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

July 20, 2021

Re: K210666
Trade/Device Name: Chest-CAD
Regulation Number: 21 CFR 892.2070
Regulation Name: Medical image analyzer
Regulatory Class: Class II
Product Code: MYN
Dated: June 9, 2021
Received: June 10, 2021

Dear Dr. 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,

For

Thalia T. Mills, Ph.D.
Director
Division of Radiological Health
OHT7: Office of In Vitro Diagnostics
and 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)*
K210666

Device Name
Chest-CAD

Indications for Use *(Describe)*
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.

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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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

1. SUBMITTER

Applicant:	Imagen Technologies, Inc. 151 West 26th Street, Suite 1001 New York, NY 10001
Contact and Primary Correspondent:	Robert Lindsey, Ph.D. Chief Science Officer Imagen Technologies, Inc. 151 West 26th Street, Suite 1001 New York, NY 10001 917-830-4721 rob@imagen.ai
Secondary Correspondent:	Becky Ditty Consultant Biologics Consulting 1555 King St., Suite 300 Alexandria, VA 22314 269-888-2516 bditty@biologicsconsulting.com
Date Prepared:	July 12th, 2021

2. DEVICE

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

3. PREDICATE DEVICE

On January 22, 2020, FDA published the final rule down-classifying medical image analyzers (product code MYN) from Class III to Class II. Therefore, Riverain Technologies' RapidScreen™ RS-2000 (P000041) has been identified as the predicate device for Chest-CAD.

4. DEVICE DESCRIPTION

Chest-CAD is a computer-assisted detection (CADe) software device designed to assist physicians in identifying suspicious regions of interest (ROIs) in adult chest X-rays. Suspicious ROIs identified by Chest-CAD are assigned to one of the following categories: Cardiac, Mediastinum/Hila, Lungs, Pleura, Bones, Soft Tissues, Hardware, or Other. Chest-CAD detects suspicious ROIs by analyzing radiographs using deep learning algorithms for computer vision and provides relevant annotations to assist physicians with their interpretations.

For each image within a study, Chest-CAD generates a DICOM Presentation State file (output overlay). If any suspicious ROI is detected by Chest-CAD in the study, the output overlay for all images includes the text "ROI(s) Detected:" followed by a list of the category/categories for which suspicious ROI(s) were found, such as "Lungs, Bones". In addition, if suspicious ROI(s) are detected in the image, bounding boxes surrounding each detected suspicious ROI are included in the output overlay. If no suspicious ROI is detected by Chest-CAD in the study, the output overlay for each image will include the text "No ROI(s) Detected" and no bounding boxes will be included. Regardless of whether a suspicious ROI is detected, the overlay includes text identifying the X-ray study as analyzed by Chest-CAD and a customer configurable message containing a link to or instructions for users to access labeling. The Chest-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

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.

6. SUBSTANTIAL EQUIVALENCE

Comparison of Indications

The predicate device for Chest-CAD (Riverain Technologies' RapidScreen™ RS-2000) has the following FDA-approved Indications for Use:

> *The RapidScreen™ RS-2000 is a computer-aided detection (CAD) system intended to identify and mark regions of interest (ROIs) on digitized frontal chest radiographs. It identifies*

features associated with solitary pulmonary nodules from 9 to 30 mm in size, which could represent early-stage lung cancer. The device is intended for use as an aid only after the physician has performed an initial interpretation of the radiograph.

RapidScreen™ RS-2000 and Chest-CAD both analyze chest radiographs, and both identify regions of interest (ROI) in the chest. Chest-CAD detects ROIs and assigns each ROI to one of eight categories compared to RapidScreen™ RS-2000 that detects ROIs and assigns ROIs to a single category (i.e., features associated with pulmonary nodules). RapidScreen™ RS-2000 is indicated for use as a second read, while Chest-CAD is indicated for use as a concurrent read. However, both devices are only intended as an aid to the physician and not intended to replace the diagnosis by the physician. 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 Chest-CAD to the predicate RapidScreen™ RS-2000.

Table 1: Technological Comparison

	Proposed Device	**Predicate**
Number	K210666	P000041
Applicant	Imagen Technologies	Riverain Medical Group
Device Name	Chest-CAD	RapidScreen™ RS-2000
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	Identify and mark regions of interest (ROIs) on chest radiographs
Clinical Finding	Identified ROIs are assigned to one of the following categories: Cardiac, Mediastinum/Hila, Lungs, Pleura, Bones, Soft Tissues, Hardware, or Other	Identified ROIs are assigned to a single category (i.e., features associated with solitary pulmonary nodules from 9 to 30 mm in size)
Intended Users	Physician	Physician
Intended User Workflow	Device intended for use as a reading aid for physicians interpreting chest radiographs	Device intended for use as a reading aid for physicians interpreting chest radiographs
Patient Population	Adults with Chest Radiographs	Adults with Chest Radiographs
Algorithm Methodology	Artificial Neural Networks	Artificial Neural Networks

	Proposed Device	Predicate
Platform	Secure cloud-based processing and delivery of chest radiographs	Secure on-premise processing and delivery of chest radiographs
Image Source	Digital X-ray	Film X-ray
Image Viewing	Image displayed on PACS system	Image displayed on video monitor

Chest-CAD's intended end-users, imaging modality, output display on X-ray studies, and assistive functionality during chest radiograph interpretation workflows are similar to those of RapidScreen™ RS-2000. Chest-CAD differs from RapidScreen™ RS-2000 in that Chest-CAD detects ROIs and assigns each ROI to one of eight categories compared to RapidScreen™ RS-2000 that detects ROIs and assigns ROIs to a single category (i.e., features associated with pulmonary nodules). Chest-CAD operates on digital X-rays from a DICOM node, whereas RapidScreen™ RS-2000 operates on digitized X-ray films. RapidScreen™ RS-2000 was approved when digital X-rays were not standard of care, however, the Riverain device was approved by FDA to process digital X-rays in P000041/S001. The fundamental purpose of both devices is to identify ROIs on chest X-rays for further consideration by the physician, and these 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 Chest-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 20,000 chest radiograph cases from 12 hospitals, outpatient centers, and specialty centers in the United States representative of the

intended use population. The results of the standalone testing demonstrated that Chest-CAD detects suspicious ROIs with high sensitivity (0.908; 95% Wilson's Confidence Interval: 0.905, 0.911), high specificity (0.887; 95% Wilson's Confidence Interval: 0.885, 0.889), and high Area Under the Curve (AUC) of the Receiver Operating Characteristic (ROC) curve (0.976, 95% Bootstrap Confidence Interval: 0.975, 0.976).

The AUC of the ROC curve was also estimated for each Chest-CAD category and Figure 1 shows AUCs remained high across the eight categories (further detail described in Table 2). The highest AUCs of the ROC curve were for Hardware (0.994) and the lowest were for Mediastinum/Hila (0.921). Sensitivity and specificity were calculated for each of the Chest-CAD categories. As shown in Table 3, sensitivity was highest for Hardware (0.967) and was lowest for Bones (0.854). Specificity was highest for Hardware (0.960) and lowest for Mediastinum/Hila (0.830). The Free-Response ROC (FROC) curve was also estimated for each Chest-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 Chest-CAD predictions.

Figure 1: Chest-CAD ROC Curve by Category

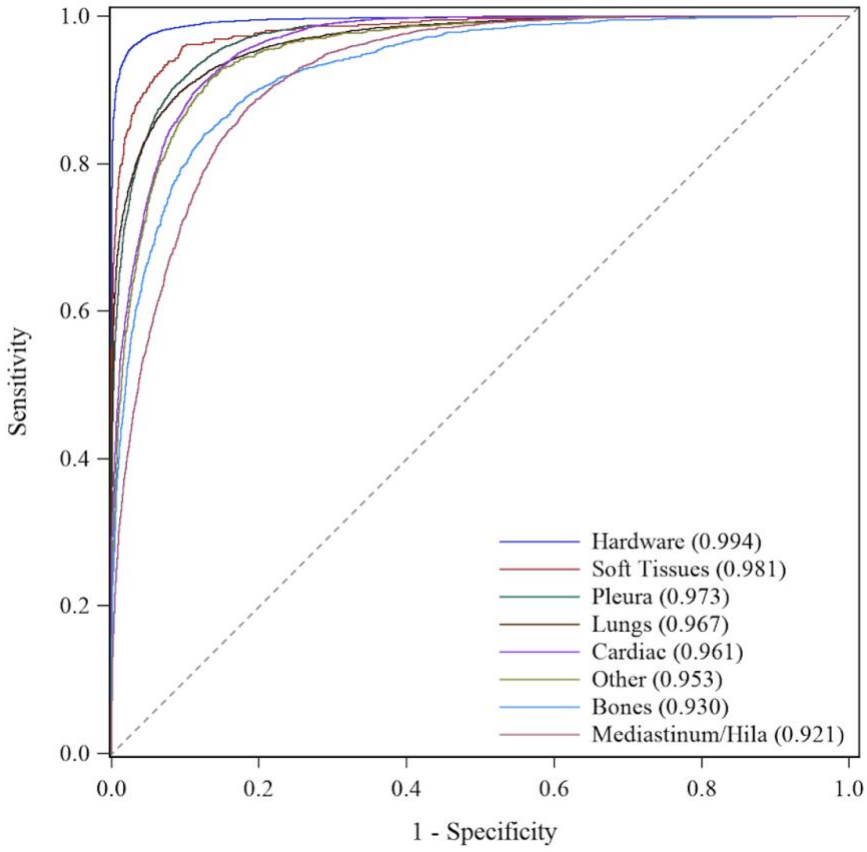


Table 2: AUC of the ROC Curve for Chest-CAD Model Predictions by Category

Category	AUC	95% Bootstrap CI
Cardiac	0.961	0.959, 0.963
Mediastinum/Hila	0.921	0.918, 0.924
Lungs	0.967	0.966, 0.969
Pleura	0.973	0.972, 0.975
Bones	0.930	0.926, 0.934
Soft Tissues	0.981	0.977, 0.985
Hardware	0.994	0.994, 0.995
Other	0.953	0.950, 0.957

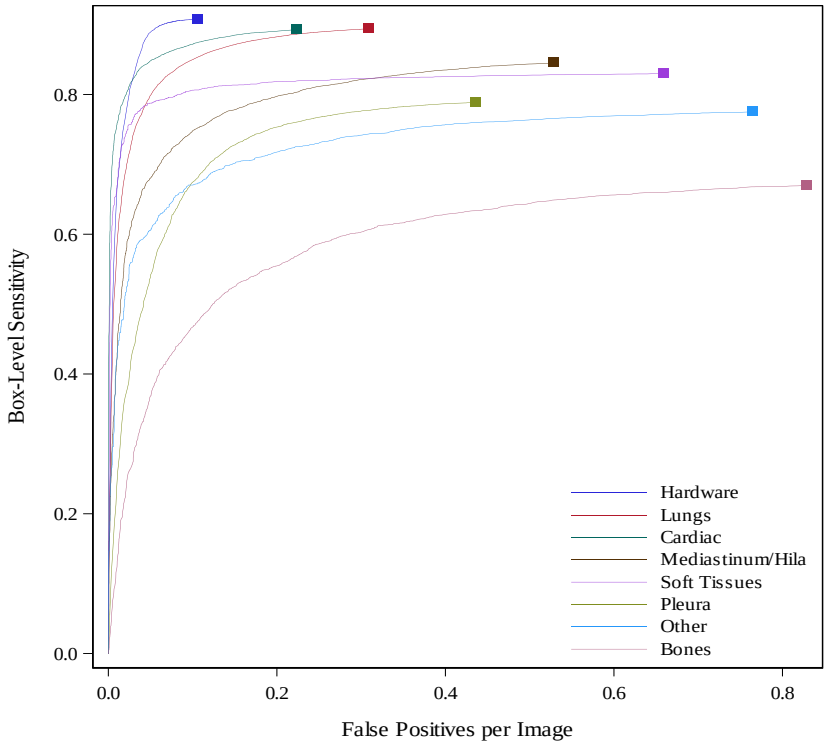
Abbreviations: AUC= Area Under the Curve; CI= Confidence Interval.

Table 3: Sensitivity and Specificity for Chest-CAD Model Predictions by Category

Category	Sensitivity	Specificity
	95% Wilson's CI	95% Wilson's CI
Cardiac	0.889 (0.881, 0.897)	0.892 (0.887, 0.897)
Mediastinum/Hila	0.856 (0.844, 0.867)	0.830 (0.824, 0.835)
Lungs	0.888 (0.882, 0.893)	0.915 (0.908, 0.921)
Pleura	0.919 (0.912, 0.925)	0.899 (0.894, 0.904)
Bones	0.854 (0.838, 0.868)	0.856 (0.850, 0.861)
Soft Tissues	0.938 (0.916, 0.955)	0.919 (0.916, 0.923)
Hardware	0.967 (0.963, 0.970)	0.960 (0.956, 0.964)
Other	0.906 (0.889, 0.920)	0.872 (0.867, 0.877)

Abbreviations: CI= Confidence Interval.

Figure 2: Chest-CAD Free-Response ROC (FROC) Curve by Category



Animal Testing

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

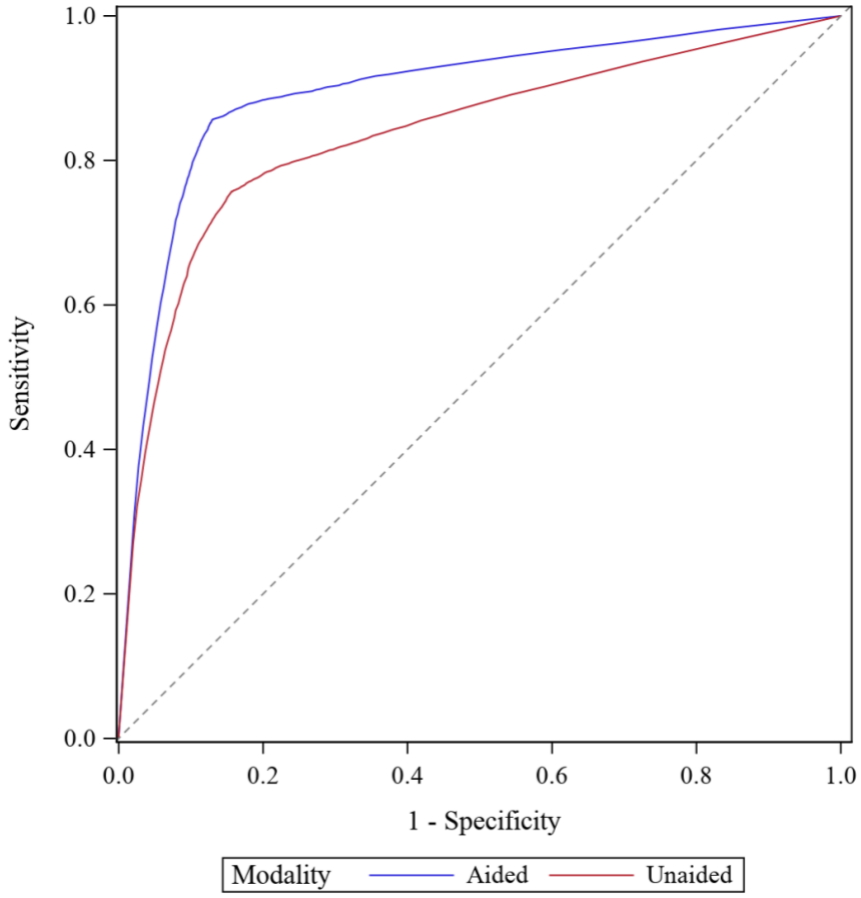
Clinical Data

Imagen conducted a fully-crossed multiple reader, multiple case (MRMC) retrospective reader study to determine the impact of Chest-CAD on reader performance in detecting suspicious ROIs in chest radiograph cases. The primary objective of this study was to determine whether the accuracy of readers aided by Chest-CAD ("Aided") was superior to the accuracy of readers when unaided by Chest-CAD ("Unaided") as determined by the case-level, across-category aggregate Area Under the Curve (AUC) of the Receiver Operating Characteristic (ROC) curve.

24 clinical readers each evaluated 238 cases in Chest-CAD's Indications for Use under both Aided and Unaided conditions. The cases were from 9 hospitals, outpatient centers, and specialty centers in the United States. 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 a suspicious ROI for each Chest-CAD category. 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 a suspicious ROI for each category and to provide a confidence score representing their certainty.

The results of the study found that the accuracy of readers in the intended use population was superior when Aided by Chest-CAD than when Unaided by Chest-CAD, as measured by the task of suspicious ROI detection using the AUC of the ROC curve as calculated by the Dorfman, Berbaum, and Metz (DBM) modeling approach.

Figure 3: Clinical Reader Study Results - Aided and Unaided ROC Curves



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

- When calculated using Wilcoxon rank-sum scores with bootstrap confidence intervals as outlined in Beiden et al. 2000[1], reader AUC estimates improved from 0.836 (95% Bootstrap CI: 0.816, 0.856) to 0.894 (95% Bootstrap CI: 0.879, 0.909).
- Reader sensitivity improved from 0.757 (95% Wilson's CI: 0.750, 0.764) to 0.856 (95% Wilson's CI: 0.850, 0.862).
- Reader specificity improved from 0.843 (95% Wilson's CI: 0.839, 0.847) to 0.870 (95% Wilson's CI: 0.866, 0.873).

[1]Beiden, S.V., Wagner, R.F., & Campbell, G. (2000). Components-of-variance models and multiple-bootstrap experiments: An alternative method for random-effects, receiver operating characteristic analysis. *Academic Radiology*, *7*, p.341-p.349.

8. CONCLUSION

The conclusions drawn from the standalone and clinical studies demonstrate that Chest-CAD is as safe, as effective, and performs as well as RapidScreen™ RS-2000. 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. Chest-CAD's intended end-users, imaging modality, output display on X-ray studies, and assistive functionality during chest radiograph interpretation workflows are similar to those of RapidScreen™ RS-2000. The technological differences identified and discussed in **Section 6** do not raise different concerns of safety and effectiveness. Thus, Chest-CAD is substantially equivalent to RapidScreen™ RS-2000 for the intended use of computer-assisted detection.