September 20, 2022

Imagen Technologies, Inc
% Robert Lindsey
Chief Science Officer
151 West 26th Street, 10th Floor
NEW YORK NY 10001

Re: K213353
Trade/Device Name: Aorta-CAD
Regulation Number: 21 CFR 892.2070
Regulation Name: Medical Image Analyzer
Regulatory Class: Class II
Product Code: MYN
Dated: August 15, 2022
Received: August 15, 2022

Dear Robert Lindsey:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part

801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Laurel Burk, Ph.D.
Assistant Director
Diagnostic X-Ray Systems Team
DHT8B: Division of Radiological Imaging
Devices and Electronic Products
OHT8: Office of Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K213353

Device Name
Aorta-CAD

Indications for Use *(Describe)*
Aorta-CAD is a computer-assisted detection (CADe) software device that analyzes chest radiograph studies for suspicious regions of interest (ROIs). The device uses a deep learning algorithm to identify ROIs and produces boxes around the ROIs. The boxes are labeled with one of the following radiographic findings: Aortic calcification or Dilated aorta.

Aorta-CAD is intended for use as a concurrent reading aid for physicians looking for ROIs with radiographic findings suggestive of Aortic Atherosclerosis or Aortic Ectasia. It does not replace the role of the physician or of other diagnostic testing in the standard of care. Aorta-CAD is indicated for adults only.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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In accordance with 21 CFR 807.87(h) (and 21 CFR 807.92) the 510(k) Summary for Aorta-CAD is provided below.

1. SUBMITTER

Applicant:	Imagen Technologies, Inc. 594 Broadway, #701 New York, NY 10012
Contact and Primary Correspondent:	Robert Lindsey, Ph.D. Chief Technology Officer Imagen Technologies, Inc. 594 Broadway, #701 New York, NY 10012 917-830-4721 rob@imagen.ai
Secondary Correspondent:	Alex J. Cadotte, Ph.D. Director, Software & Digital Health MCRA 803 7th Street, NW, 3rd Floor Washington, DC 20001 202-742-3828 acadotte@mcra.com
Date Prepared:	September 13, 2022

2. DEVICE

Device Trade Name:	Aorta-CAD
Device Common Name or Classification Name:	Medical Image Analyzer
Regulation:	21 CFR 892.2070
Regulatory Class:	II
Product Code:	MYN

3. PREDICATE DEVICE

Imagen Technologies' Chest-CAD has been identified as the predicate device for Aorta-CAD.

4. DEVICE DESCRIPTION

Aorta-CAD is computer-assisted detection (CADe) software designed for physicians to increase the accurate detection of findings on chest radiographs that are suggestive of chronic conditions in the aorta. The ROIs are labeled with one of the following radiographic findings: Aortic calcification or Dilated aorta. Aorta-CAD is intended for use as a concurrent reading aid for physicians looking for suspicious ROIs with radiographic findings suggestive of Aortic Atherosclerosis or Aortic Ectasia. Aorta-CAD's output is available for physicians as a concurrent reading aid and does not replace the role of the physician or of other diagnostic testing in the standard of care for the distinct conditions. Aorta-CAD uses modern deep learning and computer vision techniques to analyze chest radiographs.

For each image within a study, Aorta-CAD generates a DICOM Presentation State file (output overlay). If any ROI is detected by Aorta-CAD in the study, the output overlay for each image includes which radiographic finding(s) were identified and what chronic condition in the aorta is suggested by these findings, such as "Aortic calcification suggestive of Aortic Atherosclerosis." In addition, if ROI(s) are detected in an image, bounding boxes surrounding each detected ROI are included in the output overlay for that image and are labeled with the radiographic findings, such as "Aortic calcification". If no ROI is detected by Aorta-CAD in the study, the output overlay for each image will include the text "No Aorta-CAD ROI(s)" and no bounding boxes will be included. Regardless of whether an ROI is detected, the overlay includes text identifying the X-ray study as analyzed by Aorta-CAD and a customer configurable message containing a link to our instructions for users to access labeling documents. The Aorta-CAD overlay can be toggled on or off by the physician within their Picture Archiving and Communication System (PACS) viewer, allowing for concurrent review of the X-ray study.

5. INTENDED USE/INDICATIONS FOR USE

Aorta-CAD is a computer-assisted detection (CADe) software device that analyzes chest radiograph studies for suspicious regions of interest (ROIs). The device uses a deep learning algorithm to identify ROIs and produce boxes around the ROIs. The boxes are labeled with one of the following radiographic findings: Aortic calcification or Dilated aorta.

Aorta-CAD is intended for use as a concurrent reading aid for physicians looking for ROIs with radiographic findings suggestive of Aortic Atherosclerosis or Aortic Ectasia. It does not replace the role of the physician or of other diagnostic testing in the standard of care. Aorta-CAD is indicated for adults only.

6. SUBSTANTIAL EQUIVALENCE

Comparison of Indications

The predicate device for Aorta-CAD is Chest-CAD (K210666). Chest-CAD has the following FDA-cleared Indications for Use:

> *Chest-CAD is a computer-assisted detection (CADe) software device that analyzes chest radiograph studies using machine learning techniques to identify, categorize, and highlight suspicious regions of interest (ROI). Any suspicious ROI identified by Chest-CAD is assigned to one of the following categories: Cardiac, Mediastinum/Hila, Lungs, Pleura, Bones, Soft Tissues, Hardware, or Other. The device is intended for use as a concurrent reading aid for physicians. Chest-CAD is indicated for adults only.*

Chest-CAD and Aorta-CAD both analyze chest radiographs and both detect ROIs in the chest. Both devices identify and categorize ROIs. Chest-CAD and Aorta-CAD are indicated for use as a concurrent reading aid. Both devices are intended as an aid to the physician and not intended to replace the role of the physician or of other diagnostic testing in the standard of care. The differences in Indications for Use do not constitute a new intended use, as both devices are intended to assist physicians by identifying and marking ROIs in chest radiographs.

Technological Comparisons

Table 1 provides a comparison of the Technological Characteristics of Aorta-CAD to the predicate Chest-CAD.

Table 1: Technological Comparison

	Proposed Device	**Predicate**
Number	TBD	K210666
Applicant	Imagen Technologies, Inc.	Imagen Technologies, Inc.
Device Name	Aorta-CAD	Chest-CAD
Classification Regulation	892.2070	892.2070
Product Code	MYN	MYN
Image Modality	X-ray	X-ray
Study Type	Chest	Chest
Clinical Output	Identify and mark regions of interest (ROIs) on chest radiographs and label the box around the ROI as one of the following: Aortic calcification or Dilated aorta.	Identify and mark regions of interest (ROIs) on chest radiographs and label the box around the ROI as one of the following: Cardiac, Mediastinum/Hila, Lungs, Pleura, Bones, Soft Tissues, Hardware, or Other.

	Proposed Device	Predicate
Intended Users	Physicians	Physicians
Intended User Workflow	Device intended for use as a concurrent reading aid for physicians interpreting chest radiographs.	Device intended for use as a concurrent reading aid for physicians interpreting chest radiographs.
Patient Population	Adults with Chest Radiographs	Adults with Chest Radiographs
Machine Learning Methodology	Supervised Deep Learning	Supervised Deep Learning
Platform	Secure cloud-based processing and delivery of chest radiographs	Secure cloud-based processing and delivery of chest radiographs
Image Source	Digital X-ray	Digital X-ray
Image Viewing	Image displayed on PACS system	Image displayed on PACS system
Privacy	HIPAA Compliant	HIPAA Compliant

As outlined in the table above, Aorta-CAD's technological characteristics are similar to those of Chest-CAD. Aorta-CAD differs from Chest-CAD in that Aorta-CAD simultaneously identifies and categorizes ROIs as one of two categories compared to Chest-CAD which simultaneously identifies and categorizes ROIs as one of eight categories. The fundamental purpose of both devices is to identify ROIs on chest X-rays for further consideration by the physicians, and the differences in technological characteristics do not raise different concerns of safety and effectiveness.

7. PERFORMANCE DATA

Biocompatibility Testing

There are no direct or indirect patient-contacting components of the subject device. Therefore, patient contact information is not needed for this device.

Electrical Safety and Electromagnetic Compatibility (EMC)

The subject device is a software-only device. Therefore, electrical safety and EMC testing was not necessary to establish the substantial equivalence of this device.

Software Verification and Validation Testing

Software verification and validation testing were conducted, and documentation was provided as recommended by FDA's Guidance for Industry and FDA Staff, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices." The software level of concern for Aorta-CAD is Moderate since a malfunction of, or a latent design flaw in, the

software device may lead to an erroneous diagnosis or a delay in delivery of appropriate medical care that would likely lead to Minor Injury.

Bench Testing

Imagen conducted a standalone performance assessment on 5,000 chest radiograph cases representative of the intended use population. The results of the standalone testing demonstrated that Aorta-CAD detects ROIs with high sensitivity (0.910; 95% Wilson's Confidence Interval: 0.896, 0.922), high specificity (0.896; 95% Wilson's Confidence Interval: 0.889, 0.902), and high Area Under the Curve (AUC) of the Receiver Operating Characteristic (ROC) curve (0.974, 95% Bootstrap Confidence Interval: 0.971, 0.977).

The AUC of the ROC curve was also estimated for each category and **Figure 1** shows AUCs remain high across the two categories (further details in **Table 2**). The AUC of the ROC curve was 0.972 for Aortic calcification suggestive of Aortic Atherosclerosis and was 0.948 for Dilated aorta suggestive of Aortic Ectasia. Sensitivity and specificity were calculated for each category. As shown in **Table 3**, sensitivity was 0.922 for Aortic calcification suggestive of Aortic Atherosclerosis and sensitivity was 0.830 for Dilated aorta suggestive of Aortic Ectasia. Specificity was 0.897 for Dilated aorta suggestive of Aortic Ectasia and was 0.894 for Aortic calcification suggestive of Aortic Atherosclerosis. The Free-Response ROC (FROC) curve was also estimated for each Aorta-CAD category and **Figure 2** shows the box-level sensitivity versus the false positives per image. The FROC curves terminate at the device's box-level sensitivity for each category due to the cascaded nature of the Aorta-CAD predictions.

Figure 1: Standalone Results - Aorta-CAD ROC Curve by Category

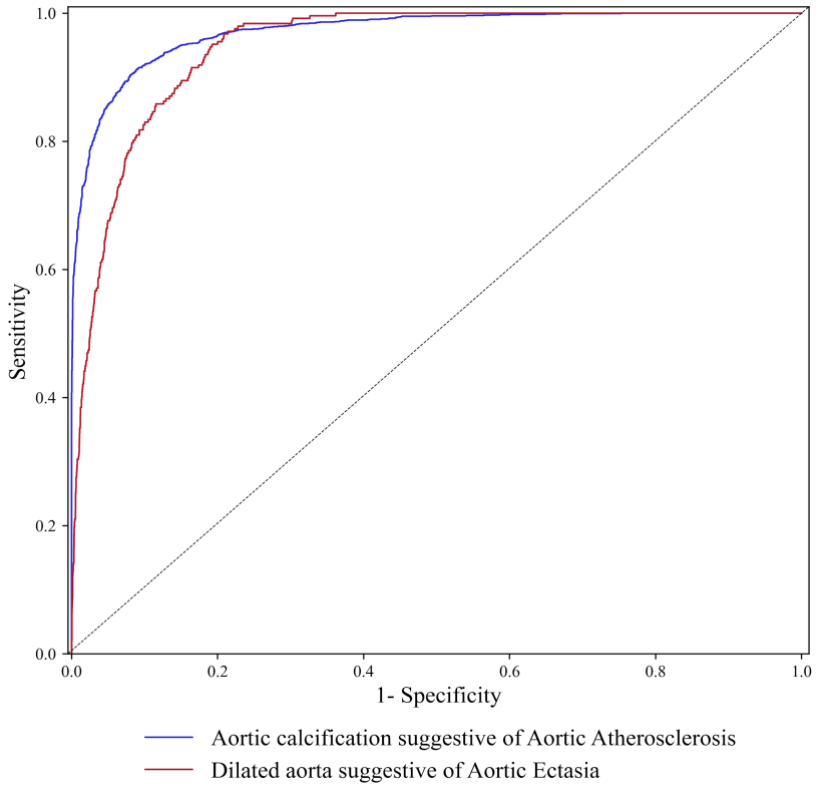


Table 2: AUC of the ROC Curve for Aorta-CAD Predictions by Category

Category	Ground Truth Positive n (%)	AUC	95% Bootstrap CI
Aortic calcification suggestive of Aortic Atherosclerosis	1662 (33.2)	0.972	0.967, 0.976
Dilated aorta suggestive of Aortic Ectasia	247 (4.9)	0.948	0.939, 0.957

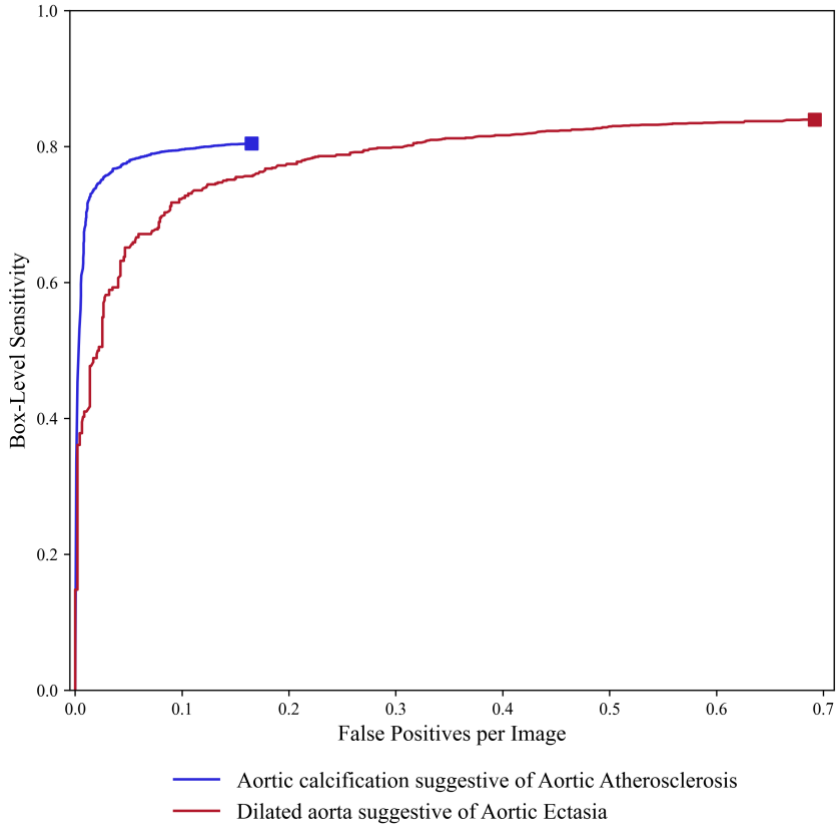
Abbreviations: AUC = Area Under the Curve; CI = Confidence Interval; ROC = Receiver Operating Characteristic.

Table 3: Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive for Aorta-CAD Predictions by Category

Category	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
	95% Wilson's CI	95% Wilson's CI	95% Wilson's CI	95% Wilson's CI
Aortic calcification suggestive of Aortic Atherosclerosis	0.922 (0.908, 0.934)	0.894 (0.883, 0.904)	0.812 (0.794, 0.829)	0.958 (0.951, 0.965)
Dilated aorta suggestive of Aortic Ectasia	0.830 (0.778, 0.872)	0.897 (0.888, 0.906)	0.296 (0.263, 0.331)	0.990 (0.987, 0.993)

Abbreviations: CI = Confidence Interval.

Figure 2: Standalone Results - Free-Response ROC (FROC) Curve by Aorta-CAD Category



Animal Testing

Not applicable. Animal studies are not necessary to establish the substantial equivalence of this device.

Clinical Data

Imagen conducted a fully-crossed multiple reader, multiple case (MRMC) retrospective reader study to determine the impact of Aorta-CAD on reader performance in detecting Aortic calcification suggestive of Aortic Atherosclerosis and Dilated aorta suggestive of Aortic Ectasia in chest radiograph cases. The primary objective of this study was to determine whether the accuracy of readers aided by Aorta-CAD ("Aided") was superior to the accuracy of readers when unaided by Aorta-CAD ("Unaided") per category as determined by the case-level Area Under the Curve (AUC) of the Receiver Operating Characteristic (ROC) curve.

Clinical readers each evaluated 244 cases in Aorta-CAD's Indications for Use under both Aided and Unaided conditions. Each case was previously evaluated by a panel of U.S. board-certified radiologists who assigned a ground truth binary label indicating the presence or absence of Aortic calcification suggestive of Aortic Atherosclerosis and Dilated aorta suggestive of Aortic Ectasia. The MRMC study consisted of two independent reading sessions separated by a washout period of at least 28 days in order to avoid memory bias. For each case, each reader was required to provide a binary determination of the presence or absence of an ROI for each category and to provide a confidence score representing their certainty.

The accuracy of readers in the intended use population was superior when aided by Aorta-CAD than when unaided by Aorta-CAD for each category as calculated by the Dorfman, Berbaum, and Metz (DBM) modeling approach. The results of the clinical study are shown in **Figure 3** and **Figure 4**.

Figure 3: **Reader Study Results - Aided and Unaided ROC Curves for Aortic calcification suggestive of Aortic Atherosclerosis**

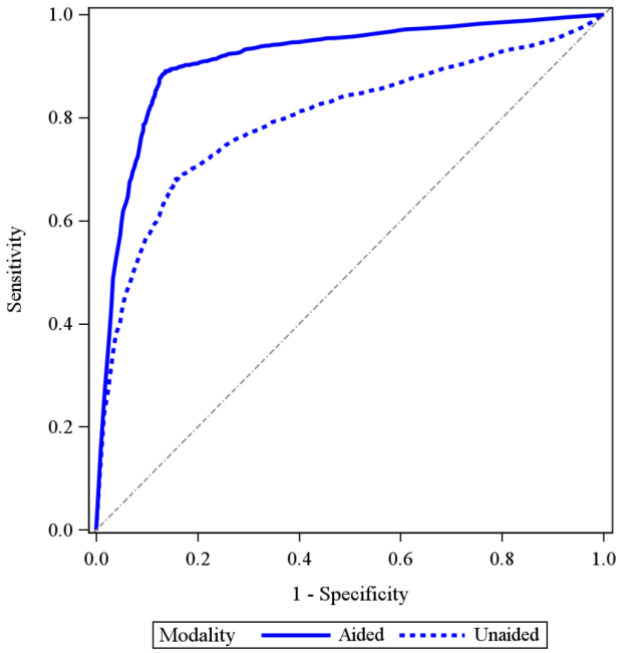
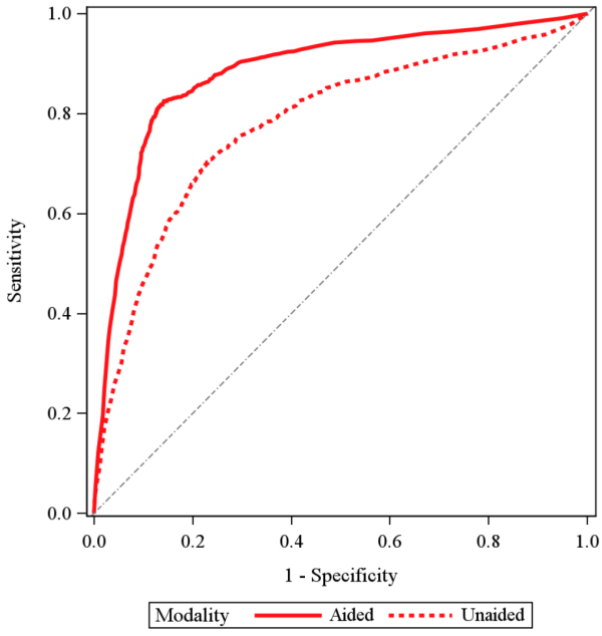


Figure 4: **Reader Study Results - Aided and Unaided ROC Curves for Dilated aorta suggestive of Aortic Ectasia**



In particular, the clinical study results demonstrated improvements when Aided versus Unaided:

- Reader AUC estimates significantly improved for both categories (p-values < 0.001).
- Reader AUC improvement for Aortic calcification suggestive of Aortic Atherosclerosis was 0.0984 (95% Confidence Interval: 0.0984, 0.0985) and for Dilated aorta suggestive of Aortic Ectasia was 0.0885 (95% Confidence Interval: 0.0885, 0.0886).

8. CONCLUSIONS

The conclusions drawn from the standalone and clinical studies demonstrate that Aorta-CAD is as safe, as effective, and performs as well as Chest-CAD. The special controls for the Medical Image Analyzer (CADe) 21 CFR 892.2070 regulation are satisfied by demonstrating effectiveness of the device in both the standalone testing and the clinical testing, showing superiority of Aided versus Unaided reads in the clinical testing, and communicating testing results in the labeling. Aorta-CAD's technological characteristics, including but not limited to the intended end-users, imaging modality, output display on X-ray studies, and assistive functionality during chest radiograph interpretation workflows, are similar to those of Chest-CAD. The technological differences identified and discussed in **§6** do not raise different concerns of safety and effectiveness. Thus, Aorta-CAD is substantially equivalent to Chest-CAD for the intended use of computer-assisted detection.