FR 11034; February 26, 1979); and (3) does not warrant preparation of a Regulatory Evaluation as the anticipated impact is so minimal. Since this is a routine matter that will only affect air traffic procedures and air navigation, it is certified that this rule will not have a significant economic impact on a substantial number of small entities under the criteria of the Regulatory Flexibility Act.

List of Subjects in 14 CFR Part 71

Airspace, Incorporation by reference, Navigation (air).

Adoption of the Amendment

In consideration of the foregoing, the Federal Aviation Administration amends 14 CFR part 71 as follows:

PART 71—DESIGNATION OF CLASS A, CLASS B, CLASS C, CLASS D, AND CLASS E AIRSPACE AREAS; AIRWAYS; ROUTES; AND REPORTING POINTS

1. The authority citation for part 71 continues to read as follows:

Authority: 49 U.S.C. 106(g), 40103, 40113, 40120; E.O. 10854, 24 FR 9565, 3 CFR, 1959–1963 Comp., p. 389.

§ 71.1 [Amended]

2. The incorporation by reference in 14 CFR 71.1 of the Federal Aviation Administration Order 7400.9E, Airspace Designations and Reporting Points, dated September 10, 1997, and effective September 16, 1997, is amended as follows:

Paragraph 6005 Class E airspace areas extending upward from 700 feet or more above the surface of the earth.

* * * * *

AGL ND E5 Crosby, ND [New]

Crosby Municipal Airport, ND
(Lat. 48°55′ 45″ N., long. 103°17′56″ W.)

That airspace extending upward from 700 feet above the surface within a 6.4-mile radius of the Crosby Municipal Airport, excluding that airspace north of lat. 49° 00′ 00″N (Canada/United States Boundary).

* * * * *

Issued in Des Plaines, Illinois, on August 25, 1998.

David B. Johnson,

Acting Manager, Air Traffic Division.

[FR Doc. 98–24290 Filed 9–9–98; 8:45 am]

BILLING CODE 4910–13–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 101

[Docket Nos. 98N–0426, 98N–0428, 98N–0427, 98N–0423, 98N–0424, 98N–0419, 98N–0422, 98N–0421, and 98N–0420]

Food Labeling: Health Claims; Reopening of Comment Period

AGENCY: Food and Drug Administration, HHS.

ACTION: Interim final rules; reopening of comment period.

SUMMARY: The Food and Drug Administration (FDA) is reopening to October 8, 1998, the comment period for the nine interim final rules that appeared in the **Federal Register** of June 22, 1998 ((63 FR 34084), (63 FR 34092), (63 FR 34097), (63 FR 34101), (63 FR 34104), (63 FR 34107), (63 FR 34110), (63 FR 34112), and (63 FR 34115)). The rules prohibit the use on food labels of claims that are not appropriately based on authoritative statements from scientific bodies or that otherwise do not meet the specifications of new legislation. Interested persons were given until September 8, 1998, to comment on the interim final rules. This action is being taken in response to requests to reopen the comment period.

DATES: Written comments by October 8, 1998.

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Christine J. Lewis, Center for Food Safety and Applied Nutrition (HFS–451), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202–205–4168.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of June 22, 1998 ((63 FR 34084), (63 FR 34092), (63 FR 34097), (63 FR 34101), (63 FR 34104), (63 FR 34107), (63 FR 34110), (63 FR 34112), and (63 FR 34115)), FDA issued nine interim final rules prohibiting the use on food labels of claims that are not appropriately based on authoritative statements from scientific bodies or that otherwise do not meet the specifications of new legislation.

Interested persons were given until September 8, 1998, to comment on the rules. FDA has received several requests for extending the comment period. After evaluating these requests, the agency has decided to reopen the comment period on the interim final rules until October 8, 1998.

To be considered, written comments regarding the interim final rules must be received by October 8, 1998, by the Dockets Management Branch (address above). Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with Docket Nos. 98N–0426, 98N–0428, 98N–0427, 98N–0423, 98N–0424, 98N–0419, 98N–0422, 98N–0421, and 98N–0420. Received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: September 4, 1998

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 98–24359 Filed 9–4–98; 4:34 pm]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 884

[Docket No. 97N–0335]

Obstetric and Gynecologic Devices; Reclassification and Classification of Medical Devices Used for In Vitro Fertilization and Related Assisted Reproduction Procedures

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is announcing that it is reclassifying instrumentation intended for use in in vitro fertilization (IVF) and related assisted reproduction technology (ART) procedures, including but not limited to gamete intrafallopian transfer (GIFT), embryo transfer (ET), and intracytoplasmic sperm injection (ICSI), from class III (premarket approval) to class II (special controls). FDA is also reclassifying assisted reproduction microscopes and microscope accessories from class III to class I. This reclassification is on the Secretary of the Department of Health and Human Services' (the Secretary's) own initiative based on new information. Accordingly, the order is being codified in the Code of Federal Regulations. Upon the effective date, this **Federal Register** document may be cited in the absence of an existing predicate device which would be used to support substantial equivalence. Elsewhere in this issue of the **Federal Register**, FDA is announcing the

availability of a draft guidance entitled ''Devices Used for In Vitro Fertilization and Related Assisted Reproduction Procedures: Submission Guidance for a 510(k).''

EFFECTIVE DATE: The regulation is effective October 13, 1998.

FOR FURTHER INFORMATION CONTACT: Elisa D. Harvey, Center for Devices and Radiological Health (HFZ–470), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301–594–1180.

SUPPLEMENTARY INFORMATION:

I. Background—Regulatory Authorities

The Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 301 *et seq.*), as amended by the Medical Device Amendments of 1976 (the 1976 amendments) (Pub. L. 94–295), the Safe Medical Devices Act of 1990 (the SMDA) (Pub. L. 101–629), and the Food and Drug Administration Modernization Act of 1997 (FDAMA) (Pub. L. 105–115), established a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the act (21 U.S.C. 360c) established three categories (classes) of devices, depending on the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three categories of devices are class I (general controls), class II (special controls), and class III (premarket approval).

Under section 513 of the act, devices that were in commercial distribution before May 28, 1976 (the date of enactment of the 1976 amendments), generally referred to as preamendments devices, are classified after FDA has: (1) Received a recommendation from a device classification panel (an FDA advisory committee); (2) published the panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) published a final regulation classifying the device. FDA has classified most preamendments devices under these procedures.

Devices that were not in commercial distribution prior to May 28, 1976, generally referred to as postamendments devices, are classified automatically by statute (section 513(f) of the act) (21 U.S.C. 360c(f)) into class III without any FDA rulemaking process. Those devices remain in class III and require premarket approval, unless and until: (1) The device is reclassified into class I or II; (2) FDA issues an order classifying the device into class I or II in accordance with new section 513(f)(2) of the act, as amended by FDAMA; or (3) FDA issues an order finding the device to be substantially equivalent, under section 513(i) of the act, to a predicate device that does not require premarket approval. The agency determines whether new devices are substantially equivalent to previously offered devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and part 807 (21 CFR part 807) of the regulations.

A preamendments device that has been classified into class III may be marketed, by means of premarket notification procedures, without submission of a premarket approval application (PMA) until FDA issues a final regulation under section 515(b) of the act (21 U.S.C. 360e(b)) requiring premarket approval.

Reclassification of classified postamendments devices is governed by section 513(f)(3) of the act, formerly section 513(f)(2) of the act. This section provides that FDA may initiate the reclassification of a device classified into class III under section 513(f)(1) of the act, or the manufacturer or importer of a device may petition the Secretary for the issuance of an order classifying the device in class I or class II. FDA's regulations in § 860.134 (21 CFR 860.134) set forth the procedures for the filing and review of a petition for reclassification of such class III devices. In order to change the classification of the device, it is necessary that the proposed new class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use.

FDAMA added a new section 513(f)(2) to the act, which addresses classification of postamendments devices. New section 513(f)(2) of the act provides that, upon receipt of a ''not substantially equivalent'' determination, a 510(k) applicant can request FDA to classify a postamendments device into class I or class II. Within 60 days from the date of such a written request, FDA must classify the device by written order. If FDA classifies the device into class I or II, the applicant has then received clearance to market the device and it can be used as a predicate device for other 510(k)'s. It is expected that this process will be used for low risk devices. This process does not apply to devices that have been classified by regulation into class III—i.e., preamendments class III devices, or class III devices for which a PMA is appropriate.

Under section 513(f)(3)(B)(i) of the act, formerly section 513(f)(2)(B)(i) of the act, the Secretary may, for good cause shown, refer a proposed reclassification to a device classification panel. The Panel shall make a recommendation to the Secretary respecting approval or denial of the proposed reclassification. Any such recommendation shall contain: (1) A summary of the reasons for the recommendation, (2) a summary of the data upon which the recommendation is based, and (3) an identification of the risks to health (if any) presented by the device with respect to which the proposed reclassification was initiated.

Section 510(l) of the act (21 U.S.C. 360(l)) provides that a class I device is exempt from the premarket notification requirements under section 510(k) of the act, unless the device is intended for a use which is of substantial importance in preventing impairment of human health or it presents a potential unreasonable risk of illness or injury. Hereafter, these are referred to as ''reserved criteria.''

Such an exemption permits manufacturers to introduce into commercial distribution generic type of class I devices without first submitting a premarket notification to FDA. If FDA has concerns about certain types of changes to a particular class I device, the agency may grant a limited exemption from premarket notification for that generic type of device.

II. Regulatory History of the Device

FDA consulted with the Obstetrics and Gynecology Devices Panel (the Panel). During an open public meeting on October 23, 1995, the Panel indicated its concurrence, given the history of safe and effective use of these devices, with FDA's intention to reclassify instrumentation intended for use in IVF and ART procedures.

Based on this input from the Panel, FDA published a proposed reclassification rule in the **Federal Register** of September 4, 1997 (62 FR 46686), proposing that the generic type of device, instrumentation intended for use in IVF and related ART procedures, should be reclassified from class III to class II, and that assisted reproduction microscopes and microscope accessories should be reclassified from class III to class I.

FDA received 10 comments from manufacturers of devices used in assisted reproduction procedures in response to the proposed rule. A summary of the comments and FDA's response is discussed in section III of this document. The comments primarily addressed issues relating to clarification of the proposed rule, and suggestions for the special controls required for the various categories of assisted reproduction devices. It should be noted

that while clinical studies have been identified as a special control for the class II devices, FDA only intends to require clinical studies on a case-by-case basis where, based on the design or function of the device, the performance in its intended use can only be validated with clinical data.

III. Summary and Analysis of Comments and FDA's Response

A. General Comments

1. One comment stated that it would be helpful to state in the reclassification final rule that the final rule itself can be used to support substantial equivalence, obviating the need to cite existing predicate devices.

FDA agrees with this comment, and has included such a statement in the summary section of the final rule. The draft guidance document entitled ''Devices Used for In Vitro Fertilization and Related Assisted Reproduction Procedures: Submission Guidance for a 510(k),'' which is the subject of a notice of availability published elsewhere in this issue of the **Federal Register**, also provides discussion of the documentation necessary to establish substantial equivalence.

2. One comment stated that the proposed date for guidance document issuance should be provided in the final rule.

FDA agrees with this comment. A notice of availability of the draft guidance document, entitled ''Devices Used for In Vitro Fertilization and Related Assisted Reproduction Procedures: Submission Guidance for a 510(k),'' is published elsewhere in this issue of the **Federal Register**, and is available through the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

3. One comment stated that although the proposed rule is clearly intended to cover devices used in GIFT procedures, the preamble to the proposed rule refers only to IVF/ET, without specifically referring to GIFT. The comment requested that FDA clarify in the final rule that it reclassifies medical devices used in GIFT, as well as IVF, ICSI, ET, and other ART procedures. The comment also provided recommended language specifying the inclusion of devices used for GIFT for the definitions of assisted reproduction needles and assisted reproduction catheters.

FDA agrees with this comment. Medical devices used during GIFT and other well-established ART procedures are included in the category of assisted reproduction catheters. The final rule has been appropriately revised to include them. In addition, the proposed language for the definitions of assisted reproduction needles and assisted reproduction catheters has been incorporated.

4. One comment pointed out the potential applicability of FDA's guidance entitled ''Convenience Kits Interim Regulatory Guidance,'' May 20, 1997, to GIFT sets or kits, and recommended that this guidance be updated to include GIFT sets as a type of device covered by this policy.

FDA disagrees with this comment. Devices used for GIFT procedures do not meet the criteria identified under ''Components.'' That is, they are not: (1) Legally marketed preamendments devices, (2) exempt from premarket notification, or (3) found to be substantially equivalent through the premarket notification process. Nevertheless, FDA anticipates that these types of kits may become eligible for consideration in time, and is willing to consider the inclusion of GIFT sets for this new regulatory approach once a sufficient 510(k) data base for these devices is obtained.

5. One comment questioned the inclusion of micropipette fabrication instruments as a category in this reclassification. The comment noted that it was not clear why the machines (micropipette fabrication instrument micropipette ''puller'') used to manufacture a regulated end product (the micropipette) should also be subject to such regulation. The comment stated that if such a device were included in this reclassification, it would mean that micropipettes would not be available commercially unless they have been processed with FDA approved instrumentation and that any IVF/ART laboratory making its own micropipettes would not be able to make those without an FDA approved instrument. The comment was concerned that this might mean that IVF/ART procedures would be stopped because there is currently no FDA approved instrument for manufacturing the micropipettes.

FDA disagrees with this comment. Only the end product device that is specifically promoted and marketed to the medical community with a claim relating to an intended use for IVF/ART will be subject to a premarket notification submission (510(k)). This applies to the micropipette itself, as well as the micropipette fabrication instrumentation. If the micropipette itself is the device marketed for that intended use, a 510(k) would be necessary, but the instrumentation to manufacture that micropipette would not require a 510(k). However, if the micropipette fabrication instrumentation itself is the device marketed for the specific intended use of IVF/ART, then a 510(k) for that device would be necessary. If neither the micropipette itself nor the micropipette fabrication instrumentation have a specific claim for use during IVF/ART, then no 510(k) is required. Thus, it is incorrect to state that this reclassification would result in a lack of commercially available micropipettes because they have not been processed with FDA approved instrumentation or that any IVF laboratory making its own micropipettes would not be able to make those without an FDA approved instrument. This classification regulation neither addresses individual IVF/ART laboratory decisions about what instruments are necessary, nor does it prohibit any individual laboratory from making its own micropipettes. However, when those devices (whether they are the micropipettes or the micropipette fabrication instrumentation) are marketed and promoted for the specific intended use of IVF/ART by the manufacturer (including a laboratory that markets the devices to others), those products become subject to section 510(k) of the act requirements.

6. One comment stated that laser microtools are also used to denude human gametes or embryos and that these devices should be classified in class II and added to pipettes and other devices under the category of assisted reproduction microtools.

FDA disagrees with this comment. The intent of this reclassification is to reclassify those devices associated with IVF/ART procedures which have a long and well-established history of safe use. Laser microtools used to manipulate and treat human gametes or embryos are relatively new. The Panel which recommended reclassification of devices used in IVF/ART did not identify laser microtools as having a sufficiently established history of reasonably safe and effective use to justify their classification in class II. Therefore, the agency believes that it is not appropriate to include laser microtools in this reclassification. As a result, laser microtools remain in class III.

7. One comment stated that there was ambiguity with respect to the classification of assisted reproduction microscopes and microscope accessories. The comment stated that fluorescence microscopes should not be classified as class I and exempt, but rather, class II because of the potential for damage to human gametes and embryos.

FDA agrees with this comment. The intent of this reclassification is to

reclassify those devices associated with IVF/ART procedures which have a long and well-established history of safe use. The use of fluorescence microscopy for the purpose of preimplantation diagnosis is relatively new. The Panel which recommended reclassification of devices used in IVF/ART did not identify fluorescence microscopes as having a sufficiently established history of reasonably safe and effective use to justify their classification in class I. Therefore, although the proposed rule did refer to fluorescence microscopy, the agency has concluded that is not appropriate to include fluorescence microscopy in this reclassification. Thus, fluorescence microscopy is retained in class III. The category of assisted reproduction microscopes and microscope accessories is intended to specifically refer to conventional optical microscopes and accessories which are used for the most common and routine IVF/ART procedures.

8. One comment stated that stylets (a tube or rod which can be inserted into a catheter or cannula to give it form and assist in its passage) are commonly used in IVF/ART procedures, but are not explicitly included in the reclassification.

FDA agrees with this comment and has amended the final rule to include stylets, which are a common component of devices used in IVF/ART procedures, in the category of assisted reproduction catheters.

9. One comment stated that the proposed definition of assisted reproduction microtools should be revised to read:

Assisted reproduction microtools are pipettes or other devices used in the laboratory to denude, micromanipulate, hold or transfer human gametes, or embryos for assisted hatching, ICSI, embryo biopsy, or other similar procedures used specifically for assisted reproduction methods, including preimplantation diagnosis.

FDA disagrees with this comment. Although devices used in preimplantation diagnosis procedures such as embryo biopsy were inadvertently included in the proposed rule, the agency does not believe this type of device should be included in this reclassification because the use of such preimplantation diagnosis procedures is relatively new. The intent of this reclassification is to reclassify those devices associated with IVF/ART procedures that have a long and well-established history of safe use, as stated in the response to comment numbers 6 and 7. The use of preimplantation diagnosis procedures such as embryo biopsy is relatively new. The Panel which recommended reclassification of devices used in IVF/ART did not identify devices associated with preimplantation diagnosis procedures as having a sufficiently established history of reasonably safe and effective use to justify their reclassification. The category of assisted reproduction microtools refers only to those devices that are used for the most common and routine IVF/ART procedures.

10. One comment recommended that catheters, accessories, and reproductive media and supplements warrant regulation as class II products, but that all other specified products intended for use during IVF/ART procedures should be considered class I products.

FDA disagrees with this comment, which did not offer any explanation for the position expressed. The agency believes that assisted reproduction needles, assisted reproduction microtools, assisted reproduction micropipette fabrication instruments, assisted reproduction micromanipulators and microinjectors, assisted reproduction labware, and assisted reproduction water and water purification systems also warrant regulation as class II medical devices. FDA has concluded that the special controls identified for these categories of devices are necessary at this time to ensure the safe and effective use of these devices. However, the agency does not rule out the possibility that these devices may be considered for further downclassification at some later date after a sufficient 510(k) data base has been obtained.

11. One comment stated that the College of American Pathologists (CAP) and the Society for Assisted Reproductive Technology (SART) references may be considered voluntary standards, but that the SART references are published patient registries, not recognized standards with which to comply or adhere.

FDA agrees with this comment. FDA recognizes that the SART reference is a patient registry and data base, and that it does not contain specific guidelines or recommendations for techniques of employing IVF/ART procedures. Nevertheless, the agency wishes to acknowledge this organization and encourage laboratories to consult this reference for its significant guidance to IVF/ART laboratories in obtaining data on the safety and effectiveness of these procedures.

12. One comment stated that validation of clinical performance is not warranted if there are no new types of safety and effectiveness questions raised.

FDA disagrees with this comment. Even if no new types of safety and effectiveness questions are raised regarding a device, clinical data may still be required in some cases to adequately assess the performance of a device based on its unique design or function, as is outlined in FDA's guidance document ''510(k) Substantial Equivalence Decision-Making Process (Detailed)'' that is available from the Division of Small Manufacturers Assistance (HFZ–220), FDA, 1350 Piccard Dr., Rockville, MD 20850, or on the World Wide Web at ''http://www.fda.gov/cdrh/k863.html''. Further information on the need for clinical data is provided in the draft guidance document on IVF decives that is being announced elsewhere in this issue of the **Federal Register**.

13. One comment stated that water purification systems have demonstrated a long history of safe and effective use in IVF/ART applications, and that placing them into class II with special controls would provide no additional benefit to end-users. The comment recommended that these devices be classified into class I and exempted from premarket notification and good manufacturing practice (GMP) requirements.

FDA disagrees with this comment. Water purification systems with specific claims for other applications (e.g., kidney dialysis) are also placed in class II and are subject to special controls. The quality of water that directly contacts human gametes or embryos in IVF/ART procedures is similar to that for dialysis. If a manufacturer of a water purification system wishes to market and promote that system with specific claim(s) for its use in IVF/ART procedures, then that device will require a 510(k). However, if a manufacturer of a water purification system wishes to market and promote that system for general purposes only, then no 510(k) is needed, and the device is not affected by this reclassification.

14. Two comments suggested using the USP ''water for injection'' requirement as the special control for the quality of water used in reconstitution of IVF media, rather than requiring type I reagent grade water. The rationale was that water meeting the latter requirement may still be corrosive to metals, causing possible exposure of metal ions to human gametes or embryos as a result of its use in final rinsing of packaging materials in a pharmaceutical washing machine. Water produced in conformance with the USP water for injection requirement has properties sufficient and appropriate for its intended use. The second comment's rationale was that their validated system producing USP

water for injection has routinely produced water which passes the mouse embryo assay test. Additionally, this same requirement should suffice for water used to wash and rinse labware.

FDA agrees with these comments. Because the USP water for injection requirement delineates testing requirements for producing water that is safe for parenteral use, it should also suffice for production of water with potential for exposure to human gametes and embryos. Therefore, FDA agrees with the comment, and the USP water for injection requirement will be used as a special control for: (1) Water specifically intended for reconstitution of reproductive media, (2) water specifically intended for washing and rinsing of labware to be used in IVF/ART procedures, and (3) purification systems specifically intended for production of water to be used for IVF/ART procedures.

15. One comment stated that regulating water quality specific to these products is not warranted because: (1) These devices are sterilized and pyrogen tested, and (2) typical use consists of flushing any lumens with media or sterile water prior to use. The comment stated that water quality is a user issue that should be addressed by Clinical Laboratory Improvement Amendments of 1988 (CLIA) or accrediting bodies.

FDA disagrees with this comment. As previously stated, the rationale for requiring water quality testing (USP water for injection testing) is that the quality of water used to reconstitute media and supplements, as well as to wash and rinse labware, is critically important to the success of ART procedures. As was also previously stated, water purification systems with specific claims for other applications (e.g., kidney dialysis) are also placed in class II and are subject to special controls. The quality of water needed for IVF/ART procedures in which human gametes or embryos are directly contacted is similar to that for dialysis. If a manufacturer of a water purification system wishes to market and promote that system with specific claim(s) for its use in IVF/ART procedures, then that device will require a 510(k). However, if a manufacturer of a water purification system wishes to market and promote that system for general purposes only, then no 510(k) is needed, and the device is not affected by this reclassification.

16. One comment stated that IVF media are products as critical as parenterals and should therefore be manufactured according to aseptic GMP conditions.

FDA agrees with this comment. Sections 820.70(c) and 820.75 of the quality system regulation, pertaining to environmental control and process validation, respectively, address this concern. These sections describe requirements for adequate control of environmental conditions to assure no adverse effect of the environment on product quality, and measures which shall be used to validate and document the manufacturing processes to assure the quality of the product. A further explanation of these portions of the quality system regulation may be found in the Association for the Advancement of Medical Instrumentation (AAMI) Guidelines entitled ''The Quality System Compendium: GMP Requirements and Industry Practice'' (Ref. 1).

17. One comment stated that because the purity of chemicals used for IVF media is critical, that FDA should require these chemicals to be of pharmacopoeial grade, with additional requirements regarding cytotoxicity, endotoxin, and sterility.

FDA disagrees with this comment. While FDA agrees that the quality of the components of IVF media is critical, FDA believes that it is not necessary to require that all chemicals be of pharmacopoeial grade, since not all desired components may be available in that grade. Additionally, there exist other special controls, including mouse embryo assay information, endotoxin testing and sterilization validation, which are sufficient to assure the safety of the product.

18. One comment recommended that human-derived or animal-derived macromolecules (such as serum albumin or hyaluronic acid) not be allowed in IVF media, and proposed the requirement that macromolecules be manufactured instead by recombinant methods. The rationale for this was: (1) The potential for transmission of pathogens such as Creutzfeld-Jacob Disease (CJD) or bovine spongiform encephalopathy (BSE) to the human gamete or embryo that may be difficult to detect; and (2) the potential for transmission of foreign deoxyribonucleic acid (DNA) into the human oocyte during ICSI. The comment also indicated that a European standard, now in preparation, would be appropriate to consider as a special control if FDA does allow use of biological macromolecules.

FDA disagrees with this comment. While FDA recognizes the previously mentioned risks, the agency believes that a requirement for the use of only recombinant macromolecules in the manufacture of IVF media is not feasible at this time due to the limited availability of these macromolecules. FDA does not currently recognize any European standard regarding the use of biological macromolecules in IVF media. However, with the controls in place for donor screening and testing, it should be appropriate to use human derived macromolecules with the proper notification and consent. In addition, there currently exist special controls for the use of animal-derived macromolecules in IVF media.

19. One comment suggested a requirement that IVF media shall be tested by the manufacturer according to the special controls listed, and that a certificate with test results be issued for each approved batch.

FDA agrees with this comment. The end-user will benefit if labeling for IVF media includes information which indicates test results for each approved batch, even if some labs opt to do further testing to supplement what is done by the manufacturer. This will also provide quality assurance to the general public without being unduly burdensome to the manufacturer.

20. One comment recommended that an acceptance criterion for endotoxin levels be set for ready-to-use IVF media.

FDA disagrees with this comment. Because there is no ''gold standard'' in the medical community for what the lower limit of acceptability of endotoxin levels is for IVF and assisted reproduction procedures, it is not possible to identify an appropriate threshold. Rather, it is important that the manufacturer perform an established USP endotoxin test, such as the limulus mebocyte lysate (LAL) or rabbit pyrogen assay, on any device potentially contacting human gametes or embryos, and identify this information in the labeling.

21. One comment stated that the category of reproductive media should also include: (1) Acid solutions (prepared from liquid or powder), which are commonly utilized to denude human gametes or embryos, (2) rinsing solutions used after acid treatment, and (3) separation media used to separate and concentrate sperm.

FDA agrees with this comment. Because these products come into direct physical contact with gametes or embryos, they will also be listed in the category of reproductive media.

22. One comment recommended that FDA require that the mouse embryo assay (MEA) test be mandatory rather than voluntary, and that the two-cell MEA be used, with an acceptance criterion of greater than 80 percent hatching.

FDA disagrees with this comment. FDA recognizes that the MEA is currently the most appropriate test for

embryotoxicity; however, there is no consensus in the medical community on whether the one-cell or the two-cell MEA is most appropriate. Both have their advantages and disadvantages, and these may be weighed differently by each end-user of a product. Therefore, it would be inappropriate for FDA to mandate one test over the other. In addition, FDA believes it would be inappropriate to mandate that the MEA be conducted, because it recognizes that some end-users will perform their own testing on the product to assure its safety, regardless of whether the manufacturer performs these tests. Requiring that the MEA be conducted would add an unnecessary burden and cost to the manufacturer. The final regulation requires each manufacturer to provide clear and prominent information both on the label and in the labeling to the user about whether and how the MEA was performed, and the results. FDA believes that this requirement to clearly label the product and provide information to the end-user in this regard will be adequate to assure appropriate testing and use of the product.

23. One comment stated that certain materials (substances which denature protein, chelate cations, bind endotoxin, or alter endotoxin's hydrophobic state) may interfere with the LAL assay used to measure endotoxin, and proposed that this reclassification state that USP methods such as the rabbit pyrogen assay may also be submitted for endotoxin testing.

FDA agrees with this comment. Manufacturers may perform either the LAL assay or the rabbit pyrogen assay in accordance with established USP test methods for determination of endotoxin levels, and must clearly identify on the label what endotoxin test was performed, as well as the results of the testing in the labeling.

24. One comment requested that the ''hybritest,'' a bioassay based on the culture of mouse hybridoma cells, be allowed as an alternative to the MEA test for embryotoxicity. The comment pointed out the limitations of the MEA test and provided documentation to support the use of the Hybritest as an alternative to the MEA.

FDA disagrees with this comment. Although FDA recognizes that there are limitations to both the one-cell and the two-cell MEA test, it is currently the most widely recognized and accepted method for determining potential embryotoxicity. Although the hybritest has potential for becoming more widely accepted in the medical community as a valid alternative to the MEA, it has not yet established sufficient history, acceptance, and validity to be acceptable as an alternative to the MEA. FDA will periodically review new information and consult with the medical community to determine if the hybritest should be included as an alternative to the MEA test.

25. One comment stated that if MEA testing is not required by the agency for assisted reproduction devices, then language stating that MEA testing was not performed is not warranted.

FDA disagrees with this comment. As previously stated, FDA believes it would be inappropriate to mandate that the MEA be conducted, because it recognizes that some end-users will perform their own testing on the product to assure its safety, regardless of whether the manufacturer performs these tests. Nevertheless, it is still essential for each manufacturer to provide information both on the label and in the labeling to the user about whether the MEA was performed. FDA believes that this requirement to clearly label the product is essential to assure that the end-user (in the laboratory) has sufficient information to determine if any further testing of the product is necessary.

26. One comment stated that the language regarding MEA testing in the special controls section of the proposed rule should be revised from, ''Whether a one-cell or two-cell MEA is used, the bioassay should duplicate, as closely as possible, the procedures used for human IVF, including acquisition, maintenance, culture, transfer (relocation) and cryopreservation of embryos'' to, ''Whether a one-cell or two-cell MEA is used, the bioassay should represent, as closely as possible, the corresponding procedures for which the device is used for human IVF, such as acquisition, maintenance, culture, transfer (relocation) or cryopreservation of embryos.''

FDA agrees with this comment. FDA is including such advice in the guidance document, for which a notice of availability is being published elsewhere in this issue of the **Federal Register**.

27. One comment stated that for assisted reproduction accessories that do not contact gametes, embryos or patients, the cited special controls of MEA testing, device sterilization validation, and/or water quality testing have no impact on mitigating risks of gamete or embryo damage.

FDA agrees with this comment. It is true that the particular special controls of MEA testing, device sterilization validation, and water quality testing are not applicable to certain assisted reproduction accessories, such as syringe pumps, incubators and cryopreservation instrumentation, which do not directly contact the human gamete, embryo, or patient. Nevertheless, the other identified special controls for design specifications, labeling and voluntary standards are applicable and can mitigate the potential risks to the human gamete or embryo associated with use of assisted reproduction accessories.

28. One comment stated that the risk of hematuria would not be mitigated by the use of design specifications, and that hematuria is primarily associated with the procedure/technique.

FDA disagrees with this comment. The agency recognizes that a risk such as hematuria is primarily associated with the procedure/technique. However, FDA believes that design specifications can help to ensure the safe and appropriate use of the product and thereby reduce the possibility of inadvertent needle puncture of the bladder.

29. One comment stated that the risk of puncture would not be mitigated by the use of design specifications, and that puncture is primarily associated with the procedure/technique.

FDA disagrees with this comment. The agency recognizes that a risk such as puncture is primarily associated with the procedure/technique. However, FDA believes that design specifications can help to ensure the safe and appropriate use of the product and thereby reduce the possibility of inadvertent needle puncture of other unintended abdominal or pelvic structures.

30. One comment stated that the risk of infection would not be mitigated by the use of MEA testing, and that instead, use of embryo-compatible materials should be advocated.

FDA agrees with this comment. The agency recognizes that a risk such as infection would not be mitigated by the use of MEA testing. However, the agency believes that the other identified special controls of endotoxin testing, device sterilization validation, water quality testing, design specifications, and labeling requirements will mitigate this risk and thereby help to ensure the safe and appropriate use of the product.

31. One comment stated that the potential complications of ectopic pregnancy, multiple gestation, or chromosomal congenital abnormalities are not device specific, and that, therefore, the statement that: ''The assisted reproduction devices most likely to present this risk are assisted reproduction needles, assisted reproduction catheters, * * * '' (62 FR 46689) should be deleted. The comment also stated that these risks would not be

mitigated by the use of design specifications.

FDA disagrees with this comment. The agency does agree that the potential complications of multiple gestation or chromosomal congenital abnormalities are not device specific, and that assisted reproduction needles do not contribute to the risk of these potential complications. Nevertheless, assisted reproduction catheters may pose a risk of increasing the rate of ectopic pregnancies following embryo transfer, either by: (1) Allowing for an increased volume of transfer fluid, or (2) being designed in such a way as to promote inadvertent location of the catheter tip in or near the fallopian tube ostium (two postulated mechanisms for the occurrence of ectopic pregnancy in IVF/ART patients). These risks would be mitigated not only by design specifications, but also by labeling and appropriate instructions for use which caution against these possibilities. Therefore, the agency has modified the statement accordingly.

32. One comment questioned whether it was appropriate to require instructions for use for disposable labware. The comment stated that generalized instructions would not be useful to the user because of the diversity of techniques, and that as laboratories become regulated by other organizations such as SART, CAP, and the Health Care Finance Administration (HCFA) under CLIA, they are generating their own written procedures to meet their own specific needs.

FDA agrees with this comment. Because of the variability in techniques from user to user, it is not feasible or helpful to provide specific instruction for use on devices such as labware. Guidance from the appropriate regulatory entities (CAP, SART, HCFA) should be followed wherever applicable, and the manufacturer should provide a general statement in the labeling to users to use the labware as appropriate for the particular technique they are employing. FDA will review the labeling to ascertain that any instructions are appropriate given the indication for use identified on the labeling.

33. One comment recommended that the statement ''labeling * * * will ensure that devices are used properly, that the user is adequately informed, that the intended use of the device is clearly understood, and that claims by the manufacturer do not exceed the intended use of the device,'' be revised to indicate that labeling ''promotes'' or ''supports reasonable assurance of'' the items listed.

FDA disagrees with this comment. The meaning intended to be conveyed by the word ''ensure'' is that the labeling should be carefully and clearly written so as to provide the user with the information necessary to use the device as intended. The agency does not believe that the recommended revisions would adequately convey this intent.

34. One comment stated that labeling requirements need to be clarified, and that boilerplate language should be suggested to provide useful information.

FDA disagrees with this comment. Because of the large number of devices identified in the several categories of assisted reproduction devices intended for this reclassification, as well as variability in techniques from user to user, it is not feasible to provide specific boilerplate language for labeling in this final rule. Guidance from the appropriate regulatory entities (CAP, SART, and HCFA) should be followed wherever applicable, and the manufacturer should provide a general statement in the labeling to the user to use the device as appropriate for the particular technique they are employing. As stated previously, FDA will review labeling to ascertain that any instructions are appropriate given the indication for use identified on the labeling. In addition, FDA will work with manufacturers to develop appropriate labeling and may revise the guidance document for these devices once an appropriate 510(k) data base has been obtained.

35. Two comments expressed a concern with respect to the requirement that all devices coming into contact with embryos and gametes must demonstrate a sterility assurance level (SAL) of 10^{-6}. Both comments stated that while a SAL of 10^{-6} may be reasonable for a terminally sterilized product, most liquid media used for the processing or culture of embryos and gametes are not compatible with existing technologies for terminal sterilization, and therefore must be aseptically filled. The comments proposed that a SAL of 10^{-3} be stipulated for aseptically filled products.

FDA agrees with this comment. A SAL of 10^{-3} is recommended for reproductive media used for the processing or culture of embryos and gametes. Products which are processed in this way must clearly identify the SAL, and that they were ''aseptically processed'' or ''membrane filtered'' both on the label and in the labeling.

36. One comment stated that the identification for assisted reproduction needles should be revised from ''Assisted reproduction needles are devices used to obtain gametes, * * *'' to ''Assisted reproduction needles are devices used to obtain gametes from the body * * *''.

FDA agrees with this comment and has revised this identification accordingly.

After reviewing the data presented before the Panel and considering the Panel's recommendation, as well as the comments received on the proposed reclassification, FDA, based on the information set forth, is reclassifying instrumentation intended for use in IVF and related ART procedures, and substantially equivalent devices of this generic type, from class III to class II, and assisted reproduction microscopes and microscope accessories, and substantially equivalent devices of this generic type, from class III to class I.

FDAMA added a new section 510(l) to the act. New section 510(l) of the act provides that a class I device is exempt from the premarket notification requirements under section 510(k) of the act, unless the device is intended for a use which is of substantial importance in preventing impairment of human health or it presents a potential unreasonable risk of illness or injury. Hereafter, these are referred to as ''reserved criteria.'' FDA has considered assisted reproduction microscopes and microscope accessories in accordance with the reserved criteria and determined that the device does not require premarket notification. Such an exemption permits manufacturers to introduce into commercial distribution generic types of devices without first submitting a premarket notification to FDA.

Accordingly, as required by § 860.134(b)(6) and (b)(7) of the regulations, FDA is reclassifying instrumentation intended for use in IVF and related ART procedures, and substantially equivalent devices of this generic type, from class III to class II, and assisted reproduction microscopes and microscope accessories, and substantially equivalent devices of this generic type, from class III to class I. In addition, FDA is codifying the reclassification of the device by adding 21 CFR part 884 subpart G which consists of §§ 884.6100, 884.6200, 884.6300, 884.6400, 884.6500, 884.6600, 884.6700, 884.6800, 884.6900, and 884.7000.

B. Special Controls

The following special controls have been identified for assisted reproduction devices classified into class II:

1. Mouse Embryo Assay Information

The manufacturer should provide information to the user on whether an MEA was performed for toxicity and functionality testing of assisted reproduction needles, catheters, microtools, water or water purification systems, reproductive media, labware or other devices coming into contact with gametes and/or embryos. The rationale for requiring information on this test as a special control for class II assisted reproduction devices is that the MEA is a good surrogate indicator of potential toxicity of materials used in assisted reproduction devices to gametes and/or embryos. Both one-cell and two-cell assays are used. FDA will not dictate to the manufacturer which MEA should be used during the manufacture of a particular product, or even that any MEA is performed. Rather, if the mouse embryo assay is conducted, the manufacturer should provide clear information to the user about how the assay was performed and the assay results, both on the label and in the labeling. The bioassay should duplicate, as closely as possible, the procedures used for human IVF, including the acquisition, maintenance, culture, transfer (relocation) and cryopreservation of embryos. If no MEA is used, then this information must also be clearly provided to the user.

2. Endotoxin Testing

The rationale for requiring endotoxin testing as a special control for class II assisted reproduction devices is that it will provide a mechanism for ensuring that devices coming into contact with gametes, embryos, and/or the patient have been tested for levels of endotoxin released from gram-negative bacteria, which is the major pyrogen of concern. Of primary concern, endotoxin can be harmful to embryos and thus potentially affect development of the embryo, implantation and pregnancy rates. An established USP endotoxin assay (LAL or rabbit pyrogenicity) must be performed on any device, including needles, catheters, microtools, labware, water or water purification systems and media coming into contact with gametes, embryos, and/or the patient.

3. Sterilization Validation

The rationale for requiring sterilization validation as a special control for class II assisted reproduction devices is that it will provide a mechanism for ensuring that devices, including needles, catheters, microtools, labware, water or water purification systems, and media coming into contact with gametes and/or embryos are sterile to a SAL of 10^{-6}. The SAL for media should be 10^{-3} or better. Established sterilization validation testing must be performed on all devices according to AAMI guidelines. The label should clearly identify the method of sterilization (for media, whether they were aseptically processed or membrane filtered) and SAL.

4. Water Quality

The rationale for requiring this test as a special control for class II assisted reproduction devices is that water quality is critically important to successful assisted reproductive technology procedures. The quality of water that directly contacts human gametes or embryos in IVF/ART procedures is similar to that for dialysis. Water used to reconstitute reproductive media and to wash and rinse labware, whether generated in-house using purification systems or obtained in bottled form from vendors, should be in conformance with USP water for injection requirements. As stated previously, general purpose water purification systems without a specific assisted reproduction claim will not be affected by this proposed rule.

5. Design Specifications

Particular design specifications may be identified for each type of device which assure minimally acceptable standards. The rationale for including design specifications as a special control for all class II assisted reproduction devices is that it will help to reduce the incidence of adverse events such as bleeding, pain or perforation which could be due to suboptimal device design. For example, assisted reproduction needles may be specified to be 16 to 18 gauge, 22 to 23 centimeters long, 45 to 60 degree beveled stainless steel, and sterile to assure safe and adequate access to ovarian follicles.

6. Labeling Requirements

Specific labeling which identifies the intended use, indication for use, contraindications, precautions, warnings, instructions for use and other information will be required. The rationale for including labeling as a special control for all class II assisted reproduction devices is that it will ensure that devices are used properly, that the user is adequately informed, that the intended use of the device is clearly understood, and that claims by the manufacturer do not exceed the intended use of the device. The label and labeling should also include information on the mouse embryo assay (see section III.B.1 of this document), the method of sterilization (for media, whether they were aseptically processed or membrane filtered) and SAL (see section III.B.3 of this document), and endotoxin levels (see section III.B.2 of this document).

7. Biocompatibility Testing

Aside from concerns with gamete- or embryotoxicity, devices which are patient-contacting should demonstrate that the materials of which they are comprised are biocompatible with their intended use using conventional biocompatibility testing. Tests performed should conform to those recommended by international standard ISO–10993, ''Biological Evaluation of Medical Devices, Part 1: Evaluation and Testing.''

8. Clinical Testing

Certain device designs may not conform to conventional configurations used in assisted reproduction today, e.g., a specially-configured embryo transfer catheter. Although the device designs envisioned for this special control do not raise new types of safety and effectiveness questions, clinical data may still be required in some cases to adequately assess the performance of a device for its intended use. As stated previously, FDA does not intend to routinely require clinical testing; instead, clinical testing will be required on a case-by-case basis, where, based on the design or function of the device, the performance in its intended use can only be validated with clinical data.

C. Summary of Other Changes

In addition, FDA would like to note the following changes from the proposed rule which are incorporated into the final rule:

(1) Although devices used for preimplantation diagnosis procedures such as embryo biopsy were inadvertently included in the proposed rule, the agency does not believe this type of device should be included in this reclassification because the use of such devices for this intended use is relatively new (see comment 9 of this document).

(2) Voluntary standards have been omitted as a special control from the final rule. While several organizations such as the CAP and the SART have provided significant guidance to IVF/ART laboratories, FDA recognizes that standards and recommendations from these organizations do not include specific guidelines for devices (see comment 11 of this document).

(3) The special control of water quality testing has been modified to require conformance with USP water for

injection requirements (see comment 14 of this document).

(4) The special control of sterilization validation has been modified to allow a SAL of 10^{-3} for reproductive media rather than 10^{-6} (see comment 36 of this document).

(5) The special control of biocompatibility testing for patient-contacting devices has been added to the appropriate categories of assisted reproduction devices.

In light of the general controls and special controls proposed for these devices, and the known risks and benefits of the devices, there exists reasonable assurance that these devices are safe and effective for their intended use.

IV. Environmental Impact

The agency has determined under 21 CFR 25.34(b) that this reclassification is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

V. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866 and the Regulatory Flexibility Act (Pub. L. 96–354) as amended by subtitle D of the Small Business Regulatory Fairness Enforcement Act of 1996 (Pub. L. 104–121), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104–4)). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety and other advantages, distributive impacts, and equity). The agency believes that this final rule is consistent with the regulatory philosophy and principles identified in the Executive Order. In addition, the final rule is not a significant regulatory action as defined by the Executive Order and so is not subject to review under the Executive Order. The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Reclassification of these devices from class III to class II or class I will relieve all manufacturers of the device of the cost of complying with the premarket approval requirements in section 515 of the act. Because reclassification will reduce regulatory costs with respect to this device, it will impose no significant economic impact on any small entities, and it may permit small potential competitors to enter the marketplace by lowering their costs. The agency therefore certifies that this final rule will not have a significant economic impact on a substantial number of small entities. In addition, this final rule will not impose costs of $100 million or more on either the private sector or State, local, and tribal governments in the aggregate, and therefore a summary statement or analysis under section 202(a) of the Unfunded Mandates Reform Act of 1995 is not required.

VI. Paperwork Reduction Act of 1995

FDA has determined that this final rule does not contain any information collection requirements and, therefore, is not subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995.

VII. References

The following reference has been placed on display in the Dockets Management Branch and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Association for the Advancement of Medical Instrumentation (AAMI) Guideline, ''The Quality System Compendium: GMP Requirements and Industry Practice.''

List of Subjects in 21 CFR Part 884

Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 884 is amended as follows:

PART 884—OBSTETRICAL AND GYNECOLOGICAL DEVICES

1. The authority citation for 21 CFR part 884 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

2. Subpart G, consisting of §§ 884.6100 through 884.6190, is added to read as follows:

Subpart G—Assisted Reproduction Devices

Sec.

884.6100 Assisted reproduction needles.
884.6110 Assisted reproduction catheters.
884.6120 Assisted reproduction accessories.
884.6130 Assisted reproduction microtools.
884.6140 Assisted reproduction micropipette fabrication instruments.
884.6150 Assisted reproduction micromanipulators and microinjectors.
884.6160 Assisted reproduction labware.
884.6170 Assisted reproduction water and water purification systems.
884.6180 Reproductive media and supplements.
884.6190 Assisted reproductive microscopes and microscope accessories.

Subpart G—Assisted Reproduction Devices

§ 884.6100 Assisted reproduction needles.

(a) *Identification.* Assisted reproduction needles are devices used in in vitro fertilization (IVF), gamete intrafallopian transfer (GIFT), or other assisted reproduction procedures to obtain gametes from the body or introduce gametes, zygote(s), preembryo(s) and/or embryo(s) into the body. This generic type of device may include a single or double lumen needle and component parts, including needle guides, such as those used with ultrasound.

(b) *Classification.* Class II (special controls) (mouse embryo assay information, endotoxin testing, sterilization validation, design specifications, labeling requirements, biocompatibility testing, and clinical testing).

§ 884.6110 Assisted reproduction catheters.

(a) *Identification.* Assisted reproduction catheters are devices used in in vitro fertilization (IVF), gamete intrafallopian transfer (GIFT), or other assisted reproduction procedures to introduce or remove gametes, zygote(s), preembryo(s), and/or embryo(s) into or from the body. This generic type of device may include catheters, cannulae, introducers, dilators, sheaths, stylets, and component parts.

(b) *Classification.* Class II (special controls) (mouse embryo assay information, endotoxin testing, sterilization validation, design specifications, labeling requirements, biocompatibility testing, and clinical testing).

§ 884.6120 Assisted reproduction accessories.

(a) *Identification.* Assisted reproduction accessories are a group of devices used during assisted reproduction procedures, in conjunction with assisted reproduction needles and/or assisted reproduction catheters, to aspirate, incubate, infuse, and/or maintain temperature. This generic type of device may include:

(1) Powered aspiration pumps used to provide low flow, intermittent vacuum for the aspiration of eggs (ova).

(2) Syringe pumps (powered or manual) used to activate a syringe to infuse or aspirate small volumes of fluid during assisted reproduction procedures.

(3) Collection tube warmers, used to maintain the temperature of egg (oocyte)

collection tubes at or near body temperature. A dish/plate/microscope stage warmer is a device used to maintain the temperature of the egg (oocyte) during manipulation.

(4) Embryo incubators, used to store and preserve gametes and/or embryos at or near body temperature.

(5) Cryopreservation instrumentation and devices, used to contain, freeze, and maintain gametes and/or embryos at an appropriate freezing temperature.

(b) *Classification.* Class II (special controls) (design specifications, labeling requirements, and clinical testing).

§ 884.6130 Assisted reproduction microtools.

(a) *Identification.* Assisted reproduction microtools are pipettes or other devices used in the laboratory to denude, micromanipulate, hold, or transfer human gametes or embryos for assisted hatching, intracytoplasmic sperm injection (ICSI), or other assisted reproduction methods.

(b) *Classification.* Class II (special controls) (mouse embryo assay information, endotoxin testing, sterilization validation, design specifications, labeling requirements, and clinical testing).

§ 884.6140 Assisted reproduction micropipette fabrication instruments.

(a) *Identification.* Assisted reproduction micropipette fabrication devices are instruments intended to pull, bevel, or forge a micropipette or needle for intracytoplasmic sperm injection (ICSI), in vitro fertilization (IVF) or other similar assisted reproduction procedures.

(b) *Classification.* Class II (special controls) (design specifications, labeling requirements, and clinical testing).

§ 884.6150 Assisted reproduction micromanipulators and microinjectors.

(a) *Identification.* Assisted reproduction micromanipulators are devices intended to control the position of an assisted reproduction microtool. Assisted reproduction microinjectors are any device intended to control aspiration or expulsion of the contents of an assisted reproduction microtool.

(b) *Classification.* Class II (special controls) (design specifications, labeling requirements, and clinical testing).

§ 884.6160 Assisted reproduction labware.

(a) *Identification.* Assisted reproduction labware consists of laboratory equipment or supplies intended to prepare, store, manipulate, or transfer human gametes or embryos for in vitro fertilization (IVF), gamete intrafallopian transfer (GIFT), or other assisted reproduction procedures. These include syringes, IVF tissue culture dishes, IVF tissue culture plates, pipette tips, dishes, plates, and other vessels that come into physical contact with gametes, embryos or tissue culture media.

(b) *Classification.* Class II (special controls) (mouse embryo assay information, endotoxin testing, sterilization validation, design specifications, labeling requirements, and clinical testing).

§ 884.6170 Assisted reproduction water and water purification systems.

(a) *Identification.* Assisted reproduction water purification systems are devices specifically intended to generate high quality, sterile, pyrogen-free water for reconstitution of media used for aspiration, incubation, transfer or storage of gametes or embryos for in vitro fertilization (IVF) or other assisted reproduction procedures. These devices may also be intended as the final rinse for labware or other assisted reproduction devices that will contact the gametes or embryos. These devices also include bottled water ready for reconstitution available from a vendor that is specifically intended for reconstitution of media used for aspiration, incubation, transfer, or storage of gametes or embryos for IVF or other assisted reproduction procedures.

(b) *Classification.* Class II (special controls) (mouse embryo assay information, endotoxin testing, sterilization validation, water quality testing, design specifications, labeling requirements, biocompatibility testing, and clinical testing).

§ 884.6180 Reproductive media and supplements.

(a) *Identification.* Reproductive media and supplement are products that are used for assisted reproduction procedures. Media include liquid and powder versions of various substances that come in direct physical contact with human gametes or embryos (including water, acid solutions used to treat gametes or embryos, rinsing solutions, sperm separation media, supplements, or oil used to cover the media) for the purposes of preparation, maintenance, transfer or storage. Supplements are specific reagents added to media to enhance specific properties of the media (e.g., proteins, sera, antibiotics, etc.).

(b) *Classification.* Class II (special controls) (mouse embryo assay information, endotoxin testing, sterilization validation, design specifications, labeling requirements, biocompatibility testing, and clinical testing).

§ 884.6190 Assisted reproductive microscopes and microscope accessories.

(a) *Identification.* Assisted reproduction microscopes and microscope accessories (excluding microscope stage warmers, which are classified under assisted reproduction accessories) are optical instruments used to enlarge images of gametes or embryos. Variations of microscopes and accessories used for these purposes would include phase contrast microscopes, dissecting microscopes and inverted stage microscopes. This device is exempt from the premarket notification procedures in subpart E of part 807 of this chapter subject to the limitations in § 884.9.

(b) *Classification.* Class I.

Dated: August 25, 1998.

D.B. Burlington,

Director, Center for Devices and Radiological Health.

[FR Doc. 98–24242 Filed 9–9–98; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HOUSING AND URBAN DEVELOPMENT

24 CFR Part 570

[Docket No. FR–4269–F–01]

RIN 2528–AA06

Hispanic-Serving Institutions Work Study Program

AGENCY: Office of the Assistant Secretary for Policy Development and Research, HUD.

ACTION: Final rule.

SUMMARY: On February 25, 1998, HUD published an interim rule that broadened the eligibility for public and private non-profit two-year institutions of higher education to participate in the Hispanic-serving Institutions Work Study Program (HSI–WSP). This final rule makes final that interim rule without changes.

EFFECTIVE DATE: October 13, 1998.

FOR FURTHER INFORMATION CONTACT: Jane Karadbil, Office of University Partnerships, U.S. Department of Housing and Urban Development, Room 8110, 451 Seventh Street, SW, Washington, D.C. 20410, telephone (202) 708–1537, extension 218. Hearing- or speech-impaired individuals may call HUD's TTY number (202) 708–1455, or 1–800–877–8399 (Federal Information Relay Service TTY). (Other than the ''800'' number, these are not toll-free numbers.) Ms. Karadbil can also be contacted via the Internet at Jane__.R.__Karadbil@hud.gov.