Federal Register

Wednesday
July 21, 1999

Part IV

Department of Health and Human Services

Centers for Disease Control and Prevention

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

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

ACTION: Final notice.

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 the CDC, develop a model program for the certification of embryo laboratories, to be carried out voluntarily by interested States.

This notice sets forth the model certification program requirements, including definitions, administrative requirements, and embryo laboratory standards. The model program incorporates comments received by CDC on the proposed model certification program that was published in the **Federal Register** on November 6, 1998 (63 FR 60178).

FOR FURTHER INFORMATION CONTACT: Robert Martin, Dr.P.H., Division of Laboratory Systems, CDC, telephone (770) 488–8295

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 the 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 the 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 officials who are to receive 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. Inspections are to be unannounced or be announced in circumstances in which the likelihood of discovering deficiencies in the operations of an embryo laboratory is not diminished. Section 3(g) also requires the Secretary to seek public comment on the circumstances under which announced inspections may be conducted. 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 determine 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 in 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 the 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 the 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 Register** 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. The second report, 1996 Assisted Reproductive Technology Success Rates: National Summary and Fertility Clinic Reports, was published in February 1999. Copies of these reports may be obtained by contacting CDC by calling 1–770–488–5372 or via the Internet at www.cdc.gov/nccdphp/drh/art96/.

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.

Background

In accordance with the FCSRCA, in developing the model certification program, the CDC consulted with individuals, professional organizations and consumer groups with expertise and interest in ART. The organizations represented reproductive medicine—the American Society for Reproductive Medicine (ASRM) and the Society for Assisted Reproductive Technology, laboratory professionals—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. The CDC also sought input from State programs and Federal agencies with regulatory responsibilities related to laboratory practice, tissue banking and ART.

A useful example in developing the model certification program was the voluntary Reproductive Laboratory Accreditation Program (RLAP) developed jointly by the CAP and the ASRM, and administered by the CAP. The CAP/ASRM RLAP currently provides oversight of at least one third of embryo laboratories affiliated with ART programs and clinics in the United States and served as the basis for many of the standards in the proposed model program. Standards and guidelines from other professional organizations, State, Federal, and international programs were also used as resources, and the CDC made a number of site visits to embryo laboratories to observe the daily operation of these facilities. In addition, between November 1996 and August 1997, the CDC held several work sessions with technical consultants to obtain individual expert input on specific issues related to the embryo laboratory and the model certification program, including personnel qualifications and responsibilities, quality assurance and quality control (quality management), recordkeeping, specific definitions as they would apply to the model certification program, and State administration of the program.

Subsequently, on November 6, 1998, the CDC published in the **Federal Register** (63 FR 60178) a notice soliciting public comment on a proposed model program for the certification of embryo laboratories. As mentioned above, the FCSRCA required 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 during the public comment period, the CDC highlighted the following issues in the preamble to the proposed model program:

- Based on the comments received during the previously mentioned work sessions with technical consultants (63 FR 60170), 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 were interested in receiving comments on the following issue which was not specifically addressed in the proposed model certification program but could have been 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.

During the 60-day comment period the public had the opportunity to submit concerns and recommendations in response to the issues highlighted above, as well as any other aspect of the proposed model program. The letters we received provided helpful information for finalizing the model certification program. A summary of the comments and our responses to them are included below.

Other information that was useful in finalizing this model certification program for embryo laboratories was data provided in a Survey of Assisted Reproductive Technology Embryo Laboratory Procedures and Practices, conducted under a CDC Task Order Contract with Research Triangle Institute and performed by Analytical Sciences, Inc. The purpose of this survey was to provide the CDC with an enumeration of those ART embryo laboratory procedures and practices that are currently in use. The final report of the survey was completed on January 29, 1999, and can be accessed via the Internet at www.phppo.cdc.gov/dls/pdf/art/ARTsurvey.pdf. A copy of the report may also be obtained by calling the CDC at (770) 488–8295.

Responses to Comments

In response to our request for comments to the proposed model certification program, we received a total of 15 letters, four of which were from professional organizations, one from a consumer advocacy group, one from a manufacturer, and the rest from individuals employed in embryo laboratories or affiliated with infertility clinics/programs. The letters contained approximately 60 comments, 14 of which were in response to the issues highlighted for consideration in the proposed model program. Six of the commenters, which included two

professional organizations, expressed support for and/or complimented our efforts to develop a model certification program. There was no opposition to the model in its entirety, but rather the respondents provided comments on specific aspects of the proposed model. Comments to the highlighted issues and additional comments are addressed below.

1. Are the revised definitions for ''assisted reproductive technology'' and ''embryo laboratory'' appropriate and accurate for use in the model certification program?

One commenter believed that the definition for ''assisted reproductive technology'' was overly broad and could be interpreted as including intra uterine insemination (IUI) and intra vaginal culture (IVC), procedures which do not require the same level of quality control, quality assurance, etc., as do other ART procedures. The commenter suggested that the model be revised to contain new categories for IUI and IVC with requirements consistent with the complexity level of the procedures. Another commenter stated that while the term ''embryo laboratory'' is technically correct, these laboratories would be more appropriately named ''embryology laboratories'' to reflect the science of the work performed in them.

Response: The proposed definition for assisted reproductive technology (ART) was based on the definition of ART provided in the FCSRCA, which was modified for clarity based on the comments received during our work sessions with technical consultants. We do not agree with the comment that the ART definition is overly broad for use in the model certification program. The definition appropriately and accurately specifies ART as ''all clinical and laboratory treatments which involve the handling of human oocyte and sperm, or embryos, with the intent of establishing a pregnancy.'' The commenter's interpretation is incorrect; IUI is not covered by this definition of ART, as IUI is a procedure that involves the manipulation of sperm only rather than oocytes and sperm. However, IVC is covered by the ART definition, since it is a procedure in which oocytes and sperm are mixed and incubated together. In addition, we disagree with this commenter's viewpoint that IVC does not require the same level of quality control or quality assurance as other ART laboratory procedures. In performing IVC, oocytes and embryos must be accurately identified just as they are for other ART laboratory procedures, requiring qualified personnel with appropriate training and expertise, written procedures and policies outlining criteria for the identification of oocytes and embryos, etc., to ensure quality patient care.

In response to the comment suggesting that the term ''embryology laboratory'' be used in place of ''embryo laboratory'', we are retaining ''embryo laboratory'' because it is the term used throughout the statute (FCSRCA). Although embryology refers to the science of studying the origin and development of an individual organism, in using the term embryo, we are specifically referring to the intended goal of the procedures performed in these laboratories—the manipulation of human gametes to produce viable human embryos.

2. 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 are there circumstances that should require unannounced inspections?

Five commenters, two of which were professional organizations, expressed concern with the proposed model's option to permit unannounced inspections for complaint investigations. The commenters cited the potential for disrupting embryo laboratory procedures and interfering with patient treatment. Maintaining patient confidentiality during an inspection was also of concern. Three commenters suggested providing the laboratory 48 hours notice to allow rescheduling of patient procedures or other alternative measures to reduce the risk to eggs, sperm and embryos. The consumer advocacy group supported unannounced inspections if precautions are taken to prevent interference with patient treatment and safeguard patient confidentiality.

Response: We understand the commenters' concerns, and agree that the nature of the work performed in embryo laboratories is delicate and time sensitive, and that disruptions or delays in the process could have deleterious effects. We also agree that maintaining patient confidentiality during a laboratory inspection is of utmost importance. When performing inspections, it is not the intent to disrupt the laboratory's operations or divulge confidential patient information. In general, Federal, State and professional accreditation organization laboratory inspectors are health professionals with pertinent education, qualifications, and experience. They receive special training and are instructed to make every effort to avoid interrupting the routine workflow when conducting an inspection. They are also aware of the importance of safeguarding confidential patient information.

The proposed model program did not mandate that unannounced inspections *must* be performed for complaint investigations, but it did provide the State that chooses to adopt the model the option to do so. We included this option so that investigations of complaints of truly egregious behavior could be conducted immediately and unannounced. In addition, this option would allow the State to incorporate embryo laboratory inspections into an already existing laboratory or health care facility regulatory program that may require unannounced complaint inspections. Based on the comments we received, and because of the unique nature of the procedures performed in embryo laboratories, we agree that in some cases there may be a need to allow 48 hours notice prior to conducting a complaint inspection. This could be done to give the laboratory time to reschedule ART procedures, if necessary, and to ensure that adequate staffing and the appropriate individuals are available on the day of inspection. In addition, we do not believe that a 48 hour notice would significantly diminish the likelihood of discovering systemic deficiencies in a laboratory's operation. Therefore, if a State determines that it is appropriate to provide some advance notice of a complaint inspection, the model certification program as written allows the State to provide the laboratory a 48 hour notice.

3. Is two years an appropriate period of time for the term of certification of a laboratory (i.e., renew biennially)?

Two individuals provided comments on the time period for the term of certification. One of the commenters viewed a two year term as reasonable. The other commenter suggested that three to five years would be more appropriate as long as there was no significant change in the laboratory's personnel, no change in the laboratory's location, or no complaints registered against the laboratory.

Response: A two year term of laboratory certification is consistent with other similar laboratory licensure or accreditation programs currently in existence. Maintaining this consistency among programs may allow for easier coordination of inspections if a laboratory participates in more than one program offered by the same organization or agency. For example, a facility that has both a clinical laboratory and a reproductive laboratory accredited by the CAP may be able to have a joint inspection for both of the programs. For this reason, we agree with

the commenter who stated that a two year term is reasonable, and have not revised this requirement in the model certification program.

4. Do the proposed embryo laboratory standards provide a sufficient means for monitoring laboratory performance or should a standard requiring PT be included in the model?

Each of the four professional organizations commenting on the proposed model addressed the issue of PT. Three of the organizations did not support the inclusion of a PT requirement in the model certification program. They did not believe appropriate PT was available or could be developed and standardized due to the specimens (human gametes and embryos) used in the embryo laboratory. They stated this is especially true if the purpose of PT is to measure a laboratory's performance by replicating ART laboratory procedures. One organization strongly believed PT must be applied to embryo laboratories as it is applied to laboratories performing clinical laboratory testing; not doing so would undermine any potential effectiveness of the model program.

Response: We agree that, at this time, the inclusion of PT in the model certification program for embryo laboratories is not appropriate. Proficiency testing monitors laboratory performance by comparing the laboratory's evaluation or measurement of external samples that mimic patient samples to known test results, or results obtained by standardized methods. Proficiency testing results should be comparable to results that would be obtained when testing similar patient samples. Definitive PT programs are available for andrology procedures (sperm counts and microscopic semen evaluations), however, the one program currently available for embryo laboratories evaluates whether a laboratory's bioassay system can detect toxicity in culture media samples sent to the laboratory by the program. It does not test a laboratory's ability to examine oocytes and embryos, or successfully perform other embryo laboratory procedures. Standardized methods for monitoring these laboratory procedures have not yet been developed, in part due to the fact that the ultimate measure of the performance of most embryo laboratory procedures is a viable human embryo.

Proficiency testing is only one measure of a laboratory's quality. Other measures such as quality control, personnel standards, and monitoring laboratory practices must also be considered in determining the overall quality of laboratory performance. As mentioned in the preamble to the proposed model, these measures are all included in the model certification program. Since appropriate, standardized PT is not available at this time for embryo laboratory procedures, we have not included it in the model certification program. At such time as definitive PT becomes available for embryo laboratory procedures, States that adopt the model certification program or develop an equivalent program should consider including it in their program as an additional indicator of laboratory performance.

5. Additional comments.

Comment: One commenter requested clarification of what regulations take priority, or must be met, when there is a conflict/difference between Federal and State laboratory requirements.

Response: A laboratory must meet all applicable Federal, State and local requirements, and when differences exist among regulations, the laboratory must meet the most stringent requirement. By doing this, the laboratory should meet corresponding regulations that are less stringent.

Comment: One professional organization strongly urged the CDC to approve accreditation organizations for embryo laboratory certification purposes. The organization believes that CDC approval of the CAP/ASRM Reproductive Laboratory Accreditation Program (RLAP) and others that could be developed would be the best means to protect the public health without creating overly burdensome and redundant regulation. An additional commenter endorsed the existing CAP/ASRM RLAP as the means to assure constructive assessment of embryologic methods and improvement in the quality of ART programs.

Response: The CDC recognizes there are existing voluntary accreditation programs currently available that provide oversight of ART embryo laboratories and have had a positive impact on laboratory quality without Federal oversight. These programs were reviewed and served as examples in developing the model certification program for embryo laboratories, and could provide an excellent resource for States that wish to develop their own certification program. One such program is the CAP/ASRM RLAP, mentioned above.

While we agree that Federal approval of an accreditation organization(s) could be beneficial to laboratories in States which do not adopt the model or have an equivalent certification program, as explained below, this would go beyond the proposed model's implementation plan which permits States to approve accreditation organizations to certify laboratories within their respective State. As stated earlier in the preamble, the FCSRCA authorizes the Secretary and States to charge fees to cover the costs of the model certification program. Since this is a voluntary program, and laboratories have not indicated they would opt into such a self-supporting program, at this time, the CDC is deferring the implementation of the approval and subsequent monitoring of accreditation organizations to States that choose to adopt the model certification program and wish to use an accreditation organization for State certification purposes.

Although we have not officially approved any accreditation programs or determined their equivalency to the model certification program, as data become available, the CDC will publish the certification/accreditation status of embryo laboratories affiliated with ART programs or clinics in conjunction with future annual publications of the ART Success Rates reports.

Comment: One commenter asserted that any fees charged for certification must not be unduly excessive or burdensome to the laboratory. The commenter suggested the cost of certification be adjusted with respect to the laboratory's level of activity, *i.e.*, higher volume laboratories should be charged more than smaller volume laboratories. A professional organization commented that the Federal government should share the costs of the certification and accreditation programs.

Response: It will be up to each State that adopts the model program to develop fee schedules and the methodology for determining fees charged to the laboratory for certification. Many existing licensing/certification programs do establish fees based on volume of testing or number of procedures performed. The requirement that addresses fees at Part II., B., 8. of the model certification program was included to reiterate the FCSRCA's provision (Pub. L. 102–493, sec. 7) that allows charging such fees necessary to recoup the cost of administering a certification program.

To date, the Federal government has assumed the cost of implementing the FCSRCA, in development of the laboratory standards and administrative process for the model certification program for embryo laboratories and publication of both the proposed and finalized model programs. In addition, the CDC will distribute this model program to State officials and health authorities as outlined in the statute and will provide the certification/accreditation status of embryo

laboratories affiliated with infertility clinics and ART programs in its annual publication of ART Success Rates.

Comment: Two commenters expressed concern over the model's administrative requirement for the State, or as applicable, accreditation organization to make available to the public, upon request, the laboratory's specific inspection findings, including deficiencies identified and any subsequent corrections to those deficiencies. One of the commenters believed this would discourage a laboratory's participation in the voluntary certification program and that the public would be unable to interpret the published inspection findings.

Response: The requirement to make a laboratory's inspection findings available to the public upon request was mandated by the FCSRCA. This requirement is part of the overall effort in the legislation to provide the public with consistently reliable and comparable information about the effectiveness of infertility services provided by ART clinics. It is one piece of the information that may be used by consumers in choosing a clinic for ART services. We disagree that this requirement would discourage laboratories that are maintaining good laboratory practices from participation in the voluntary model certification program. In fact, successful participation in a voluntary program such as the model certification program could be viewed as an asset for a laboratory or ART program seeking new clients. We also disagree with the commenter that the public would not be able to interpret inspection findings. The model certification program requires States and accreditation organizations to include the necessary explanatory information for the public to interpret the findings.

Comment: Two professional organizations were concerned the model did not sufficiently address due process procedures for laboratories found to be out of compliance with the certification program's standards.

Response: Due process procedures for laboratories that are not in compliance with certification program requirements are not described in the model program because such a process would be developed and performed at the State level and may vary from State to State. The reference to State development of due process procedures is found at Part II., B., 7., a. of the model certification program.

Comment: One commenter disagreed with the model's proposed guideline at Part III., A., that the laboratory employ one individual for every 90–150 ART cycles performed by the laboratory annually. The commenter suggested one individual for every 100 ART cycles is more appropriate.

Response: We disagree. We included the recommended range as a guideline for adequate staffing of a laboratory, recognizing that some embryo laboratories do not provide as extensive service as others and may not need as many employees. In addition, a laboratory's workload may vary over time, and it may not be possible to keep the staffing level at an exact number. By giving an appropriate range as a guideline for staffing, we are providing some guidance for laboratories while maintaining flexibility for the reasons stated above.

Comment: A few commenters promoted requiring board certification for laboratory directors with a doctoral degree, with one of the commenters stating, ''Board examinations are the only comprehensive measure available of a candidate's command of a unified fund of laboratory specific knowledge and are crucial in establishing a minimum competence level for laboratory directorship in our field.'' One of the commenters misinterpreted the requirements of the model, thinking it would allow an individual with a doctoral degree in English (or other non-science major) to qualify as a laboratory director.

Response: We agree it is beneficial for the director of the embryo laboratory to be board certified, especially if that certification is specific to reproductive laboratory science. However, we do not believe it is the only way to ensure that a laboratory director is qualified for this position. Therefore, while not making board certification a requirement, we are adding language at Part III., A., 1., b., recommending board certification in embryology for doctoral scientist laboratory directors.

In response to the commenter who misread the model certification program requirements for a doctoral degree, Part I., Definitions, specifies the earned doctoral degree must be in a chemical, physical, biological or medical laboratory science. This would preclude an individual with a doctoral degree in English or other nonscience from fulfilling the qualification requirements for an embryo laboratory director.

Comment: Several commenters, which included three professional organizations provided their opinions on the use of documented hours of training and numbers of ART cycles in an embryo laboratory as an appropriate qualification requirement for laboratory personnel, in particular the laboratory director. Reasons given by commenters for not requiring a specific number of hours and/or cycles of training/experience included the following:

Training should bear a logical relationship to the complexity of procedures performed. Some ART laboratory procedures may require fewer or greater number of repetitions to ensure competency, *i.e.*, intracytoplasmic sperm injection (ICSI) requires more manipulation and skill than *in vitro* fertilization (IVF) and should have a higher hour/cycle requirement assigned;

The laboratory director should determine the adequacy of each employee's training/experience and not be locked into requiring an exact number of hours and/or cycles;

Consideration must be given to the laboratory director, who may not always perform bench work;

The number of hours/cycles may be impossible to document if a current laboratory director was trained several years in the past; and

Requiring the laboratory director to have 60 cycles of experience in ART procedures including IUI, IVC, conventional IVF, gamete intrafallopian transfer (GIFT), zygote intrafallopian transfer (ZIFT), ICSI, and assisted hatching, etc., if these procedures are not offered by a facility is unreasonable.

On the other hand, one professional organization stated that, for laboratory directors, the number of ART laboratory cycles performed is a better measure of training and experience than a specific number of hours of training. This organization suggested 60 ART cycles and six months full time in an IVF laboratory is sufficient training for reproductive endocrinologists. Another professional organization agreed if the laboratory director was performing bench work, a requisite number of hours and cycles correlating with the skill level for a specific procedure should be met. Both organizations stated the model program should be flexible and accommodate future changes in embryo laboratory procedures.

Response: Professional guidelines such as the ASRM's revised minimum standards for IVF, GIFT, and related procedures (see References) were a valuable resource in developing the model certification program. The ASRM guidelines recommend the embryo laboratory director or supervisor should have had at least six months training and completed at least 60 ART procedures in a program that performs at least 100 IVF procedures per year with a minimum annual 10% IVF live birth rate per retrieval cycle. The ASRM defines an ART procedure as ''a combination of the examination of

follicular aspirates, insemination, documentation of fertilization and preparation for embryo transfer.'' These guidelines also recommend that embryo laboratory technologists have evidence of completion of 30 complete IVF procedures under continuous supervision of the laboratory director or supervisor.

The ASRM recommendations for personnel training are similar to those proposed in the model certification program. The model's proposed training requirement for the laboratory director and supervisor of one thousand hours of laboratory training is approximately equal to the ASRM's requirement of six months of full-time (40 hour week) training. The ASRM's recommendation for completion of 60 ART laboratory procedures is synonymous with the model's requirement for ''performing, at a minimum, each laboratory component of the human ART cycle 60 times''. For the reproductive biologist, the model program proposed to require training that included performing the ART laboratory procedure(s) to be performed in the laboratory, at a minimum, 30 times under direct and constant supervision.

We do not agree with the commenters who recommended we not require a specific number of hours of documented training, and/or performance of a certain number ART laboratory procedures for laboratory director, laboratory supervisor, or reproductive biologist. Although we recognize it can be difficult to impose a blanket training requirement for the skill level needed for a diverse group of laboratory procedures, we believe the requirements in the model certification program are consistent with the ASRM guidelines and appropriate (with minor revisions) as *minimum* training requirements for the majority of ART laboratory procedures and job duties to be performed by each respective personnel category. We agree with the commenters who suggested some ART laboratory procedures require more extensive technical skill and manipulation (*e.g.,* ICSI) and may need additional repetitions prior to assuring competence of an individual. As stated in the model, it is the responsibility of the laboratory director to ensure all personnel receive appropriate training, and can demonstrate reliable performance of procedures prior to working on patient specimens (Part III., A., 2., k.). If the director determines it is necessary to increase the number of repetitions for some ART laboratory procedures, he or she should require such for adequate personnel training.

For clarification of the requirements in the model certification program and for consistency with the ASRM guidelines, we have replaced the laboratory director requirement at Part III., A., 1., b., ii., and c., ii., for at least ''1000 hours'' of documented training with ''six months.'' In this same section, and at Part III., A., 3., b., ii., and c., ii., we have substituted ''each ART laboratory procedure 60 times'' for ''each laboratory component of the human assisted reproductive technology cycle 60 times.'' Although we have deleted the word ''human'' from this requirement, the model's definition for ART laboratory procedures specifies these are ''all laboratory procedures for the handling and processing of human oocytes and sperm, or embryos, with the intent of establishing a pregnancy.''

In response to the comments regarding the role of the laboratory director, as outlined in the model program, the laboratory director is responsible for the overall operation, administration, and *technical* and scientific oversight of the embryo laboratory. Although in some laboratories this may not include day-to-day performance of ART laboratory procedures, it does require the director to have knowledge and technical skills pertaining to the ART laboratory procedures selected/developed and performed in the facility. He or she must also ensure all personnel receive appropriate training for the ART laboratory procedures to be performed, and the laboratory supervisor is technically qualified for that position. Based on these responsibilities, we believe it is necessary for the laboratory director to have at least six months training in an embryo laboratory, and have performed each ART laboratory procedure at least 60 times as part of the training process.

Since the laboratory supervisor is responsible for day-to-day supervision and oversight of the embryo laboratory and may perform the laboratory director responsibilities if authorized in writing by the director, the model program also requires the supervisor to have training which includes performing each ART laboratory procedure at least 60 times. We note that in finalizing the model program, we have clarified at Part III., A., 2., that the laboratory director may delegate performance of his or her responsibilities to an individual qualified as a laboratory supervisor or laboratory director.

In response to the commenter who was concerned about documentation of an individual's training if that person had been working for a number of years, the part of the training that may be difficult to document would be the number of ART laboratory procedures performed by that individual. In such cases, laboratory worksheets or logbooks, or other forms of laboratory documentation showing completion of ART laboratory procedures by a specific individual may be used as the documentation that adequate training has been completed.

The commenter who interpreted the qualification requirements for laboratory director as being 60 cycles of IUI, IVC, * * * etc., misinterpreted the model program. As explained above, the model requires the laboratory director to perform at least 60 ART *laboratory* procedures as part of his or her training. Performing medical procedures that may be part of an ART cycle, such as IUI, GIFT, and ZIFT is not required. ART laboratory procedures do 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.'' We believe it is appropriate for both the laboratory director and laboratory supervisor to be trained in the performance of all of these procedures to adequately carry out their duties and provide oversight of reproductive biologists who are performing any of these procedures. Although procedures such as ICSI, assisted hatching or other micromanipulative techniques are laboratory procedures, they are specific techniques for oocyte insemination and assessment of embryo development. We would not expect the laboratory director and supervisor to be trained in these specialized techniques, unless they perform them in their laboratory.

Comment: One individual stated there should be a requirement for the laboratory director and supervisor to each perform at least 25 ART cycles per year.

Response: We agree with the commenter that, to maintain their skills and expertise, embryo laboratory personnel performing ART laboratory procedures should perform a minimum number of these procedures on an annual basis. The ASRM guidelines, described in the previous response, recommend each staff embryologist (including the laboratory director *or* supervisor) perform at least 20 ART procedures a year, in contrast to the 25 ART cycles suggested by the commenter. We believe performance of a minimum of 20 ART laboratory procedures per year is a reasonable number to recommend if an individual

performs ART laboratory procedures as part of his or her responsibilities. Since it is consistent with what is recommended by the ASRM professional guidelines, we are recommending at Parts III., 1., d., ii. and 3., d., ii., for the laboratory director and laboratory supervisor, that if the individual serving in either position performs ART laboratory procedures in the laboratory, he or she should perform each of these laboratory procedures at least 20 times annually. We have also added a recommendation at Part III., 5., d., ii. that each reproductive biologist perform each of the ART laboratory procedures he or she performs in the laboratory at least 20 times annually.

Comment: One commenter was concerned the proposed model's personnel qualification requirements fail to address formal and specific education in reproductive medicine and promotes on-the-job training as the only option to fulfill the educational requirement because the model program would ''grandfather'' currently employed individuals who do not have an appropriate college degree. The commenter asked that we consider adding provisions that would allow formal education in reproductive laboratory science as an option to on-the-job training. A professional organization also suggested the proposed ''grandfather'' clauses at Part III., A., 3, c., and 5., c., include a minimum educational standard, specifically a bachelor's degree for the laboratory supervisor and an associate's degree for the reproductive biologist.

Response: We agree with the commenter that it is appropriate to include reproductive laboratory science in the list of acceptable academic degrees for all categories of embryo laboratory personnel. However, we do not agree that having this degree is sufficient to delete the training or experience requirements for any of the personnel categories. In this rapidly changing field, where accurate performance of laboratory procedures is dependent on the skill and expertise of the individual performing the procedures, we believe in addition to an academic degree, it is critical to obtain adequate hands-on training and experience prior to working with human gametes and embryos. This is especially true for procedures that may differ significantly from one laboratory to another.

We do not agree with the comment made by the professional organization that minimum educational standards should be included in the ''grandfather'' clauses at Part III., A., 3, c., and 5., c. of the model certification program. In developing standards for this relatively new area of laboratory technology, we do not wish to create a situation where individuals who have been working in the field would not meet the qualifications specified for their positions. In the model certification program, we have specified educational requirements which must be met by individuals who first become employed in an embryo laboratory after the date of this **Federal Register** notice. For the reason stated above, individuals serving in these positions on or before July 20, 1999 who have the specified experience and/or training requirements for their respective positions will be considered qualified.

Comment: A professional organization and two individuals commented on the proposed requirements for the laboratory director, supervisor and reproductive biologist to obtain 12 contact hours of continuing education per year in ART or clinical laboratory practice. While the professional organization expressed the view that continuing education for non-supervisory personnel as specified in the proposed model program is acceptable, one of the individual commenters felt that 12 contact hours was excessive for non-supervisory personnel as well as costly for the ART program. This commenter suggested reducing the requirement to 12 contact hours every *two* years. The other individual commenter noted the proposed requirement at Part III., A., 2., l., made the laboratory director responsible for ensuring each employee obtain the required continuing education. The commenter felt this should also be the reproductive biologist's responsibility and that reading appropriate literature should count as continuing education.

Response: We agree with the professional organization that in this rapidly evolving field of science and technology, it is appropriate and necessary for all levels of laboratory personnel to maintain current knowledge and skills relevant to ART embryo laboratory procedures. We do not believe requiring 12 contact hours of continuing education (CE) on an annual basis is excessive. At the same time, we recognize there may be some cost to the laboratory or individual to obtain the continuing education. However, we believe the benefits outweigh the costs, especially when there are a number of ways in which CE may be provided, including video or audioconferencing seminars or self-study educational materials. As the one commenter suggested, reading relevant journal articles is another cost-effective way to obtain CE. However, we note that to meet the model's CE requirement, the specific vehicle used for earning CE contact hours must have been approved by an approved continuing education provider such as the International Association of Continuing Education and Training or other provider specified by the State implementing the model certification program.

We agree that each reproductive biologist, as well as laboratory supervisor, should be pro-active in obtaining appropriate CE. However, as stated previously, it is the laboratory director who is ultimately responsible for the overall operation, administration and technical and scientific oversight of the laboratory. This includes employing qualified personnel and ensuring they receive appropriate training and continuing education to maintain and update their knowledge and skills in ART and laboratory practice.

Comment: One commenter requested clarification of the proposed requirements at Part III., B., 1., and C., 2., which require the laboratory to have ''adequate'' space and ''sufficient'' equipment for the type and volume of ART laboratory procedures performed. Specifically, the commenter would like guidelines that address the number of procedures per square foot of space and the number of procedures per cell freezer, etc.

Response: Although we appreciate the commenter's suggestion to more specifically define adequate space and sufficient equipment for an embryo laboratory, we have not specified exact laboratory measurements or numbers of required equipment in the model certification program in an effort to allow flexibility in the configuration and arrangement of laboratory facilities and equipment contained therein. Requirements may differ depending on the number and types of procedures performed, and the number of individuals that are employed by or using each laboratory. As noted in the proposed model standards, the physical space, utilities, and laboratory equipment must be able to accommodate the volume of ART laboratory procedures performed at its busiest time, in a manner that will reduce the potential for spilled, lost or misplaced patient specimens while they are being handled or stored. The laboratory must be secure and have limited access, and must include an isolated area for performing sterile techniques under aseptic conditions. The laboratory and administrative space must be conveniently located, but separate from patient areas, and immediate communication must be

possible with the oocyte retrieval and transfer room. As long as these requirements can reasonably be met, the space and equipment are considered adequate and sufficient.

Comment: Four individuals pointed out the proposed requirement at Part III., B., 3., b., for animal specimens to be incubated separately from human specimens would disallow the use of an incubator containing human specimens when performing the mouse embryo bioassay for quality control purposes.

Response: We agree with the commenters that the proposed requirement noted above could be interpreted to prohibit quality control procedures that require mouse embryos to be held in the same incubator as human specimens. However, there are acceptable alternative procedures (i.e., human sperm survival) that may be used for quality control if a laboratory does not have access to a separate incubator for checking media, glassware, pipettes, etc. The quality control for an incubator itself includes monitoring temperature, humidity and gas concentration, and does not require a bioassay to be performed.

Although not mentioned by commenters, the use of live cells, tissues, organs from a nonhuman animal source transplanted or implanted into a human, or used for ex vivo contact with human body fluids, cells, tissues, organs that are subsequently given to a human recipient (xenotransplantation), raises a major public health dilemma. In its Guidance For Industry, Public Health Issues Posed by the Use of Nonhuman Primate Xenografts in Humans (April 1999), The Food and Drug Administration, in consultation with other Federal agencies, concluded that further scientific research, evaluation and public discussion is needed in order to obtain sufficient information to adequately assess and potentially reduce the risks (particularly the transmission of infectious agents) posed by the use of nonhuman primate cells, tissues and organs. A Federal Advisory Committee on Xenotransplantation is currently under development within the Department of Health and Human Services to address these issues, conduct discussions, and make recommendations regarding the use of nonhuman primate xenografts.

To assure consistency with applicable Federal, State or local requirements as they are developed, we are revising the requirement at Part III., B., 3. , to state, ''If live nonhuman animal cells, tissues, and/or organs are used, all applicable Federal, State and local regulations regarding their handling, storage and use must be met.'' We believe this revision is appropriate and necessary in light of the serious public health issues that need to be addressed with their use in humans.

Comment: One commenter expressed concern with the proposed requirement at Part III., C., 4., c., that states for oral requests for changes to the original written or electronic request for an ART laboratory procedure, the laboratory must receive written or electronic documentation within 24 hours from the authorized person requesting the change. The commenter states particularly in programs where the physicians and/or laboratory staff have multiple work sites, it is sometimes difficult to receive written confirmations within a 24-hour time frame.

Response: It is critical for embryo laboratories to obtain written or electronic orders for procedures to be performed and that these orders are communicated clearly in a timely manner. This enables the laboratory to ensure adequate and appropriate staffing for scheduled procedures and, more importantly, it ensures that the patient's specimens used in the ART embryo laboratory procedures are handled appropriately. Some of the procedures are of a sensitive nature, and the laboratory could be subject to liability if an unauthorized laboratory procedure is accidentally performed due to miscommunication or lack of communication. The model certification program requires a written or electronic request by an authorized person *prior* to performing any procedure. It is only when there is a change to the original request that the model allows 24 hours for written or electronic verification of the change. We do not agree with the commenter that this time frame should be extended to 48 hours. In most cases, it is desirable to have written or electronic verification of revised orders at the time the decision is made to change the patient's treatment protocol. Allowing 24 hours provides a minimal amount of leeway for extenuating circumstances.

Comment: One commenter was confused by the proposed requirement at Part III., C., 4., i., which states that clinical laboratory testing on specimens obtained by the embryo laboratory must be performed in accordance with the Clinical Laboratory Improvement Amendments of 1988 (CLIA) regulations.

Response: Examinations of materials derived from the human body to provide information for the diagnosis, prevention, or treatment of disease, or assessment of the health of human beings must be performed in accordance with the regulations (42 CFR Part 493) implementing CLIA. Examples of specimens that may be obtained by the embryo laboratory that would be subject to the CLIA regulations include blood or serum samples for endocrinology or hematology testing or microbiology culture samples. If the embryo laboratory performs this testing it must have a valid CLIA certificate for the testing to be performed, or if the laboratory is in a CLIA-exempt State it must be licensed by the State in which it is located. If the embryo laboratory refers specimens for clinical laboratory testing, the testing must be performed by a laboratory that meets the CLIA requirements. To clarify the requirement at Part III., C., 4., i., we are specifying the purpose of clinical laboratory testing is to ''provide information for the diagnosis, prevention or treatment of disease, or assessment of the health of human beings.''

Comment: One professional organization suggested the quality control standards include an additional statement at Part III., C., 6., e., iv., that ''The use of blood-based media prepared in-house is not recommended. However, if such products are used then * * *'' This statement is to preface the proposed quality management requirement that the laboratory test blood-based media supplements prepared in-house for several communicable diseases.

Response: We agree with the commenter that it is not a recommended practice for the laboratory to prepare blood-based media or a blood-based media supplement that could potentially contain and transmit communicable diseases. However, if blood-based media or supplements are prepared in-house, blood from the donor(s) used to make the media/supplement must be tested to ensure the donor(s) is negative/nonreactive for significant disease agents. We have added language to the requirement at Part III., C., 6., e., iv., to state that the in-house preparation of blood-based media or a blood-based media supplement is not recommended. In addition, we have clarified that the blood donor(s) must be tested for the communicable diseases listed using FDA licensed, approved or cleared tests for markers of these diseases. Also, to maintain consistency with the FDA's requirements for the testing of blood and tissue product donors, we have added human T-cell lymphotrophic virus, Type II, to the communicable diseases listed in this requirement.

Comment: One commenter recommended that the proposed quality assurance requirement at Part III., C., 7.,

b., for the laboratory to track and evaluate procedural outcomes (*e.g.*, fertilization rates and embryo quality) should be incorporated into the current Society for Assisted Reproductive Technology (SART) reporting computer program. The commenter believes capturing the data in the SART program would help to reduce the amount of additional paperwork for the laboratory.

Response: We recognize that for some laboratories, it may be possible to maintain the data listed at Part III., C., 7., b. in a database similar to that used by SART to collect data on ART programs and clinics. However, we do not agree this should be required by the model certification program for several reasons. First, the data collected by SART is not specific to embryo laboratory activities, but their data relates to clinical ART practices and pregnancy success rates reported by ART programs/clinics. In addition, there are many instances in which there is not a direct, one-to-one relationship between ART programs/clinics and the embryo laboratories used by these facilities, and not all ART programs report to SART. To meet the standards in the model certification program, laboratories must record and track the data described in the model. These data are part of the laboratory's internal system to monitor the ongoing quality of its activities.

Comment: One professional organization commented that the proposed ten year period for record retention is excessive and should be reduced to a five year period, while a consumer advocacy group felt indefinite record-keeping should be considered since consumers of ART procedures need to know if they, or their children, have ever had exposure to contaminants through laboratory procedures.

Response: While we appreciate the consumer advocacy group's concerns, requiring indefinite retention of all laboratory records could be extremely burdensome for some laboratories. We proposed the ten year period for record retention because it was consistent with similar requirements mandated by the Food and Drug Administration for human tissue intended for transplantation. We continue to believe this time period is reasonable and have not changed the requirement in the model certification program. However, we note that the 1998 Survey of Assisted Reproductive Technology Embryo Laboratory Procedures and Practices conducted by the CDC indicated the majority of embryo laboratories are retaining most of their records indefinitely. If consumers are concerned they may not have indefinite access to pertinent laboratory records, it may be possible for them to request the laboratory provide them with all relevant information at the time of an ART procedure. The consumer could then maintain this information for as long as desired.

Additional Revisions to the Proposed Model Certification Program

Although written comment was not received on the following, we are making a few additional revisions to the administrative requirements proposed in the model certification program for the reasons stated below.

- At Part II., B., 2., d., vi., we are extending the time frame in which the approved accreditation organization must provide the State advanced written notice of the effective date of any proposed changes in the organization's requirements from ''at least 30 days'' to ''at least 60 days.'' We believe that this revision will provide the State a more reasonable period of time to review the organization's proposed changes for continued equivalency to the State's certification program.
- At Part II., B., 4., a., we are revising the language that states ''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,'' to include a change in the laboratory's location. We believe a change in the laboratory's location may require an onsite inspection to ensure that the laboratory continues to meet the certification program's requirements for adequate space and appropriate environmental conditions. A conforming change is also being made at Part II., B., 3., ii., which requires the embryo laboratory to submit changes in its ownership or administration to the State within 30 days of the change.

A Model Program for the Certification of Embryo Laboratories

With this publication, CDC has provided a model program for the certification of embryo laboratories which incorporates the definitions and laboratory standards called for in the FCSRCA and has included administrative requirements for States which choose to adopt the model program. CDC will distribute the model certification program to State officials and health authorities as outlined in the statute, and encourage their assistance in the State adopting the program.

As stated in the preamble to the proposed model certification program, CDC will defer implementation of the approval of State certification programs or accreditation organizations, as well as Federal validation inspections of embryo laboratories certified by States adopting the model or accredited by an accreditation program for embryo laboratories. While Congress anticipated that the cost of Federal and State monitoring and oversight of embryo laboratories would be covered by the fees paid by participating laboratories, participation by embryo laboratories is voluntary and laboratories not willing to pay these fees would not be limited in their ability to operate. To date, embryo laboratories have not indicated they would opt into such a voluntary oversight program.

While the model certification program for embryo laboratories does not provide for a Federal oversight role, we believe that this model provides an excellent resource for States that wish to develop their own programs and professional organizations with an interest in establishing or adopting standards for the embryo laboratory. In addition, as mentioned previously in this preamble, as the data become available, the CDC will publish the certification/accreditation status of embryo laboratories affiliated with ART programs or clinics in conjunction with future annual publications of the ART Success Rates reports.

Organization of the Model Certification Program

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

Dated: July 14, 1999.

Thena M. Durham,

Acting Associate Director for Management and Operations, Centers for Disease Control and Prevention.

A 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, medical or reproductive 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.

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

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 ART laboratory procedure performed *e.g.*, fertilization assessment-the presence of two pronuclei in the ooplasm.

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

Sperm. The male reproductive 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 or 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 the CDC, Public Health Practice Program Office, Division of Laboratory Systems, 1600 Clifton Rd., Atlanta, GA 30333, 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 ART 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 the CDC, Public Health Practice Program Office, Division of Laboratory Systems, 1600 Clifton Rd., Atlanta, GA 30333, 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 ART programs or clinics with which each embryo laboratory is associated, for annual publication by the CDC.

f. Information about any proposed use and approval and revocation of approval of accreditation organizations in accordance with paragraphs 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 the 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—

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

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

iii. 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 purpose of conducting onsite validation inspections of laboratories; and

vi. Provide the State written notification at least 60 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. Assurances 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 ART programs or clinics with which the laboratory is associated.

ii. Submit changes in the ownership, administration, or location 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 (e.g., 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.

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, administration, or location.

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 to determine if 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 program, that it has revoked its approval of the organization within 10 days of the revocation.

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 ART program(s) or clinic(s) served by the laboratory. As a guideline, for every 90–150 ART cycles performed annually, the laboratory should employ one individual who is capable of performing all ART 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 ART 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. It is recommended that a doctoral scientist serving as a laboratory director be board certified in embryology. In addition, the laboratory director must meet the following:

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

ii. Have documented training of at least six months in an embryo laboratory which includes performing, at a minimum, each ART laboratory procedure 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 July 20, 1999 and meet the following:

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

ii. Have documented training of at least six months in an embryo laboratory which includes performing, at a minimum, each ART laboratory procedure 60 times.

Note: Documented experience and training may be acquired concurrently.

d. In addition to meeting the qualification requirements above—

i. Obtain at least 12 contact hours of continuing education annually in assisted reproductive technology or clinical laboratory practice; and

ii. If the individual serving as the laboratory director performs ART laboratory procedures in the laboratory, it is recommended that he or she performs each of these procedures at least 20 times annually.

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 ART laboratory procedures, and record and report procedural outcomes promptly, accurately and proficiently. If the laboratory director delegates performance of his or her responsibilities to an individual qualified as an embryo laboratory director or laboratory supervisor, 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 on-site, telephone or electronic consultation 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 ART laboratory procedures to be performed.

d. Ensure that ART 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 ART process under the laboratory's control.

f. Ensure that an approved procedure manual is available to all personnel responsible for performing ART 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 ART 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 ART 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 ART 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 ART laboratory procedures. In the absence of the director, the laboratory supervisor must be responsible for the proper performance of all ART 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, medical technology, clinical or reproductive laboratory science from an accredited institution; and

ii. Have documented training which includes performing, at a minimum, each ART laboratory procedure 60 times.

c. If not qualified under subparagraph 3.b. of this section, be the supervisor of an embryo laboratory on or before July 20, 1999 and have documented training which includes performing, at a minimum, each ART laboratory procedure 60 times.

d. In addition to meeting the qualification requirements above—

i. 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; and

ii. If the individual serving as the laboratory supervisor performs ART laboratory procedures in the laboratory, it is recommended that he or she performs each of these procedures at least 20 times annually.

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

a. Be accessible to laboratory personnel at all times when ART 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 ART laboratory procedures.

c. Ensure direct and constant supervision of personnel undergoing training in ART 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 ART 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, medical technology, clinical or reproductive laboratory science from an accredited institution; and

ii. Have documentation of training appropriate for the ART laboratory procedure(s) to be performed before performing the procedure(s) without direct and constant supervision on patient specimens. Training must include performing the ART 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 ART laboratory procedures in an embryo laboratory on or before July 20, 1999 and have documentation of training appropriate for the ART laboratory procedure(s) to be performed before performing the procedure(s) without direct and constant supervision on patient specimens. Training must include performing the ART laboratory procedure(s), at a minimum, 30 times under direct and constant supervision.

d. In addition to meeting the qualification requirements above—

i. Obtain at least 12 contact hours of continuing education annually in ART 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; and

ii. It is recommended that each reproductive biologist perform each of the ART laboratory procedures he or she performs in the laboratory at least 20 times annually.

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

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

b. Follow the laboratory's established policies and procedures for performing ART 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 ART 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 ART 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 ART laboratory procedures performed during peak periods of activity.

b. ART 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 ART 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/Nonhuman Animal Cells, Tissues, Organs.

a. If laboratory animals are used, all applicable Federal, State and local regulations regarding animal care and use must be met.

b. If live nonhuman animal cells, tissues, and/or organs are used, all applicable Federal, State and local regulations regarding their handling, storage and use must be met.

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 ART laboratory procedures performed and services provided. All quality management activities must be documented.

1. Procedure Manual. A written procedure manual including instructions for all ART 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 must include the following, when applicable to the ART laboratory procedure performed:

i. Principle (scientific basis) of the ART laboratory procedure;

ii. Clinical significance of the ART laboratory procedure;

iii. Requirements for specimen collection and handling;

iv. Step-by-step instructions for performance of the ART 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 ART 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 ART laboratory procedures. The laboratory must—

a. Have sufficient equipment for the type and volume of ART 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 ART 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 ART 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 ART 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 ART 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 ART 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 ART 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 chemicals, 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 ART 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 ART process that are under the laboratory's control.

c. The laboratory may perform ART 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 an 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 procedure(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 ART 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 to provide information for the diagnosis, prevention or treatment of disease, or assessment of the health of human beings 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's 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 ART 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 ART 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. While the use of blood-based media or a blood-based media supplement (*e.g.*, human fetal cord serum) prepared in-house is not recommended, if such media or supplements are prepared, the laboratory must test blood from the donor(s) used to make the media/supplement with a FDA licensed, approved, or cleared test and show the donor(s) to be negative/nonreactive for the following communicable diseases prior to use of the media/supplement:

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, Types I and II (*e.g.*, anti-HTLV I/II); 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 or 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 ART laboratory procedures.

iv. Evaluate the effectiveness of its policies and procedures for assuring employee competence in performing ART 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 ART 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 ART 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 ART 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 Society for Reproductive Medicine. Revised Minimum Standards for In Vitro Fertilization, Gamete Intrafallopian Transfer, and Related Procedures. Fertility and Sterility 1998; 70 (Suppl 2) :1S–5S.
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. 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. 63 FR 60178, Nov. 6, 1998.
8. Code of Federal Regulations, Title 42, Chapter IV, Part 493—Laboratory Requirements.

9. The College of American Pathologists/ American Society for Reproductive Medicine Reproductive Laboratory Accreditation Program. The College of American Pathologists, Northfield, Illinois, 1996.
10. The Fertility Clinic Success Rate and Certification Act of 1992 (Public Law 102–493).
11. Guidance for Industry, Public Health Issues Posed by the Use of Nonhuman Primate Xenografts in Humans. Food and Drug Administration, Center for Biologics Evaluation and Research, April, 1999.
12. Keel BA and BW Webster. CRC Handbook of the Laboratory Diagnosis and Treatment of Infertility. CRC Press, Inc., Boca Raton, Florida, 1990.
13. 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.
14. Senate Report 102–452 on H.R. 4773. Fertility Clinic Success Rate and Certification Act of 1992. 102d Congress, 2d Session, 1992.
15. Survey of Assisted Reproductive Technology Embryo Laboratory Procedures and Practices. www.phppo.cdc.gov/dls/pdf/art/ARTsurvey.pdf.
16. 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. 99–18405 Filed 7–19–99; 11:53 am]

BILLING CODE 4163–18–P