4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 864

[Docket No. FDA-2017-N-6780]

Medical Devices; Hematology and Pathology Devices; Classification of the Whole Slide Imaging System

AGENCY: Food and Drug Administration, HHS.

ACTION: Final order.

SUMMARY: The Food and Drug Administration (FDA or we) is classifying the whole slide imaging system into class II (special controls). The special controls that apply to the device type are identified in this order and will be part of the codified language for the whole slide imaging system's classification. We are taking this action because we have determined that classifying the device into class II (special controls) will provide a reasonable assurance of safety and effectiveness of the device. We believe this action will also enhance patients' access to beneficial innovative devices, in part by reducing regulatory burdens.

DATES: This order is effective [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. The classification was applicable on April 12, 2017.

FOR FURTHER INFORMATION CONTACT: Steven Tjoe, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 4550, Silver Spring, MD 20993-0002, 301-796-5866, steven.tjoe@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

Upon request, FDA has classified the whole slide imaging system as class II (special controls), which we have determined will provide a reasonable assurance of safety and effectiveness. In addition, we believe this action will enhance patients' access to beneficial innovation, in part by reducing regulatory burdens by placing the device into a lower device class than the automatic class III assignment.

The automatic assignment of class III occurs by operation of law and without any action by FDA, regardless of the level of risk posed by the new device. Any device that was not in commercial distribution before May 28, 1976, is automatically classified as, and remains within, class III and requires premarket approval unless and until FDA takes an action to classify or reclassify the device (see 21 U.S.C. 360c(f)(1)). We refer to these devices as "postamendments devices" because they were not in commercial distribution prior to the date of enactment of the Medical Device Amendments of 1976, which amended the Federal Food, Drug, and Cosmetic Act (FD&C Act).

FDA may take a variety of actions in appropriate circumstances to classify or reclassify a device into class I or II. We may issue an order finding a new device to be substantially equivalent under section 513(i) of the FD&C Act (see 21 U.S.C. 360c(i)) to a predicate device that does not require premarket approval. We determine whether a new device is substantially equivalent to a predicate by means of the procedures for premarket notification under section 510(k) of the FD&C Act (21 U.S.C. 360(k) and part 807 (21 CFR part 807).

FDA may also classify a device through "De Novo" classification, a common name for the process authorized under section 513(f)(2) of the FD&C Act. Section 207 of the Food and

Drug Administration Modernization Act of 1997 established the first procedure for De Novo classification (Pub. L. 105-115). Section 607 of the Food and Drug Administration Safety and Innovation Act modified the De Novo application process by adding a second procedure (Pub. L. 112-144). A device sponsor may utilize either procedure for De Novo classification.

Under the first procedure, the person submits a 510(k) for a device that has not previously been classified. After receiving an order from FDA classifying the device into class III under section 513(f)(1) of the FD&C Act, the person then requests a classification under section 513(f)(2).

Under the second procedure, rather than first submitting a 510(k) and then a request for classification, if the person determines that there is no legally marketed device upon which to base a determination of substantial equivalence, that person requests a classification under section 513(f)(2) of the FD&C Act.

Under either procedure for De Novo classification, FDA is required to classify the device by written order within 120 days. The classification will be according to the criteria under section 513(a)(1) of the FD&C Act. Although the device was automatically placed within class III, the De Novo classification is considered to be the initial classification of the device.

We believe this De Novo classification will enhance patients' access to beneficial innovation, in part by reducing regulatory burdens. When FDA classifies a device into class I or II via the De Novo process, the device can serve as a predicate for future devices of that type, including for 510(k)s (see 21 U.S.C. 360c(f)(2)(B)(i)). As a result, other device sponsors do not have to submit a De Novo request or premarket approval application in order to market a substantially equivalent device (see 21 U.S.C. 360c(i), defining "substantial equivalence").

Instead, sponsors can use the less-burdensome 510(k) process, when necessary, to market their device.

II. De Novo Classification

On December 1, 2016, Philips Medical Systems Nederland B.V. submitted a request for De Novo classification of the Philips IntelliSite Pathology Solution (PIPS). 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. We classify 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 that, in combination with the general controls, provide reasonable assurance of the safety and effectiveness of the device for its intended use (see 21 U.S.C. 360c(a)(1)(B)). After review of the information submitted in the request, we determined that the device can be classified into class II with the establishment of special controls. FDA has determined that these special controls, in addition to the general controls, will provide reasonable assurance of the safety and effectiveness of the device.

Therefore, on April 12, 2017, FDA issued an order to the requester classifying the device into class II. FDA is codifying the classification of the device by adding 21 CFR 864.3700. We have named the generic type of device the whole slide imaging system, and it is identified as an automated digital slide creation, viewing, and management system intended as an aid to the pathologist to review and interpret digital images of surgical pathology slides. The system generates digital images that would otherwise be appropriate for manual visualization by conventional light microscopy.

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

Table 1.--Whole Slide Imaging System Risks and Mitigation Measures

Identified Risk	Mitigation Measures/21 CFR Section
Inaccurate or missing results leading to, for example, incorrect diagnosis	General controls; Special control (1) (21 CFR 864.3700(b)(1)); and, Special control (2) (21 CFR 864.3700(b)(2))
Delayed results	General controls; Special control (1) (21 CFR 864.3700(b)(1)); and, Special control (2) (21 CFR 864.3700(b)(2))

FDA has determined that special controls, in combination with the general controls, address these risks to health and provide reasonable assurance of safety and effectiveness. For a device to fall within this classification, and thus avoid automatic classification in class III, it would have to comply with the special controls named in this final order. The necessary special controls appear in the regulation codified by this order. This device is subject to premarket notification requirements under section 510(k) of the FD&C Act.

III. Analysis of 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.

IV. Paperwork Reduction Act of 1995

This final 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 the guidance document "De Novo Classification Process (Evaluation of Automatic Class III Designation)" have been approved under OMB control number 0910-0844; the collections of information in 21 CFR part 814, subparts A through E, regarding premarket approval, have been approved under OMB control number 0910-0231; the collections of information in part 21 CFR 807, subpart E,

regarding premarket notification submissions, have been approved under OMB control number 0910-0120; and the collections of information in 21 CFR parts 801 and 809, regarding labeling, have been approved under OMB control number 0910-0485.

List of Subjects in 21 CFR Part 864

Blood, Medical devices, Packaging and containers.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 864 is amended as follows:

PART 864--HEMATOLOGY AND PATHOLOGY DEVICES

1. The authority citation for part 864 is revised to read as follows:

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

2. Add § 864.3700 to subpart D to read as follows:

§ 864.3700 Whole slide imaging system.

(a) *Identification.* The whole slide imaging system is an automated digital slide creation, viewing, and management system intended as an aid to the pathologist to review and interpret digital images of surgical pathology slides. The system generates digital images that would otherwise be appropriate for manual visualization by conventional light microscopy.

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

(1) Premarket notification submissions must include the following information:

(i) The indications for use must specify the tissue specimen that is intended to be used with the whole slide imaging system and the components of the system.

(ii) A detailed description of the device and bench testing results at the component level, including for the following, as appropriate:

(A) Slide feeder;

(B) Light source;

(C) Imaging optics;

(D) Mechanical scanner movement;

(E) Digital imaging sensor;

(F) Image processing software;

(G) Image composition techniques;

(H) Image file formats;

(I) Image review manipulation software;

(J) Computer environment; and

(K) Display system.

(iii) Detailed bench testing and results at the system level, including for the following, as appropriate:

(A) Color reproducibility;

(B) Spatial resolution;

(C) Focusing test;

(D) Whole slide tissue coverage;

(E) Stitching error; and

(F) Turnaround time.

(iv) Detailed information demonstrating the performance characteristics of the device, including, as appropriate:

(A) Precision to evaluate intra-system and inter-system precision using a comprehensive set of clinical specimens with defined, clinically relevant histologic features from various organ

systems and diseases. Multiple whole slide imaging systems, multiple sites, and multiple readers must be included.

(B) Reproducibility data to evaluate inter-site variability using a comprehensive set of clinical specimens with defined, clinically relevant histologic features from various organ systems and diseases. Multiple whole slide imaging systems, multiple sites, and multiple readers must be included.

(C) Data from a clinical study to demonstrate that viewing, reviewing, and diagnosing digital images of surgical pathology slides prepared from tissue slides using the whole slide imaging system is non-inferior to using an optical microscope. The study should evaluate the difference in major discordance rates between manual digital (MD) and manual optical (MO) modalities when compared to the reference (e.g., main sign-out diagnosis).

(D) A detailed human factor engineering process must be used to evaluate the whole slide imaging system user interface(s).

(2) Labeling compliant with 21 CFR 809.10(b) must include the following:

(i) The intended use statement must include the information described in paragraph (b)(1)(i) of this section, as applicable, and a statement that reads, "It is the responsibility of a qualified pathologist to employ appropriate procedures and safeguards to assure the validity of the interpretation of images obtained using this device."

(ii) A description of the technical studies and the summary of results, including those that relate to paragraphs (b)(1)(ii) and (iii) of this section, as appropriate.

(iii) A description of the performance studies and the summary of results, including those that relate to paragraph (b)(1)(iv) of this section, as appropriate.

(iv) A limiting statement that specifies that pathologists should exercise professional judgment in each clinical situation and examine the glass slides by conventional microscopy if there is doubt about the ability to accurately render an interpretation using this device alone.

Dated: December 26, 2017.

Leslie Kux,

Associate Commissioner for Policy.

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