

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 884

[Docket No. FDA-2014-M-1957]

Medical Devices; Obstetrical and Gynecological Devices; Classification of the Assisted
Reproduction Embryo Image Assessment System

AGENCY: Food and Drug Administration, HHS.

ACTION: Final order.

SUMMARY: The Food and Drug Administration (FDA) is classifying the Assisted
Reproduction Embryo Image Assessment System into class II (special controls). The special
controls that will apply to the device are identified in this order, and will be part of the codified
language for the Assisted Reproduction Embryo Image Assessment System classification. The
Agency is classifying the device into class II (special controls) in order to provide a reasonable
assurance of safety and effectiveness of the device.

DATES: This order is effective [INSERT DATE OF PUBLICATION IN THE FEDERAL
REGISTER]. The classification was applicable June 6, 2014.

FOR FURTHER INFORMATION CONTACT: Michael Bailey, Center for Devices and
Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm
G120, Silver Spring, MD 20993-0002, 301-796-6530.

SUPPLEMENTARY INFORMATION:

I. Background

In accordance with section 513(f)(1) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 360c(f)(1)), devices that were not in commercial distribution before May 28, 1976 (the date of enactment of the Medical Device Amendments of 1976), generally referred to as postamendments devices, are classified automatically by statute into class III without any FDA rulemaking process. These devices remain in class III and require premarket approval, unless and until the device is classified or reclassified into class I or II, or FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i), to a predicate device that does not require premarket approval. The Agency determines whether new devices are substantially equivalent to predicate devices by means of premarket notification procedures in section 510(k) of the FD&C Act (21 U.S.C. 360(k)) and part 807 (21 CFR part 807) of the regulations.

Section 513(f)(2) of the FD&C Act, as amended by section 607 of the Food and Drug Administration Safety and Innovation Act (Pub. L. 112-144), provides two procedures by which a person may request FDA to classify a device under the criteria set forth in section 513(a)(1) of the FD&C Act. Under the first procedure, the person submits a premarket notification under section 510(k) of the FD&C Act for a device that has not previously been classified and, within 30 days of receiving an order classifying the device into class III under section 513(f)(1), the person requests a classification under section 513(f)(2) of the FD&C Act. Under the second procedure, rather than first submitting a premarket notification under section 510(k) of the FD&C Act and then a request for classification under the first procedure, the person determines that there is no legally marketed device upon which to base a determination of substantial

equivalence and requests a classification under section 513(f)(2) of the FD&C Act. If the person submits a request to classify the device under this second procedure, FDA may decline to undertake the classification request if FDA identifies a legally marketed device that could provide a reasonable basis for review of substantial equivalence with the device, or if FDA determines that the device submitted is not of “low-moderate risk”, or that general controls would be inadequate to control the risks and special controls to mitigate the risks cannot be developed.

In response to a request to classify a device under either procedure provided by section 513(f)(2) of the FD&C Act, FDA will classify the device by written order within 120 days. This classification will be the initial classification of the device.

On August 3, 2012, FDA issued an order classifying the EEVA System into class III, because it was not substantially equivalent to a device that was introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, or a device which was subsequently reclassified into class I or class II. On August 23, 2012, Auxogyn, Inc., submitted a de novo request for classification of the EEVA System under section 513(f)(2) of the FD&C Act. The manufacturer recommended that the device be classified into class II (Ref. 1).

In accordance with section 513(f)(2) of the FD&C Act, FDA reviewed the request in order to classify the device under the criteria for classification set forth in section 513(a)(1) of the FD&C Act. FDA classifies devices into class II if general controls by themselves are insufficient to provide reasonable assurance of safety and effectiveness, but there is sufficient information to establish special controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use. After review of the information submitted in the

request, FDA determined that the device can be classified into class II with the establishment of special controls. FDA believes these special controls, in addition to general controls, will provide reasonable assurance of the safety and effectiveness of the device.

Therefore, on June 6, 2014, FDA issued an order to the requestor classifying the device into class II. FDA is codifying the classification of the device by adding § 884.6195 (21 CFR 884.6195).

Following the effective date of this final classification administrative order, any firm submitting a premarket notification (510(k)) for an Assisted Reproduction Embryo Image Assessment System will need to comply with the special controls named in the final administrative order.

The device is assigned the generic name Assisted Reproduction Embryo Image Assessment System, and it is identified as a prescription device that is designed to obtain and analyze light microscopy images of developing embryos. This device provides information to aid in the selection of embryo(s) for transfer when there are multiple embryos deemed suitable for transfer or freezing.

FDA has identified the following risks to health associated with this type of device and the measures required to mitigate these risks in Table 1:

Table 1.--Assisted Reproduction Embryo Image Assessment System Risks and Mitigation Measures

Identified Risk	Mitigation Measures
Damage or Destruction of the Embryo	Non-Clinical Performance Testing Software Verification, Validation & Hazard Analysis Clinical Testing Electromagnetic Compatibility Testing Electrical Safety Testing Labeling Training
Infection (Contamination of Device, Labware, and Incubator)	Cleaning and Disinfection Validation Labeling Training
Incorrect Embryo Development Prediction	Non-Clinical Performance Testing Software Verification, Validation & Hazard Analysis Clinical Testing

	Labeling Training
Electromagnetic Interference/Electrical Safety Issues	Electromagnetic Compatibility Testing Electrical Safety Testing Labeling
Use Error	Labeling Training

FDA believes that the following special controls, in addition to the general controls, address these risks to health and provide reasonable assurance of safety and effectiveness:

- Clinical performance testing must demonstrate a reasonable assurance of the safety and effectiveness of the device to predict embryo development. Classification performance (sensitivity and specificity) and predictive accuracy (Positive Predictive Value and Negative Predictive Value) must be assessed at the subject and embryo levels.
- Software validation, verification, and hazard analysis must be provided.
- Non-clinical performance testing data must demonstrate the performance characteristics of the device. Testing must include the following:
 - Total light exposure and output testing;
 - a safety analysis must be performed based on maximum (worst-case) light exposure to embryos, which also includes the safety of the light wavelength(s) emitted by the device;
 - simulated-use testing;
 - Mouse Embryo Assay testing to assess whether device operation impacts growth and development of mouse embryos to the blastocyst stage;
 - cleaning and disinfection validation of reusable components;
 - package integrity and transit testing ;
 - hardware fail-safe validation;
 - electrical equipment safety and electromagnetic compatibility testing; and

- prediction algorithm reproducibility.
- Labeling must include the following:
 - A detailed summary of clinical performance testing, including any adverse events;
 - specific instructions, warnings, precautions, and training needed for safe use of the device;
 - appropriate electromagnetic compatibility information;
 - validated methods and instructions for cleaning and disinfection of reusable components; and
 - information identifying compatible cultureware and explain how they are used with the device.

An Assisted Reproduction Embryo Image Assessment System is a prescription device restricted to patient use only upon the authorization of a practitioner licensed by law to administer or use the device. (See 21 CFR 801.109 (Prescription devices).)

Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C Act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device. For this type of device, FDA has determined that premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device. Therefore, this device type is not exempt from premarket notification requirements. Persons who intend to market this type of device must submit to FDA a premarket notification, prior to marketing the device, which contains information about the Assisted Reproduction Embryo Image Assessment System they intend to market.

II. Environmental Impact

The Agency has determined under 21 CFR 25.34(b) that this action 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.

III. Paperwork Reduction Act of 1995

This final administrative order establishes special controls that refer to previously approved collections of information found in other FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in part 807, subpart E regarding premarket notification submissions have been approved under OMB control number 0910-0120 and the collections of information in 21 CFR part 801, regarding labeling, have been approved under OMB control number 0910-0485.

IV. Reference

The following reference has been placed on display in the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. K120427: De Novo Request from Auxogyn, Inc., dated August 23, 2012.

List of Subjects in 21 CFR Part 884

Medical devices, Obstetrical and Gynecological 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. Section 884.6195 is added to subpart G to read as follows:

§ 884.6195 Assisted Reproduction Embryo Image Assessment System.

(a) Identification. An Assisted Reproduction Embryo Image Assessment System is a prescription device that is designed to obtain and analyze light microscopy images of developing embryos. This device provides information to aid in the selection of embryo(s) for transfer when there are multiple embryos deemed suitable for transfer or freezing.

(b) Classification. Class II (special controls). The special control(s) for this device are:

(1) Clinical performance testing must demonstrate a reasonable assurance of safety and effectiveness of the device to predict embryo development. Classification performance (sensitivity and specificity) and predictive accuracy (Positive Predictive Value and Negative Predictive Value) must be assessed at the subject and embryo levels.

(2) Software validation, verification, and hazard analysis must be provided.

(3) Non-clinical performance testing data must demonstrate the performance characteristics of the device. Testing must include the following:

(i) Total light exposure and output testing;

(ii) A safety analysis must be performed based on maximum (worst-case) light exposure to embryos, which also includes the safety of the light wavelength(s) emitted by the device;

(iii) Simulated-use testing;

(iv) Mouse Embryo Assay testing to assess whether device operation impacts growth and development of mouse embryos to the blastocyst stage;

- (v) Cleaning and disinfection validation of reusable components;
- (vi) Package integrity and transit testing;
- (vii) Hardware fail-safe validation;
- (viii) Electrical equipment safety and electromagnetic compatibility testing; and
- (ix) Prediction algorithm reproducibility.

(4) Labeling must include the following:

- (i) A detailed summary of clinical performance testing, including any adverse events;
- (ii) Specific instructions, warnings, precautions, and training needed for safe use of the

device

- (iii) Appropriate electromagnetic compatibility information;

- (iv) Validated methods and instructions for cleaning and disinfection of reusable components; and

- (v) Information identifying compatible cultureware and explain how they are used with the device.

Dated: February 20, 2015.

Leslie Kux,

Associate Commissioner for Policy.

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