Guidance for Industry,
FDA Reviewers/Staff and Compliance

Devices Used for In Vitro Fertilization and Related Assisted Reproduction Procedures

Draft Guidance – Not for Implementation

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Obstetrics and Gynecology Devices Branch
Division of Abdominal, Reproductive and ENT Devices
Office of Device Evaluation

Preface

Public Comment:

For 90 days following the date of publication in the Federal Register of the notice announcing the availability of this guidance, comments and suggestions regarding this document should be submitted to the Docket No. assigned to that notice, Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 12420 Parklawn Drive (HFA-305), Room 1-23, Rockville, MD 20857.

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Devices Used for *In Vitro* Fertilization and Related Assisted Reproduction Procedures: Submission Guidance for a 510(k)

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INTRODUCTION

This document outlines the information to be submitted in a 510(k) premarket notification for medical devices which are intended to be used for *in vitro* fertilization (IVF), gamete intrafallopian transfer (GIFT), zygote intrafallopian transfer (ZIFT), intracytoplasmic sperm injection (ICSI), embryo transfer (ET), and related assisted reproduction technology (ART) procedures. It follows the publication in the Federal Register of first a proposed rule (Docket No. 97N-0335; published 9/4/97) and then a final rule (Docket No. **xxx-xxxx**; published **xx/xx**/98), which downclassified these types of devices from Class III, effective on **xx/xx**/98. The Federal Register reclassification notification itself can be used to support substantial equivalence in the absence of any existing predicate devices.

For general information regarding 510(k) requirements, contact CDRH's Division of Small Manufacturer's Assistance (DSMA) at (800) 638-2041 or (301) 443-6597.

For additional information regarding these types of medical devices, contact:

Obstetrics and Gynecology Devices Branch
Office of Device Evaluation (HFZ-470)
9200 Corporate Boulevard,
Rockville, Maryland 20850
(301) 594-1180

It should be noted that, for certain IVF/ART devices, additional information other than that outlined in this document, including clinical data, may be needed. In addition, certain devices intended for use in IVF/ART which are not covered in this guidance may require premarket approval. The following list identifies the medical devices, with their respective descriptions, which are covered by this guidance document and are appropriate to submit in a 510(k).

DEVICE CATEGORIES (See Section F for more detail on Special Controls)

A. Assisted reproduction needles

Class: II Procode: 85 MQE CFR#: 884.6100

Assisted reproduction needles are devices in IVF, GIFT, or other ART procedures used to either: (a) obtain gametes from the body, or (b) 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.

Special Controls: Mouse Embryo Assay Information, Endotoxin Testing, Sterilization Validation, Design Specifications, Labeling Requirements, Biocompatibility Testing, Clinical Testing.

Assisted reproduction catheters

Class: II Procode: 85 MQF CFR#: 884.6110

Assisted reproduction catheters are devices used in IVF, 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.

Special Controls: Mouse Embryo Assay Information, Endotoxin Testing, Sterilization Validation, Design Specifications, Labeling Requirements, Biocompatibility Testing, Clinical Testing.

C. Assisted reproduction accessories

Class: II Procode: 85 MQG CFR#: 884.6120

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.

Special Controls: Design Specifications, Labeling Requirements, Clinical Testing.

D. Assisted reproduction microtools

Class: II Procode: 85 MQH CFR#: 884.6130

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, or other assisted reproduction methods.
Note: This category does not include 1) laser microtools, or 2) devices intended for use during preimplantation diagnosis procedures, including embryo biopsy.

Special Controls: Mouse Embryo Assay Information, Endotoxin Testing, Sterilization Validation, Design Specifications, Labeling Requirements, Clinical Testing.

E. Assisted reproduction micropipette fabrication instruments

Class: II Procode: 85 MQI CFR#: 884.6140

Assisted reproduction micropipette fabrication devices are instruments intended to pull, bevel, or forge a micropipette or needle for ICSI, IVF or other similar assisted reproduction procedures.

Note: Only the device that is promoted and marketed to the medical community with a claim relating to an intended use for IVF/ART will require a premarket notification [510(k)] submission. This applies to the micropipettes or micropipette fabrication instrumentation. If the micropipette is the device marketed for that intended use, it would require a 510(k), 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 intended use of IVF/ART, then it would require a 510(k). If the device (whether it is the micropipette itself or the micropipette fabrication instrumentation) does not have a specific claim for use during IVF/ART, then no 510(k) is required. The individual IVF laboratory is not prohibited by FDA from using any instrumentation they deem necessary.

Special Controls: Design Specifications, Labeling Requirements, Clinical Testing.

F. Assisted reproduction micromanipulators and microinjectors

Class: II Procode: 85 MQJ CFR#: 884.6150

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.

Special Controls: Design Specifications, Labeling Requirements, Clinical Testing.

G. Assisted reproduction labware

Class: II Procode: 85 MQK CFR#: 884.6160

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) or other assisted reproduction techniques. 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.

Special Controls: Mouse Embryo Assay Information, Endotoxin Testing, Sterilization Validation, Design Specifications, Labeling Requirements, Clinical Testing.

H. Assisted reproduction water and water purification systems

Class: II Procode: 85 MTW CFR#: 884.6170

Assisted reproduction water purification systems are devices 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 IVF or other assisted reproduction procedures. It may also be intended as the final rinse for labware or other assisted reproduction devices which will contact the gametes or embryos. This also includes bottled water, available from a vendor, which 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.

Note: 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 importance of 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.*

The USP Water For Injection (WFI) standard will be used as a special control because it delineates testing procedures for producing water which is safe for parenteral use, which should also suffice for production of water with potential for exposure to human gametes and embryos. It will apply to water 1) specifically intended for reconstitution of reproductive media, 2) specifically intended for washing and rinsing of labware to be used in ART procedures, and 3) purification systems specifically intended for production of water to be used for ART procedures.

Special Controls: Mouse Embryo Assay Information, Endotoxin Testing, Sterilization Validation, Design Specifications, Labeling Requirements, Biocompatibility Testing, Clinical Testing.

I. Reproductive media and supplements:

Class: II Procode: 85 MQL CFR#: 884.6180

Reproductive media and supplements are products that are used for assisted reproduction procedures. Media include liquid and powder versions of various substances which 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, or oil used to

cover the media) for the purposes of preparation, maintenance, transfer or storage, and supplements, including specific reagents added to media to enhance specific properties of the media (e.g., proteins, sera, antibiotics, etc.).

Note: Media should be manufactured according to aseptic GMP conditions in accordance with sections 820.70(c) and 820.75 of the Quality System Regulation, pertaining to Environmental Control and Process Validation, respectively. 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."

If human- or animal-derived macromolecules (such as serum albumin or hyaluronic acid) are proposed for inclusion in IVF media, justification should be provided (including controls in place for donor screening and testing, as well as proper patient notification and consent), since these macromolecules present a potential risk for transmission of pathogens such as Creutzfeld-Jacob Disease (CJD) or bovine spongiform encephalopathy (BSE) to the human gamete or embryo which may be difficult to detect. In addition, there exists the potential for transmission of foreign DNA into the human oocyte during intracytoplasmic sperm injection (ICSI). FDA recognizes that the technology for production of these macromolecules by recombinant means is still developing. In addition, FDA's Center for Biologics Evaluation and Research (CBER) may be contacted for information on currently existing special controls for the use of animal-derived macromolecules in IVF media.

IVF media should be issued with labeling which indicates test results for endotoxin testing, and information on mouse embryo assay (MEA) testing for that batch (see Special Controls section). This will provide quality assurance to the user and inform them as to whether any further testing is needed.

Special Controls: Mouse Embryo Assay Information, Endotoxin Testing, Sterilization Validation, Design Specifications, Labeling Requirements, Biocompatibility Testing, Clinical Testing.

J. Assisted reproduction microscopes and microscope accessories:

Class: I Procode: 85 MTX CFR#: 884.6190

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 microscope accessories used for these purposes would include phase contrast microscopes, dissecting microscopes and inverted stage microscopes.

Note: These devices are Class I and exempt from 510(k) unless the device is part of a larger assisted reproduction system (e.g., laser-assisted hatching work station), OR includes a fluorescence microscope used for preimplantation diagnosis procedures. This category is intended to specifically refer to conventional optical microscopes and accessories which are used for the most common and routine IVF/ART procedures, which have a long and well-established history of safe use.

Recommended 510(k) Contents:

A. Device Name and Predicate Device Name

Identify both the trade and proprietary name of the device, as well as the common or usual name for the device. Also, identify as specifically as possible either the legally marketed device(s) to which the new device will be compared, **OR** the category of assisted reproduction device to which the device will be compared, referencing the Notice of the Final Rule published in the Federal Register, and the specific CFR classification regulation number for the device, as well as its classification. When identifying a predicate device, be as specific as possible, e.g., propietary and common name, manufacturer, model number, 510(k) reference number, etc. The 510(k) should include a tabbed section with product literature (description, specifications, label, labeling and instructions, promotional materials).

EXAMPLE:

Device	Class	CFR Reference	Procode
Reproductive Media	II	884.6180	85 MQL
Labware	II	884.6160	85 MQK

B. Administrative Information

Establishment Registration Number
Contact Person and Title
Telephone number and Fax number
Truthful and Accurate Statement
Indication For Use Statement (using FDA form)
510(k) Statement or 510(k) Summary

C. Device Description, Intended Use and Directions For Use

This section identifies the information necessary to evaluate the device. Additional information may be needed depending on the individual design and function of the device.

1) Device Description: May consist of system block diagrams (if applicable), schematic diagrams, photographs, and drawings in addition to a written description. Wherever possible, please provide diagrams and/or drawings to illustrate how the device achieves its intended use.

2) All components and materials making up the device should be clearly and specifically identified in tabular format, with identification of whether the material is patient-contacting, gamete- or embryo-contacting, or neither. The results of biocompatibility testing (including the raw data and reports as well as summaries) performed on the finished device, or certification that identical materials are used in a legally marketed device with a similar intended use, are also needed. For additional information on biocompatibility, please refer to the Blue Book Memorandum "Use of International Standard ISO-10993, 'Biological Evaluation of Medical Devices Part 1: Evaluation and Testing'," available from the Division of Small Manufacturers Assistance (DSMA).

3) Intended Use: The 510(k) should provide a clear and specific statement of the intended use of the device, including the indication(s) for use.

4) Safety Requirements: If applicable, please provide information relating to thermal, electrical, or electromagnetic safety, identifying applicable standards of UL or IEC 601 and providing either certification that the device complies with the applicable electrical safety standards, or test results which guarantee a similar level of protection.

D. Hazard Analysis

The hazard analysis should identify each potential hazard to the patient (or the gamete/embryo), the cause of the hazard, the level of concern, and the steps taken to address the hazard.

E. Comparison Table

Provide a table that lists the similarities and differences between your device and any identified predicate device(s). The table should include: intended use, indications, contraindications, patient- or gamete/embryo-contacting materials, design features, safety features, and any other relevant device characteristics.

F. Performance Standards/Special Controls

Performance standards under Section 514 of the Act have not been developed for these devices. However, the following Special Controls have been identified in order to provide reasonable assurance of the safety and effectiveness of devices used in assisted reproduction procedures.

Due to the wide variety of designs and intended uses of assisted reproduction devices, FDA may request additional information, including possible clinical studies, for particular devices as deemed necessary.

It is important to note that any special controls for these devices apply only to products that are specifically labeled and marketed for assisted reproduction. General purpose devices (e.g., incubators, freezers, and water purification systems), which are not specifically labeled and promoted for assisted reproduction, are not subject to the regulatory controls described in this guidance document.

The following Special Controls should be addressed, **where applicable**, in any 510(k) for a medical device specifically labeled and marketed for use in assisted reproduction, which is submitted to FDA:

1. Mouse Embryo Assay Information

The mouse embryo assay (MEA) is used for toxicity and functionality testing of reproductive media, labware **or any device 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 it is a good surrogate indicator of potential toxicity of materials used in assisted reproduction devices to gametes and/or embryos. FDA recognizes that the MEA is currently the most appropriate test for embryotoxicity; however, there is no definitive 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. This would add an unnecessary burden and cost to the manufacturer. Rather, it will be essential for 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.

Both one-cell and two-cell assays are used, and these are identical except that one-cell embryos are flushed from the mouse oviduct earlier than two-cell embryos. There are advantages to either test. Some believe that a two-cell MEA is preferable because it assures that one is testing a viable cleaving embryo from the onset. If cleaving does not proceed to the expanding or hatching blastocyst stage, then the test material is suspect for toxicity to the embryo. A one-cell MEA may not be as reassuring because lack of cleavage may be due either to embryo toxicity or to an intrinsically compromised embryo. The two-cell MEA is also easier to use because of timing of oviductal flushing and the fact that the embryos release easily from their mass of cumulus cells. Others believe that one-cell

embryos are more sensitive to toxic conditions and better represent the actual conditions of *in vitro* fertilization and embryo development than the two-cell embryo.

If the MEA is performed, whether a one-cell or two-cell MEA is used, the bioassay should represent, as closely as possible, the corresponding procedures used for which the device is used for human IVF, such as the acquisition, maintenance, culture, transfer (relocation) and cryopreservation of embryos.

Currently, alternative methods of assessing potential gamete- or embryotoxicity, such as the Hybritest, a bioassay based on the culture of mouse hybridoma cells, are not acceptable in lieu of the MEA. 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.

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 gram-negative bacterial endotoxin, the major pyrogen of concern. Endotoxin can be harmful or lethal to embryos and thus may potentially affect development of the embryo, implantation and pregnancy rates.

An established USP endotoxin assay using the Limulus Amebocyte Lysate (LAL) test or Rabbit Pyrogen Assay should be performed on any device, including needles, catheters, labware, water (including bottled water or water purification systems) and media, coming into contact with gametes, embryos, and/or the patient.

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. 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 of acceptability. Rather, it is important that the manufacturer perform an established USP endotoxin test such as the Limulus Amebocyte Lysate (LAL) or Rabbit Pyrogen assay on any device potentially contacting human gametes or embryos, and identify this information in the labeling.

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 coming into contact with gametes and/or embryos are sterile to a sterility assurance level (SAL) of 10^{-6}. A SAL of 10^{-3} may reasonably be expected for reproductive media and supplements used for the processing or culture of embryos and gametes. Products which are processed in this way should clearly identify the SAL, and that they were "aseptically processed" or "membrane-filtered," both on the label and in the labeling. Because IVF media are products as critical as others intended for parenteral use, they should therefore be manufactured according to aseptic GMP conditions. Please refer to 21 CFR Sections 820.70(c) and 820.75 of the Quality System Regulation, pertaining to Environmental Control and Process Validation, respectively. 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"

Established sterilization validation testing should be performed on all devices according to AAMI guidelines. Also refer to Please refer to the Blue Book Memorandum K90-1, "510(k) Sterility Review Guidance" for the sterilization information necessary in a 510(k) submission. If reuse of any device is intended, clear instructions for the method of reprocessing should be provided. A "Status Reprocessing Instructions Validation Certification" form, available from the Division of Small Manufacturers Assistance (DSMA) should also be completed. Packaging information should also be included in this section.

4. Water Quality (May, 1996 [Ref. 10])

The importance of quality of water needed for IVF/ART procedures in which human gametes or embryos are directly contacted is similar to that for dialysis. 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. 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 wishes to market and promote that system for general purposes only, then a 510(k) is not necessary.

The USP Water For Injection standard 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 ART procedures, and 3) water purification systems specifically intended for production of water to be used for ART procedures. Water produced in conformance with this standard has properties sufficient and appropriate for the intended use of IVF/ART.

5. Design/Performance Specifications

The rationale for including design specifications as a special control for 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. Particular design specifications should identified for each type of device to assure minimally acceptable standards. For example, assisted reproduction needles may be specified to be 16-18 gauge, 22-23 cm long, 45-60 degree beveled stainless steel, with a specially treated tip to be echogenic, and sterile, to assure safe and adequate access to ovarian follicles. Identify any performance specifications, and provide bench data and/or a plan to demonstrate that these specifications have been met. In addition, describe any safety features which are incorporated into the device.

6. Labeling Requirements

The rationale for including labeling requirements as a special control for 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. Specific labeling which clearly identifies the intended use, indication(s) for use, contraindications, precautions, warnings and instructions for use is needed. For instance, assisted reproduction catheters will should have labeling which specifies its intended use as "For transvaginal retrieval of oocytes," or "For delivery of embryos into the fallopian tube." Labeling should also include an indication of the volume of media considered appropriate for that catheter. The instructions should specify where the catheter is intended to place gametes/embryos, the appropriate patient position, and patient preparation instructions (disinfection/cleaning of the vagina).

The label and package insert should also indicate endotoxin testing results, and whether a one-cell or two-cell mouse embryo assay, or no assay at all, was performed, as well as the method of sterilization used. For additional information on labeling, please refer to the guidance titled "Medical Device Labeling – Suggested Format and Content" (DRAFT; issued 4/25/97). Particular attention should be paid to the section on Essential Prescribing Information (EPI).

FDA recognizes that because of variability in techniques from user to user, it may not be feasible or helpful to provide specific instruction for use on some devices, such as labware. Guidance from the appropriate regulatory entities (CAP, SART, HCFA) should be followed wherever applicable, and a general statement in the labeling should be made 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.

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 or timely to provide specific boilerplate language for labeling in this guidance. Again, guidance regarding labeling from the appropriate regulatory entities (CAP, SART, CLIA) should be followed wherever applicable. 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) database has been obtained.

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

Clinical testing will not be routinely requested for devices used in IVF/ART procedures. However, certain device designs or functions may not conform to conventional configurations used in assisted reproduction today, e.g., a specially-configured embryo transfer catheter. Even if the device designs envisioned for this special control do not raise new types of safety and effectiveness questions, additional testing may still be necessary to validate the performance of the device, as outlined in FDA's "510(k) Substantial Equivalence Decision-Making Process (Detailed)." Therefore, clinical data may be needed in some cases to adequately assess the performance of a device in its intended use. For example, if the claim is made that use of a particular type of reproductive media will result in improved pregnancy rates, then that claim can only be substantiated with clinical data. Likewise, if a claim is made that a particular GIFT catheter is safer or easier to use, then those claims would need to be supported by a clinical study validating that claim. FDA encourages manufacturers with questions regarding the need for clinical data for a particular device to contact the Obstetrics and Gynecology Devices Branch for further discussion.

G. Kits

Devices used for IVF/ART procedures do not yet meet the criteria identified under FDA's "Convenience Kits Interim Regulatory Guidance (May 20, 1997)." That is, they are neither 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 IVF/ART sets for this new regulatory approach once a sufficient 510(k) database for these devices is obtained.

H. Voluntary Standards

CDRH will accept a declaration of conformity (as defined below) for CDRH-recognized voluntary standards in place of data or procedural description. **Declaration of conformity** is described as "a statement made by the submitter that a particular device was tested and meets the requirements of a recognized standard." It should clearly specify 1) any element of the standard that was not applicable; 2) if the standard is part of a family of standards which provides collateral and/or particular parts, a statement regarding the collateral and/or particular parts that were met; 3) any deviations from the standards that were applied; 4) what differences exist , if any, between the tested device(s) and the device to be marketed, and a justification of the test results in those areas of difference; and 5) the name and address of any test laboratory or certification body involved and a reference to any accreditation of those organizations.

The following currently recognized standards may apply to devices in these categories:

UL-2601-1	Standard for Medical Electrical Equipment
IEC-60601-1	Medical Electronics Equipment
UL 544	Electrical Safety
ISO-10993	Biological Evaluation of Medical Devices
AAMI TIR No. 12-1994	Reprocessing Reusable Medical Devices
IEEE Std 730-1989	Software Quality Assurance
IEEE Std 828-1990	Software Configuration Management Plans
IEEE Std 830-1993	Software Requirements Specifications
IEEE Std 1016-1987	Software Design Descriptions

Additional Standards (Examples):

1) College of American Pathologists (CAP)--Reproductive Laboratory Accreditation Program
2) Society for Assisted Reproductive Technology (SART)

These organizations have already identified many standards which may be applicable to assisted reproduction devices. FDA recognizes that the SART database consists of published patient registries, and that it does not contain specific guidelines or recommendations for devices used in IVF/ART procedures or recognized standards with which to comply or adhere. Nevertheless, the Agency feels it is important to acknowledge this organization for its significant guidance to IVF/ART laboratories in obtaining data on the safety and effectiveness of these procedures. Guidance may include recommended tests and equipment, as well as acceptable techniques in the use of many assisted reproduction devices. Please specifically identify any standards promulgated by these or other organizations to which your device conforms.

IV. References

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