Friday,
November 6, 1998

Part VI

Department of Health and Human Services

Centers for Disease Control and Prevention

Implementation of the Fertility Clinic Success Rate and Certification Act of 1992; Proposed Model Program for the Certification of Embryo Laboratories; Notice

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Centers for Disease Control and Prevention

Implementation of the Fertility Clinic Success Rate and Certification Act of 1992; Proposed Model Program for the Certification of Embryo Laboratories

AGENCY: Centers for Disease Control and Prevention (CDC), Department of Health and Human Services (HHS).

ACTION: Notice and request for comments.

SUMMARY: The Fertility Clinic Success Rate and Certification Act of 1992 (Pub. L. 102–493, 42 U.S.C. 263a–1 et seq.) requires that the Secretary, HHS, through CDC, develop a model program for the certification of embryo laboratories, to be carried out voluntarily by interested States. The model certification program is to be developed in consultation with appropriate consumer groups and professional organizations with knowledge and expertise in assisted reproductive technology.

This notice sets forth a description of the proposed model certification program, including the proposed definitions, administrative requirements, and embryo laboratory standards. Accordingly, CDC solicits comments on the proposed model certification program and reserves the right to revise the program based upon the comments it receives.

DATES: To assure consideration, written comments on the proposed model certification program for embryo laboratories as described in this notice must be received at the address indicated below on or before January 5, 1999.

ADDRESSES: Address all written comments to: Model Certification Program—**Federal Register** Notice, Centers for Disease Control and Prevention, Mail Stop K–66, 4770 Buford Highway N.E., Atlanta, Georgia 30341–3724.

Due to staffing and resourcing limitations, we cannot accept facsimile (FAX) copies of comments nor can we accept comments by telephone.

FOR FURTHER INFORMATION CONTACT: Nancy Anderson or Carol Cook, Division of Laboratory Systems, telephone (770) 488–8047 or (770) 488–8029.

SUPPLEMENTARY INFORMATION:

Introduction

The Fertility Clinic Success Rate and Certification Act of 1992 (FCSRCA), Public Law 102–493 (42 U.S.C. 263a–1 et seq.), was intended to provide the public with comparable information concerning the effectiveness of infertility services and to assure the quality of such services by providing for the certification of embryo laboratories.

Section 2 of the statute requires that the Secretary, HHS, through CDC, define pregnancy success rates, and seek public comment on the proposed definitions. In addition, Section 2 requires each assisted reproductive technology (ART) program to annually report its pregnancy success rates to CDC, along with the identity of each embryo laboratory used by the program, and whether the laboratory is certified under Section 3 or has applied for such certification. Section 2 was addressed in a **Federal Register** notice published on August 26, 1997 (62 FR 45259).

Section 3(a) of the FCSRCA requires that the CDC ''develop a model program for the certification of embryo laboratories . . . to be carried out by the States.'' In developing the model certification program, CDC is to consult with ''appropriate consumer and professional organizations with expertise in using, providing, and evaluating professional services and embryo laboratories associated with assisted reproductive technology programs.''

Section 3(b) lists State official who are to received a description of the model certification program, and requires that the Secretary encourage States to adopt such a program.

Section 3(c) includes the requirements for administration of the certification program by the States, with provisions for the inspection and certification of embryo laboratories by States or approved accreditation organizations, and the requirement for application to the State by an embryo laboratory that seeks certification.

Section 3(d) specifies the embryo laboratory standards that are to be in the model certification program. These include a standard to assure consistent performance of laboratory procedures; a standard for a quality assurance and quality control program; standards for the maintenance of all laboratory records (including laboratory tests and procedures performed, as well as personnel and equipment records); and a standard for personnel qualifications.

Section 3(e) includes provisions for a State to adopt the model certification program if it applies to the Secretary, and is approved, and Section 3(f) allows for the use of accreditation organizations, approved under the requirements described in Section 4, to inspect and certify embryo laboratories in States that have adopted the program.

Section 3(g) requires that States which qualify to adopt the model certification program conduct embryo laboratory inspections to determine if the laboratories meet the requirements of the program. Section 3(g) also requires the Secretary to seek public comment on the conditions under which announced inspections may be conducted without diminishing the likelihood of discovering deficiencies in the operations of an embryo laboratory. In addition, inspection results (including deficiencies and any subsequent corrections to those deficiencies) are to be reported and made available to the public.

Section 3(h) provides for the Secretary to conduct validation inspections of embryo laboratories certified by a State or an approved accreditation organization to determines if the laboratories are being operated in accordance with the standards in the model certification program. If a validation survey demonstrates that an embryo laboratory is not in compliance with such standards, the statute specifies requirements for notification of the State, or as applicable, the accreditation organization. A subsequent investigation and inspection of additional certified embryo laboratories are to be conducted to determine if the State or accreditation organization is reliably identifying laboratory deficiencies. The Secretary may revoke the approval of the State certification program or accreditation organization if requirements applicable to the program are not being met.

Section 3(i) limits the Secretary is developing the model certification program, and the States in adopting such program, from establishing any regulation, standard, or requirement that has the effect of exercising supervision or control over the practice of medicine in ART programs.

Section 3(j) states that the Secretary may define the term of the certification issued by a State or an accreditation organization in a State, through the public comment process, and provides for application for recertification to be submitted when there is a change in ownership or administration of a certified embryo laboratory.

Section 4 calls for the Secretary, through CDC, to promulgate criteria and procedures for the approval and use of accreditation organizations to inspect and certify embryo laboratories in States which have adopted the model certification program, as well as in States which have not adopted the program. The section also includes

provisions for annual evaluation of approved accreditation organizations by the Secretary, through the inspection of a representative sample of accredited embryo laboratories and other such appropriate means.

Section 5 specifies the conditions under which a certification issued by a State or an accreditation organization shall be revoked or suspended, and the effect that such revocation or suspension would impose on the certification and application for recertification of the laboratory.

Section 6 mandates that the Secretary, through CDC, annually publish pregnancy success rates as reported by ART programs (Section 2); the names of ART programs that fail to report pregnancy success rates; the identity and certification status of each embryo laboratory located in a State which has adopted the model certification program; the identity of each embryo laboratory in a State which has not adopted the certification program and which has been certified by an approved accreditation organization; and in the case of an embryo laboratory which is not certified, whether the laboratory has applied for certification. The annual publication is to be distributed to States and the public. This section was also addressed in the previously mentioned **Federal Egister** notice published on August 26, 1997 (62 FR 45259). The first report, 1995 Assisted Reproductive Technology Success Rates: National Summary and Fertility Clinic Reports, was published in December 1997. Copies of the report may be obtained by contacting RESOLVE, a national consumer organization helping infertile couples and individuals, at 1–888–299–1585 or via the Internet at www.resolve.org.

Section 7 authorizes the Secretary to charge sufficient fees to cover the cost of administering the FCSRCA and authorizes States adopting the certification program to charge sufficient fees to cover the cost of administering their program.

Section 8 includes a definition of assisted reproductive technology and provides for seeking public comment on any proposed expansion of the definition.

Actions Taken To Develop the Proposed Model Certification Program

In accordance with the FCSRCA, CDC consulted with individuals, professional organizations and consumer groups with expertise and interest in ART throughout the development of the proposed model certification program for embryo laboratories. Consultation was provided by organizations representing reproductive medicine, including the American Society for Reproductive Medicine (ASRM) and the Society for Assisted Reproductive Technology, laboratory organizations such as the College of American Pathologists (CAP) and the American Association of Bioanalysts, and a consumer group that serves to educate the public on infertility diagnosis and treatment (RESOLVE). CDC also worked closely with several State programs throughout the process to ensure that the proposed model certification program, when finalized, could easily be adopted and implemented by interested States, and sought input from Federal agencies with regulatory responsibilities related to laboratory practice, tissue banking and ART.

A useful example in developing the proposed model certification program was the voluntary accreditation program for reproductive laboratories that is currently administered by the CAP. This program was developed jointly between the CAP and the ASRM, and has been in existence since 1993. More than one third of the embryo laboratories associated with ART programs in the United States currently participate in this voluntary program. As CDC began drafting the proposed model certification program, an initial step was to meet with representatives from the CAP to gather information on the CAP/ASRM Reproductive Laboratory Accreditation Program, including the laboratory standards and inspection checklists used by CAP inspectors and reproductive laboratories. CDC also used a variety of guidelines and standards from other professional organizations, State, Federal, and international programs as resources (see References), and made a number of site visits to embryo laboratories to observe the daily operation of these facilities.

Between November 1996 and August 1997, CDC held several work sessions with technical consultants to obtain input on specific issues related to the embryo laboratory and the proposed model certification program, including personnel qualifications and responsibilities, quality assurance and quality control (quality management), recordkeeping, specific definitions as they apply to the model certification program, and State administration of the program. The individuals who participated in these work sessions were asked to provide consultation because of their expertise and interest in ART laboratory procedures, or experience with clinical laboratory testing. The input provided by each consultant was used by CDC to assist in its internal deliberations to develop a practical and effective model certification program for embryo laboratories. No group consensus was sought at any of the sessions.

On-going Review of Embryo Laboratories

In passing the FCSRCA, Congress anticipated that the cost of Federal and State monitoring and oversight of embryo laboratories would be covered by the fees they pay. Section 7 of the statute provides for the collection of sufficient fees from participating embryo laboratories to cover these costs. However, participation by embryo laboratories is voluntary; laboratories not willing to pay these fees would not be limited in their ability to operate.

CDC plans to implement oversight and monitoring under the FCSRCA to the extent the roughly 350 embryo laboratories are willing to voluntarily pay sufficient fees to cover oversight costs. At this time, embryo laboratories have not indicated they would opt into such an oversight program. CDC will continue to review embryo laboratories' interest in, and willingness to pay for, a formalized Federal oversight program, and adjust CDC's plans accordingly.

CDC has, however, developed these proposed model certification standards, incorporating the definitions, administrative requirements and laboratory standards that are called for in the FCSRCA, and is publishing them to provide an opportunity for public comment. The model certification program will be revised as necessary, based on these comments, published as a final notice in the **Federal Register,** and the final model will be distributed to State officials and health authorities as outlined in the statute.

At this time, CDC will defer implementation of the approval of state certification programs or accreditation organizations. In addition, Federal validation inspections of embryo laboratories certified by States adopting the model or accredited by an accreditation program for embryo laboratories will also be deferred until a sufficient number of laboratories are willing to opt into a self-supporting system. In this proposed model, implementation of these activities would be the responsibility of States that choose to adopt the model certification program.

To summarize, CDC proposes a model certification process for embryo laboratories performing assisted reproductive technology (ART). In developing this proposal, we have carefully reviewed an existing program, the CAP/ASRM Reproductive Laboratory Accreditation Program

(RLAP) which was developed by the professional community and provides oversight of embryo laboratories affiliated with ART programs and clinics. We have also taken note that there are existing voluntary programs in other areas of laboratory practice, such as the American Society of Clinical Pathologists and the American Board of Bioanalysts' laboratory personnel certification programs, that have had a beneficial impact on laboratory quality, without Federal oversight.

As mentioned previously in this preamble, the CAP/ASRM's RLAP provided the basis for many of the laboratory standards specified in the proposed model. We believe that this existing ART laboratory accreditation program likely will meet the standards we have proposed in the model and will provide an excellent resource for States which wish to develop their own certification program. In addition, other professional organizations have expressed an interest in establishing and/or adopting standards for the embryo laboratory; the proposed certification process should benefit those other groups.

While the model certification program for embryo laboratories proposed in this model does not provide for a Federal oversight role until a sufficient number of laboratories would opt into a self-supporting system, we welcome public comment on the need, desirability and specific benefits of Federal oversight.

Request for Comments on the Proposed Model Certification Program

Written comments on any aspect of the proposed model certification program included in this notice may be submitted to CDC during the public comment period at the address specified for receipt of comments. In addition, the FCSRCA requires the Secretary to facilitate public comment on specific aspects of the model certification program and the definitions as they relate to the model. To ensure appropriate consideration by commenters, the following issues are highlighted:

- Based on the comments received during the previously mentioned work sessions with technical consultants, the proposed model's definitions for ''assisted reproductive technology'' and ''embryo laboratory'', have been elaborated from the definitions specified in the FCSRCA. The issue is whether the revised definitions are appropriate and accurate for use in the model certification program.
- The proposed model permits announced initial and routine inspections and unannounced inspections for complaint investigations. The issues are under what circumstances should announced inspections be permitted so as not to diminish the likelihood of discovering deficiencies in the operation of an embryo laboratory, and whether there are circumstances that should require unannounced inspections.
- The proposed model specifies a 2-year term for embryo laboratory certification. The issue is whether this is an appropriate period of time for the term of certification of a laboratory (i.e., renew biennially).

In addition, we are interested in receiving comments on the following issue which is not specifically addressed in the proposed model certification program but may be considered for inclusion in the finalized model:

- Proficiency testing (PT) currently available for the embryo laboratory is limited to determining whether culture media samples provided by the PT program are suitable for in vitro mouse embryo culture. While the performance of PT is not required in the proposed model, the model's standards do require a laboratory to perform quality control procedures to monitor the reliability of the ART procedures performed (including culture media checks). Equipment and instrument maintenance and function checks are also required to ensure their adequate performance. In addition, the laboratory must track and evaluate procedural outcomes such as fertilization rates, cleavage rates and embryo quality as a means of monitoring the quality of the procedures and services provided by the laboratory. The issue is whether these standards provide a sufficient means for monitoring laboratory performance or if a standard requiring PT should be included in the model.

Organization of Proposed Model Certification Program

This notice describes the proposed model certification program for embryo laboratories and includes the proposed definitions (Part I), proposed administrative requirements (Part II), and proposed embryo laboratory standards (Part III). References are also provided as an addendum to this notice for background and educational purposes.

Dated: October 28, 1998.

Jeffrey P. Koplan,

Director, Centers for Disease Control and Prevention (CDC).

PROPOSED MODEL CERTIFICATION PROGRAM FOR EMBRYO LABORATORIES

Contents

Part I. Definitions

Accredited institution. A school or program which——

(a) Admits as a regular student only persons having a certificate of graduation from a school providing secondary education, or the recognized equivalent of such certificate;

(b) Is legally authorized within the State to provide a program of education beyond secondary education;

(c) Provides an educational program for which it awards a bachelor's degree or provides not less than a 2-year program which is acceptable toward such a degree, or provides an educational program for which it awards a master's or doctoral degree; and

(d) Is accredited by a nationally recognized accrediting agency or association.

This definition includes any foreign institution of higher education that HHS or its designee determines meets substantially equivalent requirements.

Approved accreditation organization. An accreditation organization that has formally applied for and received the State's approval based on the organization's compliance with this model certification program and other requirements as specified by the State.

ART. Assisted reproductive technology.

Assisted hatching. A micromanipulation technique which involves making a small opening in the zona wall of the embryo to enhance implantation.

Assisted reproductive technology. All clinical treatments and laboratory procedures which include the handling of human oocytes and sperm, or embryos, with the intent of establishing a pregnancy. This includes, but is not limited to, in vitro fertilization, gamete intrafallopian transfer, zygote intrafallopian transfer, embryo cryopreservation, oocyte or embryo donation, and gestational surrogacy.

Assisted reproductive technology cycle. Any cycle in which (1) ART has been used, (2) in which the woman has undergone ovarian stimulation or monitoring with the intent of undergoing ART, (3) a woman has donated oocytes, or (4) in the case of cryopreserved embryos, in which embryos have been thawed with the intent of transfer. ART cycles can be stimulated (use of ovulation induction) or unstimulated (natural cycle).

Assisted reproductive technology laboratory procedures. All laboratory procedures for handling and processing of human oocytes and sperm, or embryos, with the intent of establishing a pregnancy. These procedures include, but are not limited to, the examination of follicular aspirates, oocyte classification, sperm preparation, oocyte insemination, assessment of fertilization, assessment of embryo

development, preparation of embryos for embryo transfer, and cryopreservation of specimens.

Assisted reproductive technology program or clinic. A legal entity practicing under State law, recognizable to the consumer, that provides ART to couples who have experienced infertility or are undergoing ART for other reasons. This can be an individual physician or a group of physicians who practice together, and share resources and liability.

Authorized person. An individual authorized under State law to order ART procedures.

CDC. The Centers for Disease Control and Prevention.

CLIA. The Clinical Laboratory Improvement Amendments of 1988.

Certification. The certification of an embryo laboratory by a State certification program or through accreditation by an approved accreditation organization.

Certification program. The model certification program for embryo laboratories described in this notice or a State certification program for embryo laboratories which meets or exceeds the requirements of the model certification program.

Cryopreservation. A technique to preserve biologic material through freezing.

Doctoral scientist. An individual holding an earned doctoral degree in a chemical, physical, biological or medical laboratory science from an accredited institution. As defined here, doctoral scientist also includes individuals holding an earned doctoral degree in veterinary medicine.

Embryo. The normal (2 pronuclei) fertilized egg that has undergone one or more divisions.

Embryo laboratory. A facility in which human oocytes and sperm, or embryos, are subject to ART laboratory procedures.

Embryo transfer. Introduction of an embryo(s) into a woman's uterus after in vitro fertilization.

Fertilization. The penetration of the egg by the sperm and fusion of genetic materials to result in the development of a fertilized egg (or zygote).

Gamete intrafallopian transfer. An ART procedure that involves removing eggs from the woman's ovary, combining them with sperm, and immediately injecting the eggs and sperm into the fallopian tube. Fertilization takes place inside the fallopian tube.

HHS. The U.S. Department of Health and Human Services, or its designee.

Intracytoplasmic sperm injection. The placement of a single sperm into the ooplasm of an oocyte by micro-operative techniques.

In vitro fertilization. A method of assisted reproduction that involves removing eggs from a woman's ovaries, combining them with sperm in the laboratory and, if fertilized, replacing the resulting embryo(s) into the woman's uterus.

Laboratory. Unless otherwise specified in this notice, means embryo laboratory.

Micromanipulation. Microtechniques such as intracytoplasmic sperm injection and assisted hatching commonly used to overcome fertilization disorders.

Physician. An individual with a doctor of medicine or doctor of osteopathy degree who is licensed by the State to practice medicine or osteopathy within the State in which the embryo laboratory is located.

Procedural outcome. The outcome of the assisted reproductive technology laboratory procedure performed e.g., fertilization assessment—the presence of two pronuclei in the ooplasm.

Oocyte. The female reproductive cell, also called an egg.

Specimen. Human biologic material (includes human reproductive tissue such as oocytes, sperm, zygotes and embryos).

Sperm. The male reproduction cell that has completed the process of meiosis and morphological differentiation.

State. Includes, for purposes of this model certification program, each of the 50 States, the District of Columbia, the Commonwealth of Puerto Rico, the Virgin Islands, and other territories of the United States, and a political subdivision of a State where the State, acting pursuant to State law, has expressly delegated powers to the political subdivision sufficient to authorize the political subdivision to act for the State in enforcing requirements equal to or more stringent than the model certification program.

Zygote. A normal (2 pronuclei) fertilized egg before cell division begins.

Zygote intrafallopian transfer. Eggs are collected and fertilized, and the resulting zygote is then transferred to the fallopian tube.

Part II. Administrative Requirements

A. Overview

The certification program for embryo laboratories is a model program developed by the Centers for Disease Control and Prevention (CDC) in accordance with Pub. L. 102–493 (42 U.S.C. 263a–1 *et seq.*) and is to be administered by interested States.

B. Requirements for State Administration of the Model

Certification Program for Embryo Laboratories. The State may adopt and administer the model certification program for embryo laboratories described in this notice of administer a State certification program for embryo laboratories that meets or exceeds the requirements of the model certification program, and must, at a minimum, meet the following provisions—

1. Certification Under State Programs. A State may qualify to adopt and administer the model certification program if the State submits an attestation to CDC (contact to be provided in final notice) providing—

a. Assurances that the certification program for embryo laboratories administered by the State meets or exceeds the requirements of the model certification program specified in this notice.

b. An agreement that in administering the certification program, a State will not establish any regulation, standard, or requirement which has the effect of exercising supervision or control over the practice of medicine in assisted reproductive technology programs or clinics.

c. An agreement that the term of State certification/recertification issued to an embryo laboratory is for a period of not more than two years.

d. An agreement to investigate, when appropriate and to the extent necessary, complaints received about an embryo laboratory certified under the State's program.

e. An agreement to annually report to CDC, (contact to be provided in final notice) the identity and certification status of each embryo laboratory in the State as well as any such laboratory which has applied for certification, and the assisted reproductive technology programs, or clinics with which each embryo laboratory is associated, for annual publication by CDC.

f. Information about any proposed use and approval and revocation of approval of accreditation organizations in accordance with paragraph 2. and 5. of this section.

g. An agreement to make such reports as the Secretary of the Department of Health and Human Services (through CDC) may require.

2. Use and Approval of Accreditation Organizations. Accreditation organizations approved by the State may be used to inspect and accredit embryo laboratories for the purpose of State certification and such accreditation shall constitute certification. The criteria and procedures used by the

State to approve accreditation organizations must include, at a minimum, the following:

a. The accreditation organization must provide assurances satisfactory to the State that its standards and requirements for accreditation of embryo laboratories meet or exceed the requirements of the certification program;

b. The accreditation organization must, at a minimum, conduct inspections of embryo laboratories in accordance with the requirements under paragraph 4. of this section which includes making available to the public, upon request, the specific findings (with any explanatory information required to interpret the findings), including deficiencies identified in an inspection, and any subsequent corrections to those deficiencies, no later than 60 days after the date of the inspection;

c. The accreditation organization must agree to revoke or suspend a laboratory's accreditation for one year, if the accreditation organization finds, on the basis of inspections, that the owner or operator of the laboratory, or any employee of the laboratory—

A. Has been guilty of misrepresentation in obtaining the accreditation.

B. Has failed to comply with any standards of the accreditation program.

C. Has refused a request of the accreditation organization or State for permission to inspect the laboratory, its operations, and records; and

d. The accreditation organization must agree to submit such reports and maintain such records as the State, or HHS, may require, to include, but not be limited to, the following:

i. Notification to the State of each newly accredited embryo laboratory within the State within 30 days of the laboratory obtaining accreditation;

ii. Notification to the State of any embryo laboratory within the State that has its accreditation denied, suspended, withdrawn or revoked, or that has had any other adverse action taken against it by the accreditation organization within 30 days of the action taken;

iii. Notification to the State within 10 days of a deficiency identified in any accredited embryo laboratory within the State where the deficiency poses an immediate jeopardy to the laboratory's patients or a hazard to the general public;

iv. Notification to the State if the accreditation organization finds, on the basis of inspections, that the owner or operator of the laboratory, or any employee of the laboratory—

A. Has been guilty of misrepresentation in obtaining the accreditation.

B. Has failed to comply with any standards of the accreditation program.

C. Has refused a request of the accreditation organization for permission to inspect the laboratory, its operations, and records;

v. Provide inspection schedules as requested by the State for the purposes of conducting onsite validation inspections of laboratories; and

vi. Provide the State written notification at least 30 days in advance of the effective date of any proposed changes in its requirements.

3. Embryo Laboratory Application Requirements. The State must provide for the submission of an application to the State by an embryo laboratory requesting certification, in such form as may be specified by the State. Such an application must include the following:

a. Assurance satisfactory to the State that the embryo laboratory will be operated in accordance with the standards of the certification program;

b. An agreement by the embryo laboratory to—

i. Annually report to the State the assisted reproductive technology programs or clinics with which the laboratory is associated.

ii. Submit changes in the ownership or the administration of the laboratory to the State within 30 days of the change.

iii. Permit the State to conduct onsite inspections including, as applicable, initial, routine, validation and complaint inspections, upon presentation of identification to the owner, operator, or agent in charge of the laboratory, during the laboratory's regular hours of operation to determine compliance with the certification program.

iv. Permit the State to have access to all facilities, equipment, materials, records, and information which the State requires to determine if the laboratory is being operated in accordance with the standards of the certification program.

v. Permit the State to copy any material, record, or information inspected, or submit such, upon request by the State.

vi. Permit the State to make available, upon request, to the public, the laboratory's specific inspection findings (with any explanatory information required to interpret the findings), including deficiencies identified in an inspection, and any subsequent corrections to those deficiencies;

c. If the State allows certification of an embryo laboratory on the basis of the laboratory's accreditation by an approved accreditation organization (i.e., issues a certificate of accreditation), the laboratory must, in addition to the requirements of subparagraphs 3.a. and 3.b. of this section—

i. Submit proof of current accreditation;

ii. Permit the accreditation organization to have access to all facilities, equipment, materials, records, and information which the accreditation organization requires to determine if the laboratory is being operated in accordance with the standards of the accreditation organization program;

iii. permit the accreditation organization to copy any material, record, or information inspected, or submit such, upon request by the accreditation organization;

iv. Permit the accreditation organization to make available, upon request, to the public, the laboratory's specific inspection findings (with any explanatory information required to interpret the findings), including deficiencies identified in an inspection, and any subsequent corrections to those deficiencies; and

v. Agree to authorize the accreditation organization to submit to the State or HHS such laboratory-specific information or reports as the State or HHS may require; and

d. Such other information, agreements and assurances as the State finds necessary.

4. Initial, Routine and Complaint Inspections. Inspections must be conducted to determine if embryo laboratories applying for or renewing their certification meet the requirements of the certification program. In addition, inspections may be performed as part of the State's investigation of complaints received about a certified embryo laboratory. The inspections may be carried out by the State or, as applicable, by an accreditation organization approved by the State in accordance with paragraph 2. of this section.

a. Initial inspections for embryo laboratory certification must be performed during the laboratory's regular hours of operation and may be announced. Initial inspections are performed when the laboratory applies for certification and may be performed for recertification after the laboratory has had a change in ownership or administration.

b. Routine inspections for renewal of the laboratory's certification must be performed biennially, during the laboratory's regular hours of operation and may be announced.

c. Inspections to investigate complaints received by the State about a laboratory may be performed unannounced, during the laboratory's regular hours of operation.

d. Inspection of a laboratory may be made only upon the presentation of identification to the owner, operator, or agent in charge of the laboratory being inspected.

e. In conducting an inspection, the State or approved accreditation organization must have access to all facilities, equipment, materials, records, and information which the State or approved accreditation organization requires to determine if the laboratory is being operated in accordance with the standards of the certification program.

f. The State or approved accreditation organization may copy any material, record, or information inspected or require it to be submitted to the State or, as applicable, to the approved accreditation organization.

g. The specific findings (with any explanatory information required to interpret the findings), including deficiencies identified in an inspection, and any subsequent corrections to those deficiencies must be made available to the public upon request beginning no later than 60 days after the date of the inspection.

5. Validation Inspections. The State must annually evaluate the performance of each approved accreditation organization by performing validation inspections of a sufficient number of embryo laboratories within the State accredited by the organization, to allow a reasonable estimate of the performance of such organization.

a. The State may enter and inspect, during regular hours of operation, embryo laboratories which have been accredited by an approved accreditation organization for the purpose of determining whether the laboratory is being operated in accordance with the standards of the certification program.

b. A validation inspection of a laboratory may be announced and be made only upon the presentation of identification to the owner, operator, or agent in charge of the laboratory being inspected.

c. In conducting a validation inspection, the State must have access to all facilities, equipment, materials, records, and information which the State requires to determine if the laboratory is being operated in accordance with the standards of the certification program.

d. The State may copy any material, record, or information inspected or require it to be submitted to the State.

e. If the State determines as a result of a validation inspection that the embryo laboratory is not in compliance with the standards of the certification program, the State must—

i. Notify the accreditation organization which accredited the laboratory.

ii. Make available to the public the inspection findings (with any explanatory information required to interpret the findings), including deficiencies identified in the inspection, and any subsequent corrections to those deficiencies.

iii. Conduct additional inspections of other embryo laboratories accredited by the accreditation organization is reliably identifying the deficiencies of the laboratories.

f. If the State determines that the accreditation organization has not met the requirements of paragraph 2. of this section, the State may (under such notice and hearing standards to be developed by the State) revoke the approval of the accreditation program.

6. Revocation of an Accreditation Organization's State Approval. If the State revokes approval of an accreditation organization under subparagraph 5.f., of this section—

a. The State must notify each laboratory, accredited by the organization under the State certification

b. The certification of any embryo laboratory accredited by the organization will continue in effect for 60 days after the laboratory is notified by the State of the withdrawal of approval, except that the State may extend the period during which the certification may remain in effect if the State determines that the laboratory submitted an application to another approved accreditation organization for accreditation or to the State, as applicable, in a timely manner after receipt of such notice.

7. Embryo Laboratory Certification Revocation and Suspension.

a. A certification issued by a State for an embryo laboratory must be revoked or suspended if the State or, as applicable, approved accreditation organization finds, on the basis of inspections and after reasonable notice and opportunity for hearing (under such notice and hearing standards to be developed by the State) to the owner or operator of the laboratory, that the owner or operator or any employee of the laboratory—

i. Has been guilty of misrepresentation in obtaining the certification.

ii. Has failed to comply with any standards of the certification program.

iii. Has refused a request of the State or approved accreditation organization for permission to inspect the laboratory, its operations, and records.

b. If the certification of an embryo laboratory is revoked or suspended, the certification of the laboratory shall continue in effect for 60 days after the laboratory receives notice of the revocation or suspension, unless there is a finding that the laboratory's continued operation may constitute a public health threat, in which case the certification shall be immediately revoked or suspended.

c. If the certification of an embryo laboratory is revoked or suspended, the laboratory may apply for recertification after one year after the date of the revocation or suspension.

8. Fees. The State may require the payment of fees for the purpose of, and in an amount sufficient to cover the costs of, administering the certification program.

Part III. Embryo Laboratory Standards

A. Personnel Qualifications and Responsibilities

The embryo laboratory must have a sufficient number of individuals, who meet the qualification requirements, to perform the functions necessary to provide timely services appropriate for the size and volume of the assisted reproductive technology program(s) or clinic(s) served by the laboratory. As a guideline, for every 90–150 assisted reproductive technology cycles performed annually, the laboratory should employ one individual who is capable of performing all assisted reproductive technology laboratory procedures provided by the embryo laboratory. Regardless of workload, at a minimum, two qualified individuals should be available to provide the appropriate laboratory services.

1. Laboratory Director Qualifications. The laboratory director must be qualified to manage and direct the laboratory personnel and the performance of assisted reproductive technology laboratory procedures. The laboratory director must—

a. Possess a current license as an embryo laboratory director issued by the State in which the laboratory is located, if such licensing is required.

b. Be a physician or a doctoral scientist with a broad knowledge of the biochemistry, biology, and physiology of reproduction, and laboratory operations including experimental design, statistics, and problem solving and meet the following.

i. Have two years documented pertinent experience in a laboratory

performing assisted reproductive technology procedures. This experience should induce familiarity with laboratory quality control, sterile technique and cell culture; and

ii. Have documented training of at least 1,000 hours in an embryo laboratory which includes performing, at a minimum, each laboratory component of the human assisted reproductive technology cycle 60 times.

Note: Documented experience and training may be acquired concurrently.

c. If not qualified under paragraph 1.b. of this section, be the director of an embryo laboratory on or before [date of publication of final notice] and meet the following:

i. Have two years documented pertinent experience in a laboratory performing assisted reproductive technology procedures. This experience should induce familiarity with laboratory quality control, sterile technique and cell culture; and

ii. Have documented training of at least 1,000 hours in an embryo laboratory which includes performing, at a minimum, each laboratory component of the human assisted reproductive technology cycle 60 times.

Note: Documented experience and training may be acquired concurrently.

d. In addition to meeting the qualification requirements above, obtain at least 12 contact hours of continuing education annually in assisted reproductive technology or clinical laboratory practice.

2. Laboratory Director Responsibilities. The laboratory director is responsible for the overall operation, administration, and technical and scientific oversight of the embryo laboratory, including the employment of personnel who are qualified to perform assisted reproductive technology laboratory procedures, and record and report procedural outcomes promptly, accurately and proficiently. If the laboratory director delegates performance of his or her responsibilities, he or she must do so in writing. The laboratory director remains responsible for ensuring that all delegated duties are properly performed. The laboratory director must—

a. Be accessible to the laboratory to provide onsite, telephone or electronic consultations as needed.

b. Ensure that the physical plant (space, facilities and equipment) and environmental conditions of the laboratory are appropriate for the laboratory procedures performed and provide a safe environment in which employees and other occupants are protected from physical, chemical, electrical and biological hazards.

c. Establish and monitor a program to ensure that aseptic conditions are maintained in the laboratory, as appropriate, for the assisted reproductive laboratory procedures to be performed.

d. Ensure that assisted reproductive technology laboratory procedures selected or developed by the laboratory are appropriate to provide quality patient care.

e. Ensure that adequate systems are in place to maintain patient confidentiality throughout those parts of the assisted reproductive technology process under the laboratory's control.

f. Ensure that an approved procedure manual is available to all personnel responsible for performing assisted reproductive technology laboratory procedures.

g. Establish and monitor a quality management program to assure the quality of laboratory services provided and to identify failures in quality as they occur.

h. Ensure that all necessary corrective actions are taken, documented and reviewed for effectiveness whenever failures in quality are identified.

i. Provide consultation to physicians and others, as appropriate, regarding the clinical significance of laboratory findings.

j. Employ a sufficient number of qualified personnel with the appropriate education and documented experience or training to supervise and perform the work of the laboratory. Written records of the qualifications of all personnel must be maintained.

k. Ensure that all personnel receive appropriate training for the assisted reproductive technology laboratory procedures to be performed, and have demonstrated that they can perform the procedures reliably prior to working on patients' specimens. All training activities must be documented.

l. Ensure that all personnel acquire, on an annual basis, the required number of continuing education contact hours. A record of each employee's continuing education participation must be maintained.

m. Specify, in writing, the responsibilities and duties of each person who performs assisted reproductive technology laboratory procedures, identifying which procedures each individual is authorized to perform and whether supervision is required.

n. Ensure that policies and procedures are established for monitoring each employee's continued competence to perform assisted reproductive technology laboratory procedures, and whenever necessary, provide remedial training or additional continuing education to improve skills.

o. Ensure that performance evaluations for each employee are performed and documented, at a minimum, annually.

3. Laboratory Supervisor Qualifications. The embryo laboratory must have one or more qualified supervisors who, under the direction of the laboratory director, provide day-to-day supervision of laboratory personnel performing assisted reproductive technology laboratory procedures. In the absence of the director, the laboratory supervisor must be responsible for the proper performance of all assisted reproductive technology laboratory procedures. The laboratory supervisor must—

a. Possess a current license issued by the State in which the laboratory is located, if such licensing is required.

b. Meet the qualification requirements for an embryo laboratory director under paragraph 1. of this section, or meet the following:

i. Have an earned master's or bachelor's degree in a chemical, physical, biological, clinical laboratory or medical technology science from an accredited institution; and

ii. Have documented training which includes performing, at a minimum, each laboratory component of the human assisted reproductive technology cycle 60 times.

c. If not qualified under subparagraph 3.b. of this section, be the supervisor of an embryo laboratory on or before [date of publication of final notice] and have documented training which includes performing, at a minimum, each laboratory component of the human assisted reproductive technology cycled 60 times.

d. In addition to meeting the qualification requirements above, obtain at least 12 contact hours of continuing education annually in assisted reproductive technology or clinical laboratory practice. If also serving as the laboratory director, continuing education obtained to meet the laboratory director qualification requirements may be used to meet this requirement.

4. Laboratory Supervisor Responsibilities. The laboratory supervisor is responsible for day-to-day supervision or oversight of the embryo laboratory operation and personnel performing assisted reproductive technology laboratory procedures. The laboratory supervisor must—

a. Be accessible to laboratory personnel at all times when assisted

reproductive technology laboratory procedures are performed to provide on-site, telephone or electronic consultation to resolve technical problems in accordance with policies and procedures established by the laboratory director.

b. Provide day-to-day supervision of laboratory personnel performing assisted reproductive technology laboratory procedures.

c. Ensure direct and constant supervision of personnel undergoing training in assisted reproductive technology laboratory procedures to fulfill the qualification requirements for a reproductive biologist.

d. Perform laboratory director responsibilities as authorized in writing by the laboratory director.

5. Reproductive Biologist Qualifications. Each individual performing assisted reproductive technology laboratory procedures must—

a. Possess a current license issued by the State in which the laboratory is located, if such licensing is required.

b. Meet the qualification requirements for an embryo laboratory director under paragraph 1. of this section, laboratory supervisor requirements under paragraph 3. of this section, or meet the following:

i. Have an earned bachelor's degree in a chemical, physical, biological, clinical laboratory or medical technology science from an accredited institution; and

ii. Have documentation of training appropriate for the assisted reproductive technology laboratory procedure(s) to be performed before performing the procedure(s) without direct and constant supervision on patient specimens. Training must include performing the assisted reproductive technology laboratory procedure(s), at a minimum, 30 times under direct and constant supervision.

c. If not qualified under subparagraph 5.b. of this section, be performing assisted reproductive technology laboratory procedures in an embryo laboratory on or before [date of publication of final notice] and have documentation of training appropriate for the assisted reproductive technology laboratory procedure(s) to be performed before performing the procedure(s) without direct and constant supervision on patient specimens. Training must include performing the assisted reproductive technology laboratory procedure(s), at a minimum, 30 times under direct and constant supervision.

d. In addition to meeting the qualification requirements above, obtain at least 12 contact hours of continuing education annually in assisted reproductive technology or clinical laboratory practice. If also serving as the laboratory director or laboratory supervisor, continuing education obtained to meet the laboratory director or laboratory supervisor qualification requirements may be used to meet this requirement.

6. Reproductive Biologist Responsibilities. The reproductive biologist is responsible for performing assisted reproductive technology laboratory procedures, and recording and reporting procedural outcomes promptly, accurately and proficiently. The reproductive biologist must—

1. Perform only those assisted reproductive technology laboratory procedures that are authorized by the laboratory director, and for which training has been documented. If appropriate training has not been documented, perform assisted reproductive technology laboratory procedures only under direct and constant supervision.

b. Follow the laboratory's established policies and procedures for performing assisted reproductive technology laboratory procedures, and recording and reporting procedural outcomes.

c. Adhere to the laboratory's quality management policies, document all specimen and procedure management, quality control and quality assurance activities, and equipment and instrument calibration, function verification and maintenance performed.

d. Identify problems that may adversely affect the performance of assisted reproductive technology laboratory procedures and either immediately notify the laboratory supervisor or director, or correct the problem(s) in accordance with the laboratory's established policies and procedures and notify the laboratory supervisor or director of the problem(s) and the corrective action(s) taken.

e. Document all corrective actions taken when failures in quality are identified.

B. Facilities and Safety

The embryo laboratory must provide adequate space and the appropriate environmental conditions to ensure safe working conditions and quality performance of assisted reproductive technology laboratory procedures.

1. Requirements for Physical Space and Utilities. The laboratory must be constructed and arranged so that—

a. The laboratory space, ventilation, and utilities are adequate for the volume of assisted reproductive technology laboratory procedures performed during peak periods of activity.

b. Assisted reproductive technology laboratory procedures are carried out in a secure area with access limited to authorized personnel.

c. Movement of patient specimens and traffic around sensitive work areas is limited in order to reduce the potential for spilled or lost specimens.

d. Incubator and storage space are configured to ensure positive specimen identification and minimize the potential for errors due to misplaced specimens or retrieval of the wrong specimen.

e. Activities requiring sterile technique such as the handling, assessment and culturing of human oocytes and embryos, are performed under aseptic conditions in an area that is physically isolated from other laboratory activities.

f. All laboratory work areas (does not include administrative areas) are easily washed and disinfected.

g. The laboratory and administrative space are conveniently located, but are separate from patient areas.

h. Immediate communication can occur with the oocyte retrieval and transfer room(s).

2. Safety Requirements. Safety precautions, policies, and procedures must be established and posted, or readily available to all personnel, to ensure protection from physical, chemical, electrical and biological hazards.

a. All personnel must be knowledgeable about and abide by applicable Federal, State and local regulations regarding protection from physical, chemical, electrical and biological hazards.

b. Disposable materials should be used wherever possible for all procedures that involve exposure to tissue and body fluids.

c. The laboratory must store and dispose of tissue, body fluids, or other potentially biohazardous materials as outlined in Federal, State and local regulations.

d. Toxic chemicals, including toxic cleaning materials, must be used in a manner that is not harmful to patient specimens.

e. Radioisotopes must not be used in a laboratory that performs assisted reproductive technology procedures.

f. The laboratory must have an emergency plan appropriate for its geographical location which specifies the actions to be taken to protect employees, patients, visitors and specimens in case of a natural disaster or other potentially devastating event.

3. Laboratory Animals. If laboratory animals are used, all applicable Federal, State and local regulations regarding animal care and use must be met. Animal specimens must be—

a. Handled and stored separately from human specimens.

b. Incubated separately from human specimens, unless program/institutional approval is given for an application involving specific cell lines, i.e., animal coculture.

C. Quality Management

The embryo laboratory must establish and follow written policies and procedures for a comprehensive quality management program that is designed to monitor and evaluate the ongoing and overall quality of the assisted reproductive technology laboratory procedures performed and services provided. All quality management activities must be documented.

1. Procedure Manual. A written procedure manual including instructions for all assisted reproductive technology laboratory procedures performed must be available in the embryo laboratory and followed by all laboratory personnel. The written procedures must be in sufficient detail to assure reproducibility and competence in the performance of the laboratory procedures.

a. The procedure manual include the following, when applicable to the assisted reproductive technology laboratory procedure performed:

i. Principle (scientific basis) of the assisted reproductive technology laboratory procedure;

ii. Clinical significance of the assisted reproductive technology laboratory procedure;

iii. Requirements for specimen collection and handling;

iv. Step-by-step instructions for performance of the assisted reproductive technology laboratory procedure;

v. Preparation of required reagents, culture media, solutions, or other special supplies;

vi. Equipment and instrumentation required for the performance of the procedure, including necessary function checks and calibration protocols;

vii. Quality control procedures to be performed, including frequency of control testing, and criteria for acceptability;

viii. Remedial action to be taken when function checks, calibration or control results do not meet the laboratory's criteria for acceptability;

ix. Calculations and interpretation of procedural outcomes, including criteria for acceptable and unacceptable outcomes, and procedural outcomes requiring special notification;

x. The laboratory's system for recording and reporting procedural outcomes;

xi. Limitations in methodologies, including interfering substances and precautions;

xii. Pertinent literature references;

xiii. Description of the course of action to be taken if required equipment or instrumentation malfunctions or is inoperable;

xiv. Criteria for the referral or transfer of specimens to another embryo laboratory for the performance of an assisted reproductive technology laboratory procedure, including procedures for specimen submission and handling; and

xv. Procedure for safe and appropriate specimen disposal.

b. Manufacturers' instrument/equipment manuals and package inserts may be used, when applicable, to meet the requirements of this section.

i. Any of the items listed under subparagraph 1.a. of this section, not provided by the manufacturer must be provided by the laboratory.

ii. Any modifications to, or deviations from, the manufacturer's instructions, must be clearly documented and provided in the procedure manual.

c. Appropriate reference materials (e.g., slides, pictures, textbooks, etc.) should be available in the laboratory to allow, as needed, comparison with patient specimens.

d. Procedures must initially be approved, signed and dated by the laboratory director, and must thereafter, be reviewed by the laboratory director on an annual basis.

e. Procedures must be re-approved, signed and dated if the directorship of the laboratory changes.

f. Each change in a procedure must be approved, signed and dated by the current laboratory director.

g. The laboratory must retain a copy of each procedure with the dates of initial use and discontinuance in accordance with the requirements of section D., Maintenance of Records, of this part.

2. Equipment and Instrument Maintenance/Calibration. The embryo laboratory must perform and document equipment and instrument maintenance and, as applicable, calibration, and function verification that include(s) electronic, mechanical and operational checks necessary for the proper performance of assisted reproductive technology laboratory procedures. The laboratory must—

a. Have sufficient equipment for the type and volume of assisted reproductive technology laboratory procedures performed, which may include but is not limited to, incubators, freezers, refrigerators, hoods, thermometers, centrifuges, microscopes, pipettes, and warming devices.

b. Establish and follow written policies and procedures for equipment and instrument maintenance and, as applicable, calibration, and function checks, that ensure proper performance of the equipment and instruments used in assisted reproductive technology laboratory procedures.

The laboratory must—

i. Define acceptable limits for equipment and instrument maintenance and, as applicable, calibration, and function checks prior to their use in assisted reproductive technology laboratory procedures.

ii. Perform maintenance and, as applicable, calibration, and function checks in accordance with the equipment/instrument manufacturer's instructions and at the frequency required to ensure adequate performance of the equipment and instruments used in assisted reproductive technology laboratory procedures.

iii. Monitor environmental conditions, using an independent measuring device, in critical equipment, including but not limited to, incubators, controlled-rate freezers and liquid nitrogen storage tanks, at a frequency that ensures timely detection of conditions that are deleterious to specimens. These conditions include, if applicable:

A. Temperature;

B. Humidity;

C. Gas concentration; and

D. Liquid nitrogen levels.

iv. Maintain an alarm system on critical equipment that will immediately detect when pre-established limits for the environmental conditions listed in subparagraph 2.b.iii. (excluding humidity), of this section, are exceeded. The alarm system must be:

A. Checked periodically to ensure that it will be triggered when preestablished limits for environmental conditions are exceeded; and

B. Monitored 24 hours a day in the laboratory or at a remote site.

v. Protect critical equipment and instrumentation from fluctuations and interruptions in electrical current.

vi. Have available emergency back-up capability for critical equipment, including but not limited to, incubators, refrigerators and controlled-rate freezers.

vii. Document all maintenance, calibration, and function checks performed.

c. Identify, investigate, and correct problems with equipment or instrumentation that may adversely affect the performance of assisted reproductive technology laboratory procedures.

d. Document all corrective actions taken when problems with equipment or instrumentation are identified.

3. Labeling, Handling, and Storage of Chemicals, Reagents, Solutions, Culture Media, Materials and Supplies. The embryo laboratory must label, handle and store chemicals, reagents, solutions, culture media, materials and supplies in a manner that ensures their positive identification, optimum integrity and appropriate reactivity in assisted reproductive technology laboratory procedures. The laboratory must—

a. Have a mechanism for ensuring sufficient chemicals, reagents, solutions, culture media, materials and supplies for the type and volume of assisted reproductive technology laboratory procedures performed (e.g., inventory maintenance program).

b. Define criteria that are essential for proper storage of chemicals, reagents, solutions, and culture media, including the following, as applicable:

i. Temperature;

ii. Humidity; and

iii. Other conditions necessary for proper storage.

c. Label all chemical, reagents, solutions, and culture media to indicate the following, as applicable:

i. Identity, and when significant, batch or lot number, titer, strength, or concentration;

ii. Recommended storage conditions;

iii. Expiration date; and

iv. Other pertinent information required for proper use.

d. Verify that materials which come in contact with sperm, oocytes, and embryos have been tested and found to be non-toxic to sperm, oocytes, and embryos. Documentation supplied by the manufacturer may be used to meet this requirement.

e. Maintain records documenting the batch or lot number, date of receipt or preparation, and date placed in use, for all chemicals, reagents, solutions, and culture media.

f. Prepare, store, and handle chemicals, reagents, solutions, and culture media in a manner to ensure that they are not used when they have exceeded their expiration date, have deteriorated, or are of substandard quality.

4. Specimen and Procedure Management. The embryo laboratory must have written protocols and criteria for the laboratory procedures performed and employ and maintain a system that provides for proper patient identification and preparation; specimen collection, identification, and handling (transportation, processing, storage, preservation); and accurate recording and reporting of laboratory procedural outcomes.

a. The laboratory must have available and follow written policies and procedures for each of the following:

i. Instructions for patient preparation, if applicable;

ii. Methods used for the positive identification of patients;

iii. Specimen collection;

iv. The labeling of patient specimens to ensure positive identification from the time of specimen collection through final disposition or disposal;

v. Criteria for maintaining specimen integrity and viability during transport, storage and the performance of assisted reproductive technology laboratory procedures including, as applicable, requirements for:

A. Temperature;

B. Humidity; and

C. Gas concentration; and

vi. Criteria for specimen acceptability and, as appropriate, instructions for special handling of suboptimal specimens.

b. The laboratory must have adequate systems in place to ensure patient confidentiality throughout those parts of the assisted reproductive technology process that are under the laboratory's control.

c. The laboratory may perform assisted reproductive technology laboratory procedures only at the written or electronic request of an authorized person. Oral requests for changes to the original written or electronic request must be documented by the laboratory and followed by receipt of written or electronic documentation from an authorized person within 24 hours of the oral request. The patient's chart or medical record may be used for written authorization, but must be available to the laboratory at the time of the laboratory procedure. Written or electronic authorization must include the following:

i. The patient's name and unique identifier;

ii. When applicable, the partner's or donor's name or other unique identifier;

iii. The name and address or other suitable identifiers of the authorized person requesting the procedure, and the name of the individual communicating the request;

iv. The procedure(s) to be performed;

v. The date(s) and time(s) the procedures(s) is to be performed; and

vi. Any additional information relevant and necessary to the performance of the procedure(s) including verification of informed patient consent, and as applicable, special handling instructions and any instructions stipulated by the patient.

d. As applicable, the laboratory must establish and follow written protocols, including documented criteria, for—

i. Evaluation and assessment of oocyte morphology and maturity, fertilization, and embryo quality.

ii. Insemination schedule relative to oocyte maturity.

iii. Volume, numbers, and quality of sperm used for insemination of each oocyte.

iv. Disposition of oocytes with an abnormal number of pronuclei.

v. Disposition of excess oocytes.

vi. The time period following insemination for examination of oocytes to determine fertilization.

vii. Micromanipulation of oocytes and embryos.

viii. Re-insemination of oocytes.

ix. Cryopreservation of specimens.

x. Embryo transfer procedures, which include the following:

A. The length of time embryos are cultured prior to transfer;

B. The medium and protein supplementation used for transfer, as applicable;

C. Disposition of excess embryos;

D. Types of catheters available, with circumstances for use of each;

E. Method of transfer; and

F. Technique for post transfer catheter check.

e. The laboratory must maintain a record system, for each patient's assisted reproductive technology cycle, to ensure reliable identification and control of the patient's specimens as they are received and the laboratory procedure(s) performed. The record system must include documentation of the information specified in subparagraph 4.c. of this section, and—

i. The laboratory accession number, or other unique identification of the specimen.

ii. The date and time of specimen receipt into the laboratory and, as applicable, the number of oocytes retrieved and assessment of each oocyte or cumulus corona complex.

iii. The condition and disposition of all specimens including those that do not meet the laboratory's criteria for acceptability.

iv. The records and dates of all laboratory handling and procedures, including the following, as applicable:

A. Semen assessment before and after washing and concentration for insemination;

B. Outcome of insemination or micromanipulation procedures (e.g., fertilization);

C. Outcome of any culture (e.g., cleavage);

D. Relative timing of protocol events (incubation hours, etc.);

E. Assessment of the developmental status and quality of all embryos at transfer;

F. Verification that no embryos remain in the catheter following completion of transfer;

G. The identity and lot numbers of the media and media supplements used in each phase of the procedure; and

H. The identity of the laboratory personnel who handled the specimens and performed the procedures.

f. The laboratory must have a mechanism in place for promptly providing the authorized person who ordered the procedure a complete summary of all procedural outcomes and the occurrence of any unusual or abnormal events, including the condition and disposition of specimens that do not meet the laboratory's criteria for acceptability.

g. The laboratory must have an accurate and reliable method of tracking cryopreserved specimens ensuring positive identification of each cryopreservation container. In addition, the cryopreservation container must be labeled with the patient's name or unique identifier, and the date the specimen(s) was frozen. All labeling must be of a permanent nature. Documentation must be maintained in duplicate log books or files for each liquid nitrogen storage tank and include the following:

i. The patient's name or other unique identifier;

ii. A description of each cryopreservation container's contents;

iii. The freezing protocol used;

iv. Date frozen;

v. Type and location of cryopreservation container (e.g., straw, vial); and

vi. Final disposition/disposal of the cryopreserved specimen(s).

h. If cryopreserved specimens are received from or transferred to other facilities, the laboratory must have written policies and procedures for the receipt/transfer of cryopreserved specimens. Policies and procedures must include appropriate methods of transportation and the method for verifying the identification and number of cryopreservation containers received/transferred. In addition, documentation of the freezing protocol used, and copies of patient release forms and applicable log sheets must accompany the cryopreserved specimens.

i. Clinical laboratory testing on specimens obtained by the embryo laboratory must be performed in accordance with the regulations implementing CLIA at 42 CFR Part 493. In addition—

i. The referring embryo laboratory must not revise results or information directly related to the interpretation of results provided by the testing laboratory.

ii. The referring embryo laboratory may permit the testing laboratory to send the test result(s) directly to the authorized person who initially requested the testing. The embryo laboratory must retain or be able to produce an exact duplicate of the testing laboratory report.

iii. The authorized person who orders a clinical laboratory test must be notified by the referring embryo laboratory of the name and address of the testing laboratory.

5. Method Validation. All assisted reproductive technology procedures selected or established by the embryo laboratory must be validated by the laboratory prior to routine patient use. The laboratory must determine appropriate performance measures and demonstrate that the procedure, when performed by the laboratory's staff, meets or exceeds acceptable levels of performance as defined by the laboratory. In addition, the laboratory must periodically verify, through its quality management activities (as specified in this part), each procedure's continued acceptable level of performance. All validations must be documented.

6. Quality Control. The embryo laboratory must establish and follow written quality control procedures at a frequency appropriate to monitor the reliability of the assisted reproductive technology laboratory procedures performed. All quality control activities must be documented. The laboratory must—

a. Establish acceptability criteria for all quality control procedures.

b. Perform and document the remedial action(s) taken when problems are identified or quality control procedures do not meet the laboratory's criteria for acceptability.

c. For each laboratory procedure performed and, as applicable, culture media preparation—

i. Define and use the appropriate grade of water required.

ii. Periodically monitor water quality to ensure that its quality continues to meet the laboratory's specifications for its intended use. As applicable, adherence to manufacturers' storage and handling requirements, and expiration dates may meet this requirement.

d. As applicable, have and follow a written procedure for the preparation, washing and sterilization of glassware used in the laboratory's procedures that includes the following:

i. Rinsing all washable glassware with distilled or deionized water prior to drying; and

ii. If detergent is used, testing washed items for detergent removal.

e. Have and follow a written procedure for the quality control of culture media which includes a visual check for physical damage to the media container and evidence of media contamination prior to its use and—

i. For each batch of culture media prepared in-house, document the quality of the media by testing—

A. pH.

B. Osmolality.

C. Culture suitability using an appropriate bioassay system.

ii. For each batch of commercially prepared culture media—

A. Verify and document the quality of the media with an appropriate bioassay system. Documentation of quality control performed by the manufacturer may meet this requirement.

B. Follow the manufacturer's specifications for using the media.

iii. Test and document the quality of any media supplementation (e.g., protein), when appropriate, using a bioassay system.

iv. Test blood based media supplements (e.g., human fetal cord serum) prepared in-house with a FDA licensed, approved, or cleared test and show the supplement to be negative/nonreactive for the following communicable diseases prior to use:

A. Human immunodeficiency virus, Type 1 (e.g., anti-HIV-1);

B. Human immunodeficiency virus, Type 2 (e.g., anti-HIV-2);

C. Hepatitis B virus (e.g., HbsAg);

D. Hepatitis C virus (e.g., anti-HCV);

E. Human T-cell lymphotrophic virus, Type I (e.g., anti-HTLV-I); and

F. Such other diseases that may be later added to this list.

NOTE: A batch of media (solid, semi-solid, or liquid) consists of all tubes, plates, or containers of the same medium prepared at the same time in the laboratory; or, if received from an outside source of commercial supplier, consists of all of the plates, tubes or containers of the same medium that have the same lot numbers and are received in a single shipment.

7. Quality Assurance. The embryo laboratory must establish and follow written policies and procedures for a quality assurance program to monitor the quality of services provided by the laboratory, and resolve problems that are identified. The laboratory must have a mechanism to evaluate the effectiveness of its policies and

procedures; identify and correct problems; and assure the adequacy and competency of the staff. As necessary, the laboratory must revise its policies and procedures based on the results of those evaluations. All quality assurance activities must be documented.

a. The laboratory must have an ongoing mechanism for monitoring, evaluating and revising, if necessary, based on the results of its evaluations, the following:

i. The criteria established for patient identification and specimen collection, identification, and handling;

ii. The information requested and maintained on each patient and for each laboratory procedure performed for its completeness, relevance and necessity;

iii. The timeliness and accuracy of recording and reporting procedural outcomes;

iv. The accuracy and reliability of tracking cryopreserved specimens;

v. The appropriate storage and retrieval of laboratory records such as procedural outcomes, and other data recorded and maintained; and

vi. The corrective actions taken for—

A. Problems identified during the evaluation of equipment and instrument maintenance, calibration, and function check data.

B. Problems identified during the evaluation of quality control data.

C. Errors detected in patient or specimen identification and handling.

D. Clerical or analytical errors detected in laboratory records.

b. The embryo laboratory must have an ongoing mechanism to—

i. Identify and evaluate laboratory procedural outcomes that appear inconsistent with the patient or donor history.

ii. Track and evaluate laboratory procedural outcomes including, but not limited to, fertilization rates, cleavage rates and embryo quality.

iii. Maintain a file of adverse reactions occurring as a result of errors made during the performance of assisted reproductive technology laboratory procedures.

iv. Evaluate the effectiveness of its policies and procedures for assuring employee competence in performing assisted reproductive technology laboratory procedures.

v. Document problems that occur as a result of a breakdown in communication between the laboratory and referring physicians or others involved in the assisted reproductive technology procedures, and take corrective actions to resolve the problems and minimize future communications breakdowns.

vi. Assure that all complaints and problems reported to the laboratory are documented. Investigations of complaints must be made, when appropriate, and as necessary, corrective actions must be instituted.

vii. Document and assess problems identified during quality assurance reviews, and discuss them with the laboratory staff and, as appropriate, referring physicians and others involved in the assisted reproductive technology procedures. The laboratory must take the necessary corrective actions to prevent recurrences.

D. Maintenance of Records

The embryo laboratory must retain records of all of its policies and procedures; personnel employment, training, evaluations and continuing education activities; and quality management activities specified in this part.

1. Record Format. Laboratory records must be accurate, indelible, and legible. Records may be retained electronically, or as original paper records, or as true copies such as photocopies, microfiche, or microfilm.

2. Retention Period. Laboratory records must be retained in accordance with time frames specified by applicable Federal, State and local laws or for ten years beyond the date of final disposition or disposal of all specimens obtained during each patient's assisted reproductive technology cycle, whichever is later. Records must be retained on site for two years. Note: Transfer of cryopreserved specimens to another facility constitutes final disposition for the transferring facility.

3. Record Retrieval. Laboratory records must be maintained in a manner which ensures timely, accurate and reliable retrieval.

4. Laboratory Closure. In the event that the laboratory ceases operation, the laboratory must make provisions for these records to be maintained for the time frame required above.

Addendum

References

1. The American Association of Bioanalysts. Embryology and Andrology Review Course. American Association of Bioanalysts, St. Louis, Missouri, 1994.

2. The American Association of Tissue Banks. Standards for Tissue Banking. The American Association of Tissue Banks, McLean, Virginia, 1996.

3. The American Fertility Society. Guidelines for Human Embryology and Andrology Laboratories. Fertility and Sterility 1992;58(Suppl 1) :1S–16S.

4. Association of Clinical Embryologists. Accreditation Standards and Guidelines for IVF Laboratories. Association of Clinical Embryologists, London, England, 1996.

5. California Health and Safety Code, Division 2, Chapter 4.1—Tissue Banks. State of California, Department of Health Services, Berkeley, California, 1992.

6. Centers for Disease Control and Prevention. Reporting of Pregnancy Success Rates from Assisted Reproductive Technology Programs. 62 FR 45259, Aug. 26, 1997.

7. Code of Federal Regulations, Title 42, Chapter IV, Part 493—Laboratory Requirements.

8. The College of American Pathologists/American Society for Reproductive Medicine Reproductive Laboratory Accreditation Program. The College of American Pathologists, Northfield, Illinois, 1996.

9. The Fertility Clinic Success Rate and Certification Act of 1992 (Public Law 102–493).

10. Keel BA and BW Webster. CRC Handbook of the Laboratory Diagnosis and Treatment of Infertility. CRC Press, Inc., Boca Raton, Florida, 1990.

11. Rules and Regulations of the State of New York, Part 52 of Title 10 (Health). Tissue Banks and Non-transplant Anatomic Banks. State of New York Department of Health, Albany, New York, 1992.

12. Senate Report 102–452 on H.R. 4773. Fertility Clinic Success Rate and Certification Act of 1992. 102d Congress, 2d Session, 1992.

13. Veeck LL. The Gamete Laboratory: Design, Management and Techniques. pp. 798–820 in: Infertility: Evaluation and Treatment. Edited by WR Keye, RJ Chang, RW Rebar and MR Soules. WB Saunders, Philadelphia, Pennsylvania, 1995.

[FR Doc. 98–29374 Filed 11–5–98; 8:45 am]

BILLING CODE 4163–18–M