrated media.
 - f. The status of each oocyte should be recorded.
 - g. Written procedures for the reinsemination of oocytes and/or micromanipulation should include time frame for reinsemination, criteria for use of initial sample (i.e., minimum motile sperm and elapsed time since processing), time frame for re-examination of oocytes, and hierarchy for embryo transfer of reinseminated oocytes.
 - h. Written policies should be developed for disposition of oocytes with evidence of abnormal fertilization (i.e., disposal, culture, freezing, micromanipulation, IRB-approved research with consent).
7. Embryo transfer and embryo grading
- a. The procedure should be performed using sterile technique.
 - b. The stage of zygote or embryo development at transfer should be documented.
 - c. The protocol for embryo transfer should include type of medium; time from oocyte retrieval and/or insemination to transfer; stage of embryo development at transfer; fate of excess embryos; type of catheter used; alternate catheters available and circumstances for use of each; method of transfer; technique for catheter flushing; and conditions and timing of transfer of remaining embryos.
 - d. If the embryo transfer facility is separated from the embryo lab, appropriate equipment and techniques should be used to maintain media temperature and pH during the procedure (e.g., infant isolette, oil overlay, or mobile unit).
 - e. It is recommended that patients be excluded from access to the laboratory to examine ova, embryos, or for transfers.

- f. A disposable sterile transfer catheter should be used.
- 8. Oocyte/embryo freezing
 - Embryo or oocyte freezing may be considered optional.
 - a. A written protocol should include cryoprotectant used (including source and shelf life), media used, type of freezing container (e.g., straw, vial, or ampule), stage of embryo for freezing, freezing rate including procedure for manual or automatic seeding, and storage conditions.
 - b. All embryo freezing containers (e.g., each straw or vial) must be permanently labeled with at least two unique identifiers. A method of ensuring prompt, accurate retrieval of cryopreserved specimens must be employed. Duplicate records of all embryos in storage should be kept, in separate locations, exclusive of the patient chart information.
 - c. Time limits for embryo storage should be established by each individual laboratory and determined prior to freezing.
 - d. If the laboratory performs cryopreservation, there should be a system in place for the detection of low levels of liquid nitrogen.
 - e. Procedures for thawing embryos should include cryoprotectant concentrations and media used, temperature requirements for thawing, criteria for assessing embryo viability, time period for embryo culture prior to transfer, protocol for patient preparation for frozen embryo transfers and conditions under which embryo transfers will take place.
- 9. Micromanipulation
 - Micromanipulation is considered optional at each facility.
 - a. Protocols for micromanipulation should include circumstances and screening criteria for micromanipulation, procedures for processing sperm samples, types of microtools to be made or purchased, media/protein source, and conditions for micromanipulation including temperature, pH and osmolarity, criteria for judging oocyte maturity and oocyte and embryonic quality prior to micromanipulation, viability following micromanipulation, and conditions under which embryo transfer will take place.
 - b. Personnel should have demonstrated competence in performing micromanipulation.

V. Laboratory Safety and Infection Control

Procedures and policies on lab safety must be available to all laboratory personnel and should be reviewed annually by the laboratory director. Protocols should be available for fire and electrical safety and internal and

external disaster preparedness (including provisions for equipment back-up in the event of equipment failure). In addition, the following guidelines are recommended (3):

- A. Every body fluid sample (semen, blood, follicular fluid) should be handled using universal precautions (i.e., as if it were contaminated). All donor tissues and fluids should be subjected to appropriate infectious disease screens and quarantine periods where applicable.
- B. All accredited laboratories are required to have an Exposure Control Plan. A requirement of this plan is to offer and document Hepatitis B vaccination to all laboratory personnel. Any employee that refuses is required to sign a waiver that is kept in their employment record. Testing for additional STIs may be offered, but not required, with test results to be directed as indicated by the employee.
- C. Extraordinary precautions should be taken to avoid accidental wounds from sharp instruments contaminated with body fluids.
- D. Disposable, nontoxic (non-powdered) gloves should be worn when handling fresh or frozen body fluids or any material that has come in contact with body fluids. Gloves should be removed and discarded when leaving the laboratory or handling the telephone. Gloves should never be reused.
- E. A laboratory coat or appropriate gown should be worn in the laboratory and removed upon leaving the laboratory.
- F. Safety glasses or goggles are suggested where appropriate.
- G. Hands should be washed after removing gowns and gloves and immediately if they become contaminated with body fluids. All hand washing should be done with disinfectant soap and hot water or alcohol-based solutions.
- H. Disposable laboratory supplies must be used whenever possible.
- I. Contaminated laboratory equipment and/or work surfaces should be disinfected and sterilized after a spill (e.g., 1:10 dilution of 5.25% sodium-hypochlorite household bleach in water or other procedures approved by the Centers for Disease Control and Prevention [CDC]).
- J. Mechanical pipetting devices should be used for the manipulation of liquids in the laboratory. Mouth pipetting is never permitted.
- K. All procedures and manipulation of body fluids should be performed to minimize the creation of droplets and aerosols. Complete facemasks or the use of appropriate hoods should be considered when procedures are conducted which have a high potential for creating aerosols or droplets. Centrifugation or vigorous mixing of open containers represents examples of this problem. Centrifuges may be

placed in exhaust hoods during use or non-aerosol centrifuges may be used. Capped tubes must be used for centrifugation.

- L. Eating, drinking, smoking, application of makeup, or manipulation of contact lenses are not permitted in the laboratory.
- M. All discarded body fluid samples and disposable laboratory supplies should be disposed of properly in a container marked BIOLOGICAL HAZARD and disposed of accordingly.
- N. Policies must be established to document all adverse laboratory incidents. All incident reports and corrective action plans should be included in the Quality Assurance review.
- O. A copy of current Material Safety Data sheets and other references that list the details of hazards and the precautions for safe handling and storage of chemicals and reagents should be available.

VI. Quality Control/Assurance

A. Quality Control (QC).

- 1. A written procedure manual must be readily available and followed by laboratory personnel. The laboratory director or designated supervisory personnel should review and update all procedures on at least an annual basis. Any changes must be approved, signed and dated by the laboratory director or by designated proxy. Copies of old or archival protocols and updated procedures should be retained for a period of at least two years.
- 2. Equipment should be maintained and calibrated on a daily, monthly, and annual basis as appropriate to the type of equipment. This includes a record of instrument calibration, functional checks of equipment when possible, and evidence of an active review of records. Documentation or corrective action when instruments and/or procedures malfunction should be kept.
- 3. All new protocols should be validated and documented.
- 4. The laboratory should define and maintain written criteria for preparation, storage, handling, and preparation of specimens. All reagents should be dated and used within the indicated expiration date.
- 5. All media and protein supplementation should be tested for quality utilizing bioassay systems such as the one- or two-cell mouse embryo culture assay, or quantitative sperm motility or viability assay. Each batch of purchased media must be tested by the vendor with an appropriate bioassay. It is up to the discretion of the laboratory to perform additional quality control assays on purchased media.
- 6. Infection control (see safety procedures above). Use HIV-1 and -2, Hepatitis B, Hepatitis C,

syphilis and HTLV-I and -II screened serum products. Use sterile techniques, appropriate disease screens, and safe laboratory procedures.

- 7. All patient worksheets should have clear patient identifying information as well as laboratory accession numbers that uniquely identify the patient during all related procedures. All Petri dishes, test tubes and other materials that serve for culture are labeled with proper identifiers. Labeling of straws or ampules for cryopreservation must be indelible.
- 8. Written and/or computer records of all laboratory aspects of the ART cycles for each patient should be maintained. All steps throughout the ART procedure must be traceable to the technical person performing the procedure, and the oocytes must be accounted for from retrieval to embryo transfer/cryopreservation or disposal.
- 9. Documentation of emergency power generator checks and automatic power transfer switch function should be made on a periodic basis. Also, system function checks should be made and documented (e.g., power off, high temp, low CO₂ alarms). After hours, alarms should be transmitted to a person who can respond to these emergencies.

B. Quality Assurance (QA)

- 1. QA is a comprehensive program designed to look at the laboratory as a whole and to identify problems or errors that exist in an attempt to improve the entire process. Indicators used in a QA program should be objective, relevant to the laboratory, and measure a broad range of specific events or aspects of treatment that reflect the quality of care. For each indicator incorporated into the laboratory's QA program, an appropriate threshold needs to be established. The threshold sets the critical level of quality laboratory performance for each indicator. Since clinical protocols are not uniform among ART laboratories, the threshold values must be specific for each individual clinical laboratory (4).
- 2. The quality assurance program should include a mechanism to review and analyze data in order to identify problems related to the quality of care provided by the laboratory. This should include, but not be limited to, the following:
 - a. Mechanisms to detect clerical, transcriptional, or analytical mistakes. When problems and/or adverse trends are identified, corrective measures should be implemented to resolve the issue to ensure quality patient care. There should be later documentation whether corrective measures instituted were able to effectively resolve the problem.
 - b. Data from the laboratory should be gathered and analyzed on a regular basis and the information gathered should be used to identify

and resolve problems. A copy of this report should be kept for review. Quality assurance also includes the turnaround time for reports and consistency of service as well as statistical analysis of outcomes data.

- c. An adverse incident file should be maintained, including but not limited to significant clerical and analytical errors as well as unusual laboratory results.
- d. The practice must participate in data collection for purposes of clinic submission in compliance with guidelines established by SART.
3. The laboratory must participate in proficiency testing for those procedures for which it is available. For those testing services in which a commercial proficiency test is not available, the laboratory must establish an internal quality assurance program. Consideration should also be given to sharing samples with other laboratories or developing other means of external quality assessment. External quality assessment serves as a companion to a laboratory's internal quality assessment program.

VII. Satellite Facilities

A satellite facility is a facility in which there is an "off-site" laboratory director whose primary directorship is at another physical facility, which has a separate identification number (SART number) and a separate medical director. ART laboratory services may be provided in satellite facilities provided the following criteria are met:

- A. A laboratory director (see above) oversees all activities in the remote location. The director will establish protocols, decide on medium preparation and source, provide training to personnel, and determine methodologies to be used.
- B. Qualified embryology technologists should be employed at the satellite facility or provided by the laboratory director as needed if the latter does not perform the procedures. Embryology technologists should meet the educational and training criteria described herein.
- C. The laboratory director should provide supervision and document appropriate lines of daily communication with satellite facilities during all IVF procedures. While the laboratory is actively treating patients, the off-site director is required to physically visit the laboratory at a frequency that will ensure the optimal functioning of the laboratory and the delivery of quality patient care.
- D. A satellite laboratory must meet the same standards as any other embryology laboratory as described in these guidelines.
- E. Equipment and laboratory space should meet all of the standards listed above as appropriate for procedures that are performed at the satellite facility.

- F. Satellite facilities may be set up to perform GIFT procedures *only* if facilities are available to provide IVF procedures as needed on site.

REFERENCES

1. U.S. Food and Drug Administration. Tissue guidances, rules and related documents. Available at: <http://www.fda.gov/cber/tissue/docs.htm>.
2. The American Society for Reproductive Medicine. 2008 Guidelines for gamete and embryo donation. *Fertil Steril* 2008;90(Suppl 3):S30-44.
3. Practice Committee of the American Society for Reproductive Medicine. Guidelines for development of an emergency plan for in vitro fertilization programs. *Fertil Steril* 2008;89:793-5.
4. Mayer JF, Jones EL, Dowling-Lacey D, et al. Total quality improvement in the IVF laboratory: choosing indicators of quality. *Reproductive BioMedicine Online* 2003;7(Comp. 1):192-6.

GUIDELINES FOR HUMAN ANDROLOGY LABORATORIES

- I. Organization of the Laboratory and Definition of Services
 - A. General Laboratory
 1. The institutional affiliation, history, definition of services, and the purpose of the laboratory should be clearly defined.
 2. The laboratory must be in compliance with any state or federal licensing requirements. As a high complexity laboratory, as defined by the federal Department of Health and Human Services (HHS), an andrology laboratory falls under the purview of Clinical Laboratory Improvement Act of 1988 (CLIA'88) regulations. These regulations undergo routine interval reviews with amendments made as appropriate. Readers are advised to consult the most recent edition of the regulations in order to ensure current applicability. Any current licenses, permits, and certification by any other groups or agencies should be listed.
 3. The laboratory must satisfy any Institutional Review Board (or equivalent Human Investigation Committee) requirements for any investigative procedures, if applicable.
 4. Laboratory animals should be maintained according to local, state, or federal requirements and/or regulations, if applicable.
 5. Andrology laboratories that cryopreserve semen for therapeutic use and/or prepare semen for use in reproductive therapies are considered manufacturers of transplantation products (sperm) according to the FDA's Cell/Tissue Transplantation regulations (1). All andrology laboratories involved in these activities must be in compliance with these FDA regulations.
 - B. Specific Laboratory Procedures

It is recognized that a single standardized protocol is inappropriate or unavailable for many andrology laboratory procedures. In the absence of a widely accepted, standardized protocol, each laboratory

must develop its own protocol for that particular procedure with appropriate controls and methodology to assure reliable, acceptable results. Andrology laboratories perform some or all of the following procedures:

1. Semen analysis and procedures: the semen analysis is essential for the diagnosis of male fertility potential. In addition to the standard semen analysis, semen may be tested for fructose, adenosine triphosphate (ATP) and other biochemical markers. Assays may include tests for sperm survival, sperm viability, sperm membrane integrity, ability of sperm to penetrate human cervical mucus in either a cross-match test or in capillary tubes (2, 3). Standards for semen analysis are detailed in the World Health Organization (WHO) Laboratory Manual for the Examination of Human Semen and Semen-Cervical Mucus Interaction (4).
2. Sperm antibody testing: the sperm antibody assays used must be able to measure the presence of sperm antibodies on the sperm as well as in the serum, cervical mucus, or seminal plasma. These assays may work either directly or indirectly on the sperm and fluids. Both positive and negative controls must be used to validate the assay. The mixed antiglobulin reaction and the immunobead test are described in the WHO Laboratory Manual (4). Other protocols are also available (5).
3. Sperm penetration assay or the zona-free hamster oocyte test: human sperm fertility potential is measured by the ability of sperm to penetrate zona-free hamster eggs. Positive controls must be utilized to validate test results. A discussion of the zona-free hamster oocyte assay is found in the WHO Laboratory Manual (4). Other descriptions of the assay are available (6).
4. Sperm cryopreservation: sperm cryopreservation involves the freezing and storage of human sperm for future use. Sperm for freezing may be obtained from either patients or donors. Guidelines for Sperm Donation have been established by The American Society for Reproductive Medicine (7) and The American Association of Tissue Banks (8).
5. Preparation of sperm for intrauterine insemination with husband, partner or donor sperm: fresh and frozen sperm may be processed for intrauterine or intracervical insemination.
6. Computer assisted semen analysis (CASA): laboratories must have a protocol that, on a periodic basis, validates that their assisted semen analysis equipment is functioning correctly.

II. Laboratory Personnel

- A. Personnel Qualifications and Responsibilities: CLIA '88 has specific qualifications and job respon-

sibilities for each type of laboratory personnel. The following descriptions include a summary of certain relevant items regarding qualifications and responsibilities of laboratory directors, general supervisors and testing personnel. Under CLIA '88, personnel qualifications and responsibilities are also defined for technical supervisors and clinical consultants (not included here). For andrology laboratories, individuals may assume the role of more than one of these jobs provided they meet all of the personnel qualifications and are able to meet all of the responsibilities cited. Laboratory personnel should possess a current license issued by the state in which the laboratory is located, if such licensing is required.

1. Laboratory Director:

- a. Qualifications. There are a number of different paths for qualifying as the director of a high complexity laboratory, such as an andrology laboratory, under CLIA '88. These include:
 - 1) An M.D. or D.O. with board-certification in anatomic or clinical pathology, or both.
 - 2) An M.D. or D.O. with laboratory training (either one year of laboratory training during medical residency or at least two years of experience directing or supervising high complexity testing).
 - 3) A board-certified Ph.D. scientist with a degree in a chemical, physical, biological or clinical laboratory science from an accredited institution and be certified by the American Board of Medical Microbiology, American Board of Clinical Chemistry, the American Board of Bioanalysis, the American Board of Medical Laboratory Immunology or other board deemed comparable by HHS.
 - 4) A person qualified under state law to direct laboratories within a state on or before February 28, 1992.
 - 5) A person serving as a laboratory director and qualified or could have qualified as director on or before February 28, 1992.
- b. Responsibilities. The director must ensure:
 - 1) The quality of testing.
 - 2) The safety of the working environment.
 - 3) That the test methodologies will provide quality results.
 - 4) That procedures are verified, accurate and reliable.
 - 5) That the laboratory is enrolled in an HHS-approved proficiency testing program.
 - 6) That QA and QC programs are established and maintained.
 - 7) That acceptable levels of analytical performance for each test system is established and maintained.

- 8) That all necessary remedial actions are taken and documented whenever significant deviations from the laboratory's established performance specifications are identified, and that patient test results are reported only when the system is functioning properly.
 - 9) That reports of test results include pertinent information required for interpretation.
 - 10) That consultation is available to the laboratory's clients.
 - 11) That the general supervisor provides on-site supervision of high complexity test performance by qualified testing personnel with high school degrees.
 - 12) That the laboratory has sufficient number of qualified personnel to perform testing.
 - 13) That personnel have appropriate education and experience before performing testing.
 - 14) That policies and procedures are established to monitor individual testing performance.
 - 15) That an approved procedure manual is available to all personnel responsible for testing.
 - 16) That the responsibilities and duties of each consultant, each supervisor, and each testing personnel are specified, in writing.
- c. The laboratory director must be accessible to the laboratory to provide on-site, telephone or electronic consultation as needed.
 - d. An individual may serve as a director of a maximum of five (5) certified laboratories.
2. Laboratory General Supervisor. The laboratory should have at least one general supervisor who, under the direction of the laboratory director, provides day-to-day supervision of testing personnel and reporting of testing results.
 - a. Qualifications. The general supervisor must have at least one of the following qualifications:
 - 1) Possess a current license issued by the state in which the laboratory is located, if such licensing is required; and be qualified as a high complexity laboratory director; or as technical supervisor.
 - 2) Be a M.D. or D.O. or have earned doctoral, master's or bachelor's degree in a chemical, physical, biological or clinical laboratory science, or medical technology from an accredited institution; and have at least one year of laboratory training or experience, or both, in high complexity testing.
 - 3) Qualify as testing personnel and have at least two years of laboratory training or experience, or both, in high complexity testing.
 - b. Responsibilities. The laboratory general supervisor must:
 - 1) Be accessible, either on-site or via electronic means, to testing personnel at all times testing is being performed.
 - 2) Provide day-to-day supervision of high complexity test performance by testing personnel.
 - 3) Must be on-site to provide direct supervision when high complexity testing is performed by qualified testing personnel with high school degrees.
 - 4) Monitor testing analyses and specimen examination to ensure that acceptable levels of analytic performance are maintained.
 - c. The laboratory director or technical supervisor may delegate to the laboratory general supervisor the responsibility for:
 - 4) Have previously qualified or could have qualified as a general supervisor on or before February 28, 1992.
 - 5) On or before September 1, 1992, have served as a general supervisor of high complexity testing and as of April 24, 1995, have graduated from an approved medical laboratory or clinical laboratory training program approved by the Accrediting Bureau of Health Education Schools (ABHES), the Commission on Allied Health Education Accreditation (CAHEA), or other organization approved by HHS; and have at least two years of clinical laboratory training or experience, or both, in high complexity testing.
 - 6) On or before September 1, 1992, have served as a general supervisor of high complexity testing and as of April 24, 1995, be a high school graduate or equivalent and have successfully completed an official U.S. military medical laboratory procedures course of at least 50 weeks duration and have held the military enlisted occupational specialty of Medical Laboratory Specialist; and have at least two years of clinical lab training or experience, or both, in high complexity testing.
 - 7) On or before September 1, 1992, have served as a general supervisor of high complexity testing; and be a high school graduate or equivalent and have had at least ten years of laboratory training and experience, or both, in high complexity testing, including at least six years of supervisory experience between September 1, 1982 and September 1, 1992.

- 1) Assuring that all remedial actions are taken whenever test systems deviate from the laboratory's established performance specifications.
 - 2) Ensuring that patient test results are not reported until all corrective actions have been taken and the test system is properly functioning.
 - 3) Providing orientation to all testing personnel.
 - 4) Evaluating and documenting the performance of all testing personnel on an annual basis.
3. Testing Personnel. The laboratory must have a sufficient number of people qualified as testing personnel to perform high complexity testing.
- a. Qualifications. Testing personnel must meet at least one of the following requirements:
- 1) Be a M.D. or D.O. in the state in which the laboratory is located or have earned a doctoral, master's or bachelor's degree in a chemical, physical, biological or clinical laboratory science, or medical technology from an accredited institution.
 - 2) Have earned an associate degree in a laboratory science or medical laboratory technology from an accredited institution.
 - 3) Have education and training equivalent to that required for an associate degree that includes at least 60 semester hours, or equivalent, from an accredited institution. This should include either a) 24 semester hours of medical laboratory technology courses, or b) 24 semester hours of science courses that include (1) six semester hours of chemistry; (2) six semester hours of biology; (3) twelve semester hours of chemistry, biology, or medical laboratory technology in any combination, and training that includes either of the following:
 - (a) Completion of a clinical laboratory training program approved or accredited by the ABHES, the CAHEA, or other organization approved by HHS.
 - (b) At least 3 months documented laboratory training in each specialty in which the individual performs high complexity testing.
 - (c) Have previously qualified or could have qualified as a technologist on or before February 28, 1992.
 - (d) On or before April 24, 1995, be a high school graduate or equivalent and have either graduated from a medical laboratory or clinical laboratory training program approved or accredited by the ABHES, CAHEA or other organization approved by HHS; or have successfully completed an official U.S. military medical laboratory training course of at least 50 weeks duration and have held the military enlisted occupational specialty of Medical Laboratory Specialist.
- 4) Until September 1, 1997, have earned a high school diploma or equivalent; and have documentation of training appropriate for the testing performed prior to analyzing patient specimens. Such must ensure that the individual must have: a) the skills required for proper specimen collection, including patient preparation (if applicable), labeling, handling, preservation or fixation, processing or preparation, transportation and storage of specimens; b) the skills required for implementation of all standard laboratory procedures; c) the skills required for performing each test method and for proper instrument use; d) the skills required for performing preventive maintenance, troubleshooting and calibration procedures related to each test performed; e) a working knowledge of reagent stability and storage; f) the skills required to implement the quality control policies and procedures of the laboratory; g) an awareness of the factors that influence test results; h) the skills required to assess and verify the validity of patient test results through the evaluation of quality control sample values prior to reporting patient test results. As of September 1, 1997, have qualified under the terms of this section provided the individual performed high complexity testing prior to April 24, 1995.
- b. Responsibilities. Each individual performing high complexity testing must:
- 1) Follow the laboratory's procedures for specimen handling and processing, test analyses, reporting and maintaining records of patient test results.
 - 2) Maintain records that demonstrate that proficiency testing samples are tested in the same manner as patient specimens.
 - 3) Adhere to the laboratory's quality control policies, document all quality control activities, instrument and procedural calibrations and maintenance performed.
 - 4) Follow the laboratory's established corrective action policies and procedures whenever test systems are not within the laboratory's established acceptable levels of performance.
 - 5) Be capable of identifying problems that may adversely affect test performance or

reporting of test results and either must correct the problems or immediately notify the general supervisor, technical supervisor, clinical consultant or director.

- 6) Document all corrective actions taken when test systems deviate from the laboratory's established performance specifications.

B. Personnel Records

There must be written documentation of compliance with the section described above. This should include the following items:

1. A list of all personnel, their job descriptions, and shifts, if applicable.
2. A list of the education, training, and qualifications of all laboratory personnel.
3. An organizational chart documenting the chain of command so that a responsible individual can always be identified. A qualified individual must be on duty or on call at all times.
4. Document and maintain records of personnel training for each specific laboratory test offered. Definitive training programs for all procedures should be established.
5. Documentation of personnel participation in continuing education.
6. Annual performance reviews for personnel.

III. Laboratory Space and Design

The andrology laboratory should have adequate space and a design that is appropriate for the volume and type of procedures performed and that ensures safe and comfortable working conditions.

- A. The andrology laboratory may share space physically with other laboratory activity. However, any activity requiring sterile technique (i.e., sperm preparation for intrauterine insemination) should be physically separated from other activities.
- B. Adequate space should be provided for record keeping, data entry, and related administrative functions.
- C. Material for laboratory construction, ventilation of the area, and cleanliness should be appropriate to the laboratory work. The use of carpet in tissue culture or work areas is prohibited.

IV. Laboratory Policy and Procedure Manuals

- A. There should be a manual(s) in the laboratory written in National Committee for Clinical Laboratory Standards (NCCLS) publication GP-2A format, that describes all procedures in sufficient detail to assure reproducibility and competence in handling of mammalian gametes. Procedure manuals should include, but are not limited to the following:
 1. Patient instructions for proper collection, labeling, and delivery of specimens. Each patient

should have a unique identification number. A requisition slip or a form designating the patient's name, unique identification number, assay(s) to be performed, and the referring physician's name should accompany the specimen.

2. Procedure sheets for the tests performed by the laboratory including the principles of the test, preparation of any standards or controls, the methodology used, references, and criteria for unacceptable results, if appropriate. If specimens are to be rejected, the criteria for rejection and procedure for safe disposal of the specimen must be established.
3. Laboratory manuals should be reviewed and revised annually by the director and signed. Auxiliary personnel should be updated and trained in any revised procedures.

- B. Laboratories should have a procedure for specimen log-in with the appropriate information on the specimen and patient. For example, given a patient name and date, the laboratory should be able to document whether or not a specimen was tested, the results of the test, the referring physician, and some unique code that identifies the patient.

- C. The location of all patient test records must be recorded in a manual. The test records should identify the person performing the test, the test results, as well as reference ranges. The results should be reviewed by the laboratory director or supervisor and signed. These test results should be kept for a minimum of two years.

- D. Maintenance manuals for all laboratory equipment must be kept in the laboratory. This manual should include records of equipment performance and maintenance.

- E. All policy manuals should be maintained in the laboratory. These policies should include, but are not limited to, procedures for record keeping, result reporting, laboratory communication, and consent procedures (if required by the institution).

V. Laboratory Equipment and Supplies (9)

A. Laboratory Equipment/Facilities

Laboratories are required to maintain or have access to equipment necessary to perform andrology services. It is the responsibility of the laboratory director to ensure that the proper equipment is in place to perform the necessary assays.

1. Certain laboratory equipment (i.e., laminar flow hoods, biohazard lab hoods, balances) must be certified by a qualified agency on an annual basis. Certifications must be maintained on file for review.
2. The laboratory should have a program for checking and calibrating laboratory equipment such as pipettors, thermometers, pH meters, centrifuges, and refrigerators on a regular basis.

Manufacturer supplied manuals or maintenance manuals for all laboratory equipment must be maintained in the laboratory.

3. There must be a mechanism for the safe handling and disposal of biohazardous waste material in the laboratory.
4. All material that comes in contact with sperm that is being prepared for cryopreservation or intrauterine insemination must be tested for toxicity. This testing requires the use of an appropriate bioassay.
5. All laboratory chemicals and reagents must be labeled with the date received and date opened and should be stored as recommended by the supplier/manufacturer.

B. Culture Medium Preparation and Quality Control Testing

1. Culture medium formulated de novo should utilize dedicated reagents, glassware, and tissue-culture-grade water (or its equivalent) in its preparation. Quality control testing is required utilizing an appropriate bioassay system, such as the one- or two-cell mouse embryo culture assay, or quantitative sperm motility or viability assay.
2. Quality control testing is optional when commercial media is purchased and used within its labeled expiration period. Documentation of quality control testing using an appropriate bioassay system must be supplied by the manufacturer.
3. When semen is processed for use in patient therapy, the use of human serum or human albumin or any other biologic product from any human source with the exception of the patient's own serum (autologous serum), will require documentation of transmissible disease testing, such as HIV-1 and -2, hepatitis B, hepatitis C, syphilis and HTLV I/II. Similarly, when semen is processed for cryopreservation with the potential for use in future patient therapy, the use of human serum or human albumin or any other biological product from any human source with the exception of the patient's own serum (autologous serum), will require documentation of transmissible disease testing.
4. Cryopreservation medium for sperm freezing. Similar to standards for other media, each lot of cryopreservation medium should have undergone quality control testing utilizing an appropriate bioassay.

VI. Laboratory Safety and Infection Control

A laboratory safety manual must be available to all personnel and should be included in employee orientation. Laboratory procedures and policies on lab safety should be reviewed annually by the laboratory director. Protocols should be available for fire and electrical safety and internal and external disas-

ter preparedness. Policies must be established to document all adverse laboratory incidents. All incident reports and corrective action plans should be included in the Quality Assurance review. Copies of current Material Safety Data Sheets and other references that list the details of hazards and the precautions for safe handling and storage of chemicals and reagents should be available. In addition, the following guidelines are recommended:

- A. The laboratory must undergo an annual safety inspection by personnel trained in this task. Results of inspections must be kept on file for reference. This includes fire inspection, storage of hazardous materials, infection control, and storage of volatile or hazardous materials. Adequate fire and safety precautions must be posted. The facility should be well lighted and ventilated.
- B. All body fluids should be handled utilizing universal precautions (i.e., as if they were contaminated). Safety precautions are to be taken when handling and disposing of any biological specimens. This includes wearing gloves and laboratory coats and avoiding accidental wounds from sharp instruments. Hands must be washed immediately if they become contaminated with biological materials. Disposable laboratory supplies should be used whenever possible.
- C. All procedures involving body fluids should minimize the creation of aerosols or droplets. The use of appropriate hoods should be considered when procedures are conducted that have a high potential for creating aerosols such as centrifugation. Alternatively, centrifuges designed to contain aerosols can be utilized. Tubes must be capped during centrifugation.
- D. All accredited laboratories are required to have an Exposure Control Plan. A requirement of this plan is to offer and document Hepatitis B vaccination to all laboratory personnel. Any employee that refuses is required to sign a waiver that is kept in their employment record. Testing for additional STDs may be offered, but not required, with test results to be directed as indicated by the employee.
- E. Containers must be labeled as to their contents and dated.
- F. Adequate facilities should be available for safe disposal of hazardous or biological waste. All biohazardous waste should be placed in a container marked BIOLOGICAL HAZARD and disposed of accordingly.
- G. There should be no smoking, eating, drinking, or application of makeup in the laboratory.
- H. Mechanical pipetting devices must be used for manipulation of liquids in the laboratory. Mouth pipetting is not permitted.
- I. Contaminated laboratory equipment and/or work surfaces should be disinfected and sterilized after

a spill (e.g., 1:10 dilution of 5.25% sodium-hypochlorite household bleach in water or other procedures approved by the CDC).

- J. There must be sufficient space available for working. The room temperature, ventilation, noise level, and fume removal should be adequate. Utilities, communication equipment, and housekeeping should be adequate.
- K. Radioisotopes or biohazardous chemicals cannot be used in the same room where sperm are prepared for intrauterine insemination or cryopreservation.
- L. Laboratory personnel should periodically review additional published safety guidelines as they become available (10).

VII. Quality Control/Assurance

A. Quality Control (QC)

To assure reliable results, the following recommendations must be followed:

1. All new protocols should be validated by parallel testing (when possible prior to clinical implementation. Protocol(s) documentation should include a description of the assay, standards, controls, calibration, and tolerance limits where applicable.
2. The laboratory director and/or supervisor should review and update all procedures on at least a yearly basis. Copies of old protocols and updated procedures must be kept for at least two years. Effective dates of all changes to protocols should be recorded.
3. Equipment should be maintained and calibrated against National Safety Board (NSB) Standard Reference Materials, when possible, on a regular basis. This includes a record of instrument calibration, functional checks of equipment, when possible, evidence of an active review of records, and documentation of corrective action taken when instruments malfunction.
4. All reagents, media and chemicals should have expiration dates recorded. All outdated materials should be discarded in an appropriate manner.
5. Positive and negative controls should be used when performing sperm antibody testing. Positive controls should be used when performing the sperm penetration assay.
6. Infection control: HIV-1 and -2, hepatitis B, hepatitis C, syphilis and HTLV-I and -II screened serum products should be used. Sterile techniques and universal precautions to limit microbial contamination should be employed.
7. Daily monitoring of temperature, gases, and humidity (when appropriate) for all equipment should be conducted on a daily basis.

B. Quality Assurance (QA)

The quality assurance program should include

a mechanism to review and analyze data in order to identify problems related to the quality of care provided by the laboratory. This should include, but is not limited to, the following:

1. Mechanisms to detect clerical, transcriptional, or analytical mistakes.
2. Data from the laboratory should be gathered and analyzed on a regular basis in order to identify and resolve problems. A copy of this report should be kept for review. Quality assurance should also include the turnaround time for reports and consistency of service as well as statistical analysis of outcomes data.
3. An adverse incident file should be maintained.
4. The laboratory must participate in proficiency testing for those procedures for which it is available. For those testing services in which a commercial proficiency test is not available, the laboratory must establish an internal quality assurance program. Consideration should be given to sharing samples with other laboratories or developing some other means of external quality assessment. External quality assessment serves as a companion to a laboratory's internal quality assessment program.

Acknowledgment: This report was developed under the direction of the Practice Committee of the Society for Assisted Reproductive Technology and the Practice Committee of the American Society for Reproductive Medicine as a service to their members and other practicing clinicians. While this document reflects appropriate management of a problem encountered in the practice of reproductive medicine, it is not intended to be the only approved standard of practice or to dictate an exclusive course of treatment. Other plans of management may be appropriate, taking into account the needs of the individual patient, available resources, and institutional or clinical practice limitations. This report was approved by the Executive Council of the Society for Assisted Reproductive Technology and by the Board of Directors of the American Society for Reproductive Medicine.

REFERENCES

1. U.S. Food and Drug Administration. Tissue guidances, rules and related documents. Available at: <http://www.fda.gov/cber/tissue/docs.htm>.
2. Blasco L. Clinical tests of sperm fertilizing ability. *Fertil Steril* 1984;41:177-92.
3. Kremer J. A simple penetration test. *Int J Fertil* 1965;10:209-15.
4. World Health Organization. In: WHO laboratory manual for the examination of human semen and semen-cervical mucus interaction. 4th ed. Cambridge: Cambridge University Press, 1999:1-128.
5. Bronson R, Cooper G, Rosenfeld D. Sperm antibodies: their role in infertility. *Fertil Steril* 1984;42:171-83.
6. Wolf DP, Sokoloski JE. Characterization of the sperm penetration bioassay. *J Androl* 1982;3:445-51.
7. The American Society for Reproductive Medicine. 2008 Guidelines for gamete and embryo donation. *Fertil Steril* 2008;90(Suppl 3):S30-44.
8. American Association of Tissue Banks. Standards for Tissue Banking; 2002.
9. Gerrity M. Selection and use of equipment. In: Wolf DP, Bavister BD, Gerrity M, Kopf GS, eds. *In vitro fertilization and embryo transfer: a manual of basic techniques*. New York: Plenum Press, 1988:7-24. assoc. editors.
10. Schrader SM. Safety guidelines for the andrology laboratory. *Fertil Steril* 1989;51:387-9.