4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 892

[Docket No. FDA-2018-N-1553]

Radiology Devices; Reclassification of Medical Image Analyzers

AGENCY:  Food and Drug Administration, HHS.

ACTION:  Proposed order.

SUMMARY:  The Food and Drug Administration (FDA or the Agency) is issuing this proposed order to reclassify medical image analyzers applied to mammography breast cancer, ultrasound breast lesions, radiograph lung nodules, and radiograph dental caries detection as postamendments class III (premarket approval) devices (regulated under product code MYN), into class II (special controls), subject to premarket notification.  FDA is also identifying the proposed special controls that the Agency believes are necessary to provide a reasonable assurance of safety and effectiveness of the device.  These devices are intended to direct the clinician's attention to portions of an image that may reveal abnormalities during interpretation of patient's radiology images by the clinician.  If finalized, this order will reclassify these types of devices from class III to class II and reduce regulatory burdens on industry as these types of devices will no longer be required to submit a premarket approval application (PMA) but can instead submit a less burdensome premarket notification (510(k)) before marketing their device.

DATES:  Submit either electronic or written comments on the proposed order by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].  Please see section X of this document for the proposed effective date when the new requirements apply and for the proposed effective date of a final order based on this proposed order.

ADDRESSES:  You may submit comments as follows:  Please note that late, untimely filed comments will not be considered.  Electronic comments must be submitted on or before [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].  The https://www.regulations.gov electronic filing system will accept comments until midnight Eastern Time at the end of [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].  Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

*Electronic Submissions*

Submit electronic comments in the following way:

- Federal Rulemaking Portal:  https://www.regulations.gov.  Follow the instructions for submitting comments.  Comments submitted electronically, including attachments, to https://www.regulations.gov will be posted to the docket unchanged.  Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process.  Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on https://www.regulations.gov.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

*Written/Paper Submissions*

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions):  Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD  20852.

- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

*Instructions*:  All submissions received must include the Docket No. FDA-2018-N-1553 for "Radiology Devices; Reclassification of Medical Image Analyzers."  Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at https://www.regulations.gov or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission.  You should submit two copies total.  One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION."  The Agency will review this copy, including the claimed confidential information, in its consideration of comments.  The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on https://www.regulations.gov.  Submit both copies to the Dockets Management Staff.  If you do not wish your name and contact information to be made

publicly available, you can provide this information on the cover sheet and not in the

body of your comments and you must identify this information as "confidential."

Any information marked as "confidential" will not be disclosed except in accordance

with 21 CFR 10.20 and other applicable disclosure law.  For more information about

FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015,

or access the information at:  https://www.gpo.gov/fdsys/pkg/FR-2015-09-

18/pdf/2015-23389.pdf.

*Docket*:  For access to the docket to read background documents or the electronic and

written/paper comments received, go to https://www.regulations.gov and insert the docket

number, found in brackets in the heading of this document, into the "Search" box and follow the

prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville,

MD 20852.

FOR FURTHER INFORMATION CONTACT:  Robert Ochs, Center for Devices and

Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm.

4312, Silver Spring, MD 20993-0002, 301-796-6661, Robert.Ochs@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

## I. Background--Regulatory Authorities

The Federal Food, Drug, and Cosmetic Act (the FD&C Act), as amended, establishes a

comprehensive system for the regulation of medical devices intended for human use.  Section

513 of the FD&C Act (21 U.S.C. 360c) established three categories (classes) of devices,

reflecting 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).

Devices that were not in commercial distribution prior to May 28, 1976 (generally referred to as postamendments devices), are automatically classified by section 513(f)(1) of the FD&C Act into class III without any FDA rulemaking process. Those devices remain in class III and require premarket approval unless, and until, the device is reclassified into class I or II, or FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the FD&C Act, 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 21 CFR part 807.

A postamendments device that has been initially classified in class III under section 513(f)(1) of the FD&C Act may be reclassified into class I or II under section 513(f)(3) of the FD&C Act. Section 513(f)(3) of the FD&C Act provides that FDA acting by order can reclassify the device into class I or II on its own initiative, or in response to a petition from the manufacturer or importer of the device. To change the classification of the device, the proposed new class must have sufficient regulatory controls to provide a reasonable assurance of the safety and effectiveness of the device for its intended use.

Reevaluation of the data previously before the Agency is an appropriate basis for subsequent action where the reevaluation is made in light of newly available regulatory authority (see *Bell* v. *Goddard*, 366 F.2d 177, 181 (7th Cir. 1966); *Ethicon, Inc.* v. FDA, 762 F. Supp. 382, 388-391 (D.D.C. 1991)), or in light of changes in "medical science" (*Upjohn* v. *Finch*, 422 F.2d 944, 951 (6th Cir. 1970)). Whether data before the Agency are old or new, the "new information" to support reclassification under 513(f)(3) must be "valid scientific evidence", as defined in section 513(a)(3) of the FD&C Act and 21 CFR 860.7(c)(2). (See, e.g., *General*

*Medical Co.* v. *FDA*, 770 F.2d 214 (D.C. Cir. 1985); *Contact Lens Mfrs. Assoc.* v. *FDA,* 766 F.2d 592 (D.C. Cir.1985), cert. denied, 474 U.S. 1062 (1986)). FDA relies upon "valid scientific evidence" in the classification process to determine the level of regulation for devices. To be considered in the reclassification process, the "valid scientific evidence" upon which the Agency relies must be publicly available. Publicly available information excludes trade secret and/or confidential commercial information, e.g., the contents of a pending PMA (see section 520(c) of the FD&C Act (21 U.S.C. 360j(c)).

In accordance with section 513(f)(3) of the FD&C Act, the Agency is proposing to reclassify medical image analyzers applied to mammography breast cancer, ultrasound breast lesions, radiograph lung nodules, and radiograph dental caries detection from class III into class II on the basis that there is sufficient information to establish special controls, in addition to general controls, to provide reasonable assurance of the safety and effectiveness of the device.

Section 510(m) of the FD&C Act provides that a class II device may be exempted from the 510(k) premarket notification requirements, if the Agency determines that premarket notification is not necessary to reasonably assure the safety and effectiveness of the device.

II. Regulatory History of the Devices

This proposed order covers medical image analyzers including computer-assisted/aided detection (CADe) devices for mammography breast cancer, ultrasound breast lesions, radiograph lung nodules, and radiograph dental caries detection that are assigned product code MYN. These postamendments devices are currently regulated as class III devices under section 513(f)(1) of the FD&C Act. FDA has experience reviewing and analyzing data and information for medical image analyzers since premarket approval of the first device for these uses in 1998. On June 26, 1998, the Center for Devices and Radiological Health (CDRH) approved the first CADe device

included in this reclassification order. In the December 30, 1998, *Federal Register* notice (63 FR 71930), FDA announced a PMA approval order for R2 Technology, Inc. M 1000 Image Checker and the availability of the summary of safety and effectiveness data for the device. Since 1998, 11 devices have received premarket approval for the analysis of several modalities, including mammography, ultrasound, as well as chest and dental radiographs. Based upon our review experience and consistent with the FD&C Act and FDA's regulations, FDA believes that these devices should be reclassified from class III into class II because there is sufficient information to establish special controls that can provide reasonable assurance of the device's safety and effectiveness.

This proposed order does not apply to medical image analyzers/CADe devices currently classified under § 892.2050 (21 CFR 892.2050), *Picture archiving and communication system.* FDA has regulated other CADe devices intended to aid lung nodule and colon polyp detection from computed tomography images as class II devices under § 892.2050, *Picture archiving and communication system* and assigned the following product codes:

- NWE (Colon Computed Tomography System, Computer-Aided Detection);
- OEB (Lung Computed Tomography System, Computer-Aided Detection);
- OMJ (Chest X-Ray Computer Aided Detection).

There have been no recalls for class II CADe devices. As of the date of this proposal, FDA has received three recalls for class III devices and one Medical Device Report (MDR), however, in the past 10 years only one recall for the class III devices has been received due to distribution of the CADe device without PMA approval. None of these recalls were classified as a Class I recall. There were also no MDRs related to either the class III medical image analyzers or class II CADe devices in the past 10 years. This evidence suggests that the safety profiles for

existing class III CADe devices are similar to the class II CADe, and consequently that our regulatory controls applied should be similar.

## III. Device Description

This proposed order applies to medical image analyzers including CADe devices for mammography breast cancer, ultrasound breast lesions, radiograph lung nodules, and radiograph dental caries detection that are currently regulated as class III devices as postamendment devices. These devices are intended to identify, mark, highlight, or in any other manner direct the clinicians' attention to portions of a radiology image that may reveal abnormalities during interpretation of patient radiology images by the clinicians. These devices incorporate pattern recognition and data analysis capabilities and operate on previously acquired radiology images, including mammography, radiograph, and ultrasound. These devices are not intended to replace the review by a qualified radiologist or to be used for triage. Furthermore, these devices are not intended to recommend diagnosis of any diseases.

## IV. Proposed Reclassification

The Radiological Devices Panel (the Panel) convened on March 4-5, 2008 (Ref. 1) and discussed issues relating to how medical image analyzers including CADe devices are used in clinical decisionmaking, how the performance of the devices should be evaluated, and the information needed to determine whether the device provides a reasonable assurance of its safety and effectiveness. Additional discussions were held regarding medical image analyzers for mammography and radiograph applications. Following the 2008 Panel Meeting, FDA convened a second meeting of the Panel on November 18, 2009. The 2009 Panel Meeting was asked to discuss two proposed draft guidances for the evaluation of medical image analyzers and the Agency's regulatory strategy for these devices (Ref. 2). Subsequently, the two draft guidance

documents were finalized by FDA and were made public on July 3, 2012 (Refs. 3 and 4). The

guidance document entitled "Clinical Performance Assessment: Considerations for Computer-

Assisted Detection Devices Applied to Radiology Images and Radiology Device Data--

Premarket Approval (PMA) and Premarket Notification [510(k)] Submissions" provides

guidance regarding clinical performance assessment studies for CADe applied to radiology

images and radiology device data. The guidance document entitled "Computer-Assisted

Detection Devices Applied to Radiology Images and Radiology Device Data--Premarket

Notification [510(k)] Submissions" provides guidance regarding premarket notification (510(k))

submissions for CADe applied to radiology images and radiology device data. These guidance

documents describe clinical and non-clinical methods to evaluate the safety and effectiveness of

CADe devices, including medical image analyzers covered by this proposed order. In addition to

the two guidance documents, the Panel's discussion regarding the benefits and risks of medical

image analyzers that were discussed at the 2008 and 2009 Panel meetings have been taken into

consideration by the Agency when developing the proposed special controls provided in this

proposed order below.

Since publication of these guidance documents, the Agency has gained considerable

experience in reviewing medical image analyzers using the methods described in the

aforementioned guidance documents. Further, as part CDRH's 2014-2015 strategic priority

"Strike the Right Balance Between Premarket and Postmarket Data Collection," a retrospective

review of class III devices subject to a PMA was completed to determine whether or not, based

on our current understanding of the technology, reclassification may be appropriate. During this

retrospective review, FDA determined that sufficient information exists such that the risks of

false positive and false negative results, misuse, and device failure can be mitigated, to establish

special controls that, together with general controls, can provide a reasonable assurance of the safety and effectiveness of medical image analyzers and therefore proposes these devices be reclassified from class III to class II. On April 29, 2015, FDA published a notice in the *Federal Register* entitled "Retrospective Review of Premarket Approval Application Devices; Striking the Balance Between Premarket and Postmarket Data Collection" in which FDA announced plans to consider reclassifying medical image analyzers identified with the MYN product code from class III to class II (80 FR 23798). No adverse comments were received regarding our proposed intent for MYN.

In accordance with section 513(f)(3) of the FD&C Act and 21 CFR part 860, subpart C, FDA is proposing to reclassify postamendments medical image analyzers, including CADe devices for mammography breast cancer, ultrasound breast lesions, radiograph lung nodules, and radiograph dental caries detection, from class III into class II. FDA believes that there is sufficient information to establish special controls, in addition to general controls, that would effectively mitigate the risks to health identified in section V and provide reasonable assurance of the safety and effectiveness of these devices. Absent the special controls identified in this proposed order, general controls applicable to the device are insufficient to provide reasonable assurance of the safety and effectiveness of the device.

FDA is proposing to create a separate classification regulation for medical image analyzer devices that will be reclassified from class III to II. Under this proposed order, if finalized, the medical image analyzer devices will be identified as a prescription device. As such, the prescription device must satisfy prescription labeling requirements (see § 801.109 (21 CFR 801.109), *Prescription devices*). Prescription devices are exempt from the requirement for adequate directions for use for the layperson under section 502(f)(1) of the FD&C Act (21

U.S.C. 352) and § 801.5 (21 CFR 801.5), as long as the conditions of § 801.109 are met.  In this

proposed order, if finalized, the Agency has identified the special controls under section

513(a)(1)(B) of the FD&C Act that, together with general controls, will provide a reasonable

assurance of the safety and effectiveness for medical image analyzer 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 safety and effectiveness

and, therefore, does not intend to exempt these proposed class II devices from the premarket

notification requirements.  Persons who intend to market this type of device must submit to FDA

a 510(k) and receive clearance prior to marketing the device.

This proposal, if finalized, will decrease regulatory burden on the medical device industry

and will reduce private costs and expenditures required to comply with Federal Regulations.

Specifically, regulated industry will no longer have to submit a PMA but can instead submit a

510(k) to the Agency for review prior to marketing their device.  A 510(k) is a less-burdensome

pathway to market a device which typically results in a more timely premarket review compared

to a PMA and reduces the regulatory burden on industry in addition to providing more timely

access of these types of devices to patients.

V. Risks to Health

From the Panel discussions on March 4-5, 2008, and November 18, 2009, along with the

peer-reviewed literature (Refs. 5-8) and FDA's experiences over the years in reviewing

submissions for these devices and similar devices, FDA determined the probable risks to health

associated with medical image analyzers including CADe devices for mammography breast cancer, ultrasound breast lesions, radiograph lung nodules, and radiograph dental caries detection are as follows: (1) false positive results may result in complications, such as incorrect management of the patient with possible adverse effects, and unnecessary additional radiology imaging and/or invasive procedures, such as biopsy; (2) false negative results could result in complications, including incorrect diagnosis and delay in disease management; (3) the device could be misused to analyze images from an unintended patient population or on images acquired with incompatible imaging hardware or incompatible image acquisition parameters, resulting in possibly lower device performance; (4) the device could be misused by not following the appropriate reading protocol, which may lead to lower sensitivity; and (5) device failure could result in the absence or delay of device output, or incorrect device output, which could likewise lead to inaccurate patient assessment.

## VI. Summary of the Reasons for Reclassification

After considering the information above, FDA has determined that all class III medical image analyzers currently approved by FDA should be reclassified into class II on the basis that special controls, in addition to general controls, can be established to provide reasonable assurance of the safety and effectiveness of the device. FDA believes that the risks to health associated with medical image analyzers applied to mammography breast cancer, ultrasound breast lesions, radiograph lung nodules, and radiograph dental caries detection can be mitigated with special controls and that these mitigations will provide a reasonable assurance of its safety and effectiveness. FDA's reasons for reclassification of these devices are as follows:

- The risk of false positive results and false negative results can be mitigated by demonstrating, through clinical performance assessment (e.g., reader studies), that reader

performance improves when using the medical image analyzer. In instances where a medical image analyzer has the same intended use but has different technological characteristics compared to the legally marketed device (predicate), a performance comparison of the predicate and new device evaluating with the same assessment process on the same dataset that is representative of the intended population may be sufficient to demonstrate device safety and effectiveness. The risk of false positive results and false negative results can be further mitigated by special controls that require sufficient information in labeling to provide detailed instructions for use to the user and inform the user of the expected device performance on a dataset representative of the intended population.

- The risk associated with misuse of the medical image analyzers on an unintended population can be mitigated by specifying in the labeling and indications for use of the device the intended patient population for which the device has been demonstrated to be effective. This risk can be further mitigated by special controls that require informing intended users in the labeling of foreseeable situations in which the device is likely to fail or not to operate at its expected performance level.

- The risk associated with misuse of the medical image analyzer on images acquired from unintended image acquisition hardware or image acquisition parameters can be mitigated by special controls that require including in the device labeling specifications for compatible imaging hardware and imaging protocols.

- The risk resulting from not following the intended reading protocol can be mitigated by including in the labeling the indications for use of the device, by providing adequate instructions for use including a description of the intended reading protocol, and by

special controls requiring that the device labeling provide a detailed description of user training that addresses appropriate reading protocols for the device.

- The risk of device failure can be mitigated by requiring design verification and validation testing, and special controls that require device operating instructions. This risk can be further mitigated by special controls that require informing users in the labeling of foreseeable situations in which the device is likely to fail or not to operate at its expected performance level.

## VII. Proposed Special Controls

FDA believes that the following special controls, in addition to general controls, are sufficient to mitigate the risks to health described in section V and provide a reasonable assurance of safety and effectiveness for these medical image analyzers:

- Design verification and validation must include detailed descriptions of image analysis algorithms, detailed descriptions of study protocols and datasets, results from performance testing demonstrating the device improves reader performance in the intended use population, standalone performance testing protocols and results, and appropriate software documentation. Performance testing ensures that the risk of false positive and false negative results is reduced.

- Labeling for the device must include detailed descriptions of the following: patient population, the intended reading protocol, the intended user and user training, device inputs and outputs, compatible imaging hardware and imaging protocols. In addition, the labeling for the device must also include applicable warnings, limitations, precautions, device operating instructions, and a detailed summary of the performance testing. Detailed instructions for use and expected device performance on a dataset representative

of the intended population in labeling helps minimize the risk of false positive and false

negative results.  Labeling ensures proper use of the device, including warnings to inform

users of foreseeable situations in which the device is likely to fail or not to operate at its

expected performance level.

Table 1 shows how FDA believes the special controls set forth in the proposed order will

mitigate each of the risks to health described in section V.

Table 1.--Risks to Health and Mitigation Measures for Medical Image Analyzers

| Identified Risk to Health | Mitigation Measures/21 CFR Section |
| --- | --- |
| False positive results | Special controls 1 (21 CFR 892.2070(b)(1)) and 2 (21 CFR 892.2070(b)(2)) |
| False negative results | Special controls 1 (21 CFR 892.2070(b)(1)) and 2 (21 CFR 892.2070(b)(2)) |
| Device misuse (analyzing images from an unintended patient population, images acquired with incompatible imaging hardware, or incompatible image acquisition parameters) resulting in possibly lower device performance | Special control 2 (21 CFR 892.2070(b)(2)) |
| Device misuse (not following the appropriate reading protocol) which may lead to lower sensitivity | Special control 2 (21 CFR 892.2070(b)(2)) |
| Device failure | Special control 2 (21 CFR 892.2070(b)(2)) |

In addition, FDA is proposing to limit these devices to prescription use under § 801.109.

Prescription devices are exempt from the requirement for adequate directions for use for the

layperson under section 502(f)(1) of the FD&C Act and § 801.5, as long as the conditions of

§ 801.109 are met (referring to 21 U.S.C. 352(f)(1)).  Under § 807.81, the device would continue

to be subject to 510(k) notification requirements.

If this proposed order is finalized, medical image analyzers including CADe devices for

mammography breast cancer, ultrasound breast lesions, radiograph lung nodules, and radiograph

dental caries detection will be reclassified into class II.  The reclassification will be codified in

§ 892.2070.  FDA believes that adherence to the proposed special controls, in addition to the

general controls, is necessary to provide a reasonable assurance of the safety and effectiveness of the devices. FDA intends to update the guidance document entitled "Clinical Performance Assessment: Considerations for Computer-Assisted Detection Devices Applied to Radiology Images and Radiology Device Data--Premarket Approval (PMA) and Premarket Notification [510(k)] Submissions" to make it consistent with this reclassification upon finalization of this proposed reclassification order.

## VIII. 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.

## IX. Paperwork Reduction Act of 1995

FDA tentatively concludes that this proposed order contains no new collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3520) is not required. This proposed order refers to previously approved collections of information found in other FDA regulations. These collections of information are subject to review by OMB under the PRA. The collections of information in 21 CFR part 807, subpart E have been approved under OMB control number 0910-0120 and the collections of information in 21 CFR part 801 have been approved under OMB control number 0910-0485.

## X. Proposed Effective Date

FDA proposes that any final order based on this proposed order become effective 30 days after its date of publication in the *Federal Register*.

## XI. References

The following references are on display in the Dockets Management Staff (see

ADDRESSES) and are available for viewing by interested persons between 9 a.m. and 4 p.m.,

Monday through Friday; they are also available electronically at https://www.regulations.gov.

FDA has verified the website addresses, as of the date this document publishes in the *Federal*

*Register*, but websites are subject to change over time.

1. Transcript of the FDA Radiological Devices Panel Meeting, March 4-5, 2008

(available at:

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfAdvisory/results.cfm?panel=24&searchtyp

e=1&month=0&year=&maxrows=10).

2. Transcript of the FDA Radiological Devices Panel Meeting, November 18, 2009

(available at: https://wayback.archive-

it.org/7993/20170404002254/https://www.fda.gov/downloads/AdvisoryCommittees/Committees

MeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/RadiologicalDevicesPan

el/UCM197419.pdf).

3. "Guidance for Industry and Food and Drug Administration Staff--Computer-Assisted

Detection Devices Applied to Radiology Images and Radiology Device Data--Premarket

Notification [510(k)] Submissions," issued July 3, 2012

(https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocu

ments/ucm187294.pdf).

4. "Guidance for Industry and FDA Staff--Clinical Performance Assessment:

Considerations for Computer-Assisted Detection Devices Applied to Radiology Images and

Radiology Device Data--Premarket Approval (PMA) and Premarket Notification [510(k)]

Submissions," issued July 3, 2012

(https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm187315.pdf).

5.  Dromain, C., B. Boyer, R. Ferré, et al., "Computed-Aided Diagnosis (CAD) in the Detection of Breast Cancer," *European Journal of Radiology*, 82(3): 417-423 (2013).

6. Fenton, J.J., G. Xing, J.G. Elmore, et al., "Short-Term Outcomes of Screening Mammography Using Computer-Aided Detection:  A Population-Based Study of Medicare Enrollees," *Annals of Internal Medicine*, 158: 580-587 (2013).

7. Gur, D., J.H. Sumkin, H.E. Rockette, et al., "Changes in Breast Cancer Detection and Mammography Recall Rates After the Introduction of a Computer-Aided Detection System," *Journal of the National Cancer Institute*, 96: 185-190 (2004).

8. Noble M., W. Bruening, S. Uhl, and K. Schoelles, "Computer-Aided Detection Mammography for Breast Cancer Screening: Systematic Review and Meta-Analysis," *Archives of Gynecology and Obstetrics*, 279(6):881-90 (2009).

List of Subjects in 21 CFR Part 892

Radiology devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 892 be amended as follows:

PART 892--RADIOLOGY DEVICES

1. The authority citation for part 892 continues to read as follows:

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

2. Add § 892.2070 to subpart B to read as follows:

§ 892.2070  Medical image analyzer.

(a) *Identification*.  Medical image analyzers, including computer-assisted/aided detection (CADe) devices for mammography breast cancer, ultrasound breast lesions, radiograph lung nodules, and radiograph dental caries detection, is a prescription device that is intended to identify, mark, highlight, or in any other manner direct the clinicians' attention to portions of a radiology image that may reveal abnormalities during interpretation of patient radiology images by the clinicians.  This device incorporates pattern recognition and data analysis capabilities and operates on previously acquired medical images.  This device is not intended to replace the review by a qualified radiologist, and is not intended to be used for triage, or to recommend diagnosis.

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

(1) Design verification and validation must include:

(i) A detailed description of the image analysis algorithms including a description of the algorithm inputs and outputs, each major component or block, and algorithm limitations.

(ii) A detailed description of pre-specified performance testing methods and dataset(s) used to assess whether the device will improve reader performance as intended and to characterize the standalone device performance.  Performance testing includes one or more standalone tests, side-by-side comparisons, or a reader study, as applicable.

(iii) Results from performance testing that demonstrate that the device improves reader performance in the intended use population when used in accordance with the instructions for use.  The performance assessment must be based on appropriate diagnostic accuracy measures (e.g., receiver operator characteristic plot, sensitivity, specificity, predictive value, and diagnostic likelihood ratio).  The test dataset must contain a sufficient number of cases from important cohorts (e.g., subsets defined by clinically relevant confounders, effect modifiers, concomitant

diseases, and subsets defined by image acquisition characteristics) such that the performance estimates and confidence intervals of the device for these individual subsets can be characterized for the intended use population and imaging equipment.

(iv) Appropriate software documentation (e.g., device hazard analysis; software requirements specification document; software design specification document; traceability analysis; description of verification and validation activities including system level test protocol, pass/fail criteria, and results; and cybersecurity).

(2) Labeling must include the following:

(i) A detailed description of the patient population for which the device is indicated for use.

(ii) A detailed description of the intended reading protocol.

(iii) A detailed description of the intended user and user training that addresses appropriate reading protocols for the device.

(iv) A detailed description of the device inputs and outputs.

(v) A detailed description of compatible imaging hardware and imaging protocols.

(vi) Discussion of warnings, precautions, and limitations must include situations in which the device may fail or may not operate at its expected performance level (e.g., poor image quality or for certain subpopulations), as applicable.

(vii) Device operating instructions.

(viii) A detailed summary of the performance testing, including: test methods, dataset characteristics, results, and a summary of sub-analyses on case distributions stratified by relevant confounders, such as lesion and organ characteristics, disease stages, and imaging equipment.

Dated: May 29, 2018.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2018-11880 Filed: 6/1/2018 8:45 am; Publication Date:  6/4/2018]