

**(i) Terminating Action for Certain Requirements of AD 2014–25–52**

For airplanes with an AOA configuration as identified in figure 1 to paragraph (i) of

this AD, or as identified in paragraph (m)(2) of AD 2016–12–15, Amendment 39–18564 (81 FR 40160, June 21, 2016) (“AD 2016–12–15”), as applicable: Accomplishing the upgrade required by paragraph (h) of this AD

terminates the requirements of paragraph (g) of AD 2014–25–52, and the airplane flight manual (AFM) procedure required by paragraph (g) of AD 2014–25–52 may be removed from the AFM.

**Figure 1 to paragraph (i) of this AD – AOA Sensor Installation Configurations**

AOA Sensor P/N – Captain	AOA Sensor P/N - First Officer	AOA Sensor P/N - Standby
C16291AB or C16291AA	C16291AB or C16291AA	C16291AB, C16291AA, 0861ED or 0861ED2
Note: For AOA sensor P/N C16291AA, paragraph (j) of AD 2016-12-15 requires detailed inspections and a functional heating test of that sensor.		

**(j) Terminating Action for Certain Requirements of AD 2016–25–30**

Accomplishment of the actions required by paragraph (h) of this AD terminates the requirements of paragraph (g) of AD 2016–25–30 for that airplane.

**(k) Parts Installation Prohibition**

Installation of any software or hardware of a version earlier than the one listed in table 1 to paragraphs (h) and (k) of this AD is prohibited, as required by paragraphs (k)(1) and (k)(2) of this AD, as applicable.

(1) For Group 1 airplanes: After modification of an airplane as required by paragraph (h) of this AD.

(2) For Group 2 airplanes: As of the effective date of this AD.

**(l) Other FAA AD Provisions**

The following provisions also apply to this AD:

(1) *Alternative Methods of Compliance (AMOCs)*: The Manager, International Section, Transport Standards Branch, FAA, has the authority to approve AMOCs for this AD, if requested using the procedures found in 14 CFR 39.19. In accordance with 14 CFR 39.19, send your request to your principal inspector or local Flight Standards District Office, as appropriate. If sending information directly to the manager of the International Branch, send it to the attention of the person identified in paragraph (m)(2) of this AD. Information may be emailed to: [9-ANM-116-AMOC-REQUESTS@faa.gov](mailto:9-ANM-116-AMOC-REQUESTS@faa.gov). Before using any approved AMOC, notify your appropriate principal inspector, or lacking a principal inspector, the manager of the local flight standards district office/certificate holding district office.

(2) *Contacting the Manufacturer*: For any requirement in this AD to obtain corrective actions from a manufacturer, the action must be accomplished using a method approved by the Manager, International Section, Transport Standards Branch, FAA; or the European Aviation Safety Agency (EASA); or EASA Design Organization Approval (DOA). If approved by the DOA, the approval must include the DOA-authorized signature.

(3) *Required for Compliance (RC)*: If any service information contains procedures or tests that are identified as RC, those procedures and tests must be done to comply with this AD; any procedures or tests that are not identified as RC are recommended. Those procedures and tests that are not identified as RC may be deviated from using accepted methods in accordance with the operator’s maintenance or inspection program without obtaining approval of an AMOC, provided the procedures and tests identified as RC can be done and the airplane can be put back in an airworthy condition. Any substitutions or changes to procedures or tests identified as RC require approval of an AMOC.

**(m) Related Information**

(1) Refer to Mandatory Continuing Airworthiness Information (MCAI) EASA Airworthiness Directive 2017–0246R1, dated April 6, 2018, for related information. This MCAI may be found in the AD docket on the internet at <http://www.regulations.gov> by searching for and locating Docket No. FAA–2018–0498.

(2) For more information about this AD, contact Vladimir Ulyanov, Aerospace Engineer, International Section, Transport Standards Branch, FAA, 2200 South 216th St., Des Moines, WA 98198; telephone and fax 206–231–3229.

(3) For service information identified in this AD, contact Airbus SAS, Airworthiness Office—EAL, 1 Rond Point Maurice Bellonte, 31707 Blagnac Cedex, France; telephone +33 5 61 93 36 96; fax +33 5 61 93 45 80; email [airworthiness.A330-A340@airbus.com](mailto:airworthiness.A330-A340@airbus.com); internet <http://www.airbus.com>. You may view this service information at the FAA, Transport Standards Branch, 2200 South 216th St., Des Moines, WA. For information on the availability of this material at the FAA, call 206–231–3195.

Issued in Des Moines, Washington, on May 23, 2018.

**James Cashdollar,**

*Acting Director, System Oversight Division, Aircraft Certification Service.*

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**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 August 3, 2018. 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 August 3, 2018. The <https://www.regulations.gov> electronic filing system will accept comments until midnight Eastern Time at the end of August 3, 2018. 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](mailto: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 (DC 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 postamendment 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&searchtype=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/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/RadiologicalDevicesPanel/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/GuidanceDocuments/cm187294.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).
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#### 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, 360l, 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 6-1-18; 8:45 am]

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## ENVIRONMENTAL PROTECTION AGENCY

### 40 CFR Part 52

[EPA-R04-OAR-2018-0073; FRL-9978-92—Region 4]

#### Air Plan Approval; SC; Regional Haze Plan and Prong 4 (Visibility) for the 2012 PM<sub>2.5</sub>, 2010 NO<sub>2</sub>, 2010 SO<sub>2</sub>, and 2008 Ozone NAAQS

**AGENCY:** Environmental Protection Agency (EPA).

**ACTION:** Proposed rule.

**SUMMARY:** The Environmental Protection Agency (EPA) is proposing to take the following four actions regarding the South Carolina State Implementation Plan (SIP): Approve the portion of South Carolina's September 5, 2017, SIP submittal seeking to change reliance from the Clean Air Interstate Rule (CAIR) to the Cross-State Air Pollution Rule (CSAPR) for certain regional haze requirements; convert EPA's limited approval/limited disapproval of South Carolina's regional haze plan to a full approval; remove EPA's Federal Implementation Plan (FIP) for South Carolina, which replaced reliance on CAIR with reliance on CSAPR to address the deficiencies identified in the limited disapproval of South Carolina's regional haze plan; and convert the conditional approvals of the visibility prong of South Carolina's infrastructure SIP submittals for the 2012 Fine Particulate Matter (PM<sub>2.5</sub>), 2010 Nitrogen Dioxide (NO<sub>2</sub>), 2010 Sulfur Dioxide (SO<sub>2</sub>), and 2008 8-hour Ozone National Ambient Air Quality Standards (NAAQS) to full approvals. **DATES:** Comments must be received on or before July 5, 2018.

**ADDRESSES:** Submit your comments, identified by Docket ID No. EPA-R04-OAR-2018-0073 at <http://www.regulations.gov>. Follow the online instructions for submitting comments. Once submitted, comments cannot be edited or removed from *Regulations.gov*. EPA may publish any comment received to its public docket. Do not submit electronically any information you consider to be Confidential Business Information (CBI) or other information

whose disclosure is restricted by statute. Multimedia submissions (audio, video, etc.) must be accompanied by a written comment. The written comment is considered the official comment and should include discussion of all points you wish to make. EPA will generally not consider comments or comment contents located outside of the primary submission (*i.e.*, on the web, cloud, or other file sharing system). For additional submission methods, the full EPA public comment policy, information about CBI or multimedia submissions, and general guidance on making effective comments, please visit <http://www2.epa.gov/dockets/commenting-epa-dockets>.

#### FOR FURTHER INFORMATION CONTACT:

Michele Notarianni, Air Regulatory Management Section, Air Planning and Implementation Branch, Air, Pesticides and Toxics Management Division, U.S. Environmental Protection Agency, Region 4, 61 Forsyth Street SW, Atlanta, Georgia 30303-8960. Ms. Notarianni can be reached by telephone at (404) 562-9031 or via electronic mail at [notarianni.michele@epa.gov](mailto:notarianni.michele@epa.gov).

#### SUPPLEMENTARY INFORMATION:

##### I. Background

##### A. Regional Haze Plans and Their Relationship With CAIR and CSAPR

Section 169A(b)(2)(A) of the Clean Air Act (CAA or Act) requires states to submit regional haze plans that contain such measures as may be necessary to make reasonable progress towards the natural visibility goal, including a requirement that certain categories of existing major stationary sources built between 1962 and 1977 procure, install, and operate Best Available Retrofit Technology (BART) as determined by the state. Under the Regional Haze Rule (RHR), states are directed to conduct BART determinations for such "BART-eligible" sources that may be anticipated to cause or contribute to any visibility impairment in a Class I area. Rather than requiring source-specific BART controls, states also have the flexibility to adopt an emissions trading program or other alternative program as long as the alternative provides greater reasonable progress towards improving visibility than BART. See 40 CFR 51.308(e)(2). EPA provided states with this flexibility in the RHR, adopted in 1999, and further refined the criteria for assessing whether an alternative program provides for greater reasonable progress in two subsequent rulemakings. See 64 FR 35714 (July 1, 1999); 70 FR 39104 (July 6, 2005); 71 FR 60612 (October 13, 2006).

EPA demonstrated that CAIR would achieve greater reasonable progress than BART in revisions to the regional haze program made in 2005.<sup>1</sup> See 70 FR 39104 (July 6, 2005). In those revisions, EPA amended its regulations to provide that states participating in the CAIR cap-and-trade programs pursuant to an EPA-approved CAIR SIP or states that remain subject to a CAIR FIP need not require affected BART-eligible electric generating units (EGUs) to install, operate, and maintain BART for emissions of SO<sub>2</sub> and nitrogen oxides (NO<sub>x</sub>). As a result of EPA's determination that CAIR was "better-than-BART," a number of states in the CAIR region, including South Carolina, relied on the CAIR cap-and-trade programs as an alternative to BART for EGU emissions of SO<sub>2</sub> and NO<sub>x</sub> in designing their regional haze plans. These states also relied on CAIR as an element of a long-term strategy (LTS) for achieving their reasonable progress goals (RPGs) for their regional haze programs. However, in 2008, the United States Court of Appeals for the District of Columbia Circuit (D.C. Circuit) remanded CAIR to EPA without vacatur to preserve the environmental benefits provided by CAIR. *North Carolina v. EPA*, 550 F.3d 1176, 1178 (DC Cir. 2008). On August 8, 2011 (76 FR 48208), acting on the D.C. Circuit's remand, EPA promulgated CSAPR to replace CAIR and issued FIPs to implement the rule in CSAPR-subject states.<sup>2</sup> Implementation of CSAPR was scheduled to begin on January 1, 2012, when CSAPR would have superseded the CAIR program.

Due to the D.C. Circuit's 2008 ruling that CAIR was "fatally flawed" and its resulting status as a temporary measure following that ruling, EPA could not fully approve regional haze plans to the extent that they relied on CAIR to satisfy the BART requirement and the

<sup>1</sup> CAIR created regional cap-and-trade programs to reduce SO<sub>2</sub> and NO<sub>x</sub> emissions in 27 eastern states (and the District of Columbia), including South Carolina, that contributed to downwind nonattainment or interfered with maintenance of the 1997 8-hour ozone NAAQS or the 1997 PM<sub>2.5</sub> NAAQS.

<sup>2</sup> CSAPR requires 28 eastern states to limit their statewide emissions of SO<sub>2</sub> and/or NO<sub>x</sub> in order to mitigate transported air pollution unlawfully impacting other states' ability to attain or maintain four NAAQS: The 1997 ozone NAAQS, the 1997 annual PM<sub>2.5</sub> NAAQS, the 2006 24-hour PM<sub>2.5</sub> NAAQS, and the 2008 8-hour ozone NAAQS. The CSAPR emissions limitations are defined in terms of maximum statewide "budgets" for emissions of annual SO<sub>2</sub>, annual NO<sub>x</sub>, and/or ozone-season NO<sub>x</sub> by each covered state's large EGUs. The CSAPR state budgets are implemented in two phases of generally increasing stringency, with the Phase 1 budgets applying to emissions in 2015 and 2016 and the Phase 2 budgets applying to emissions in 2017 and later years.