Avicenna.AI   May 19, 2021
℅ John J. Smith, M.D., Ph.D.
Partner
Hogan Lovells US LLP
555 13th St. NW
WASHINGTON DC 20004

Re: K210237
      Trade/Device Name: CINA CHEST
      Regulation Number: 21 CFR 892.2080
      Regulation Name: Radiological Computer aided triage and notification software
      Regulatory Class: Class II
      Product Code: QAS
      Dated: April 23, 2021
      Received: April 23, 2021

Dear Dr. Smith:

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 and Part 809); 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)*

K210237

Device Name

CINA CHEST

Indications for Use *(Describe)*

CINA CHEST is a radiological computer aided triage and notification software indicated for use in the analysis of Chest and Thoraco-abdominal CT angiography. The device is intended to assist hospital networks and trained radiologists in workflow triage by flagging and communicating suspected positive findings of (1) Chest CT angiography for Pulmonary Embolism (PE) and (2) Chest or Thoraco-abdominal CT angiography for Aortic Dissection (AD).

CINA CHEST uses an artificial intelligence algorithm to analyze images and highlight cases with detected PE and AD on a standalone Web application in parallel to the ongoing standard of care image interpretation. The user is presented with notifications for cases with suspected PE or AD findings. Notifications include compressed preview images that are meant for informational purposes only, and are not intended for diagnostic use beyond notification. The device does not alter the original medical image, and it is not intended to be used as a diagnostic device.

The results of CINA CHEST are intended to be used in conjunction with other patient information and based on professional judgment to assist with triage/prioritization of medical images. Notified clinicians are ultimately responsible for reviewing full images per the standard of care.

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

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

CONTINUE ON A SEPARATE PAGE IF NEEDED.

510(k) SUMMARY

AVICENNA.AI's CINA CHEST

I. Submitter

<u>Applicant</u>:
      AVICENNA.AI
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      13600 La Ciotat France

<u>Contact Person</u>:
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      Regulatory Manager
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<u>Date prepared</u>: January 28, 2021

II. Device Identification

Name of Device:	CINA CHEST
Classification Name:	Radiological Computer-Assisted Triage And Notification Software
Regulation No:	21 CFR § 892.2080
Product Code:	QAS
Regulatory Class:	Class II
Classification Panel:	Radiology devices

III. Predicate Device

The CINA CHEST device is substantially equivalent to the following predicate device with regard to indications for use, performance, and technological characteristics:

510(k):	K190072
Trade Name:	BriefCase
Manufacturer:	AiDoc Medical, Ltd
Classification Name:	Radiological Computer-Assisted Triage And Notification Software
Regulation No:	21 CFR § 892.2080
Product Code:	QAS
Regulatory Class:	Class II

A reference device is Avicenna.Ai's CINA (K200855), which is a Class II device under the same regulation and product code as above.

IV. Device Description

CINA CHEST is a radiological computer-assisted triage and notification software device.

The software system is based on algorithm-programmed components and is comprised of a standard off-the-shelf operating system and additional image processing applications.

DICOM images are received, recorded and filtered before processing. The series are processed chronologically by running algorithms on each series to detect suspected positive findings of a pulmonary embolism (PE) or an aortic dissection (AD), then notifications on the flagged series are sent to the Worklist Application.

The Worklist Application (on premise) displays the pop-up notifications of new studies with suspected findings when they come in, and provides both active and passive notifications. Active notifications are in the form of a small pop-up containing patient name, accession number and the type of suspected findings (PE or AD). All the chest and thoraco-abdominal CT angiography studies received by CINA CHEST device are displayed in the worklist and those on which the algorithms have detected a suspected finding (PE or AD) are marked with an icon (i.e., passive notification). In addition, a compressed, small black and white image that is marked "not for diagnostic use" is displayed as a preview function. This compressed preview is meant for informational purposes only, does not contain any marking of the findings, and is not intended for primary diagnosis beyond notification. Presenting the radiologist with notification facilitates earlier triage by allowing one to prioritize images in the PACS. Thus, the suspect case receives attention earlier than would have been the case in the standard of care practice alone.

V. Intended Use / Indications for Use

CINA CHEST is a radiological computer aided triage and notification software indicated for use in the analysis of Chest and Thoraco-abdominal CT angiography. The device is intended to assist hospital networks and trained radiologists in workflow triage by flagging and communicating suspected positive findings of (1) Chest CT angiography for Pulmonary Embolism (PE) and (2) Chest or Thoraco-abdominal CT angiography for Aortic Dissection (AD).

CINA CHEST uses an artificial intelligence algorithm to analyze images and highlight cases with detected PE and AD on a standalone Web application in parallel to the ongoing standard of care image interpretation. The user is presented with notifications for cases with suspected PE or AD findings. Notifications include compressed preview images that are meant for informational purposes only, and are not intended for diagnostic use beyond notification. The device does not alter the original medical image, and it is not intended to be used as a diagnostic device.

The results of CINA CHEST are intended to be used in conjunction with other patient information and based on professional judgment to assist with triage/prioritization of medical images. Notified clinicians are ultimately responsible for reviewing full images per the standard of care.

VI. Summary of Technological Characteristics

CINA CHEST runs on a standard "off the shelf" server/workstation and is comprised of PE and AD Image Processing Applications, which can be integrated, deployed and used with the reference device (K200855) or other compatible medical image communications devices. CINA CHEST receives CTA scans identified by the CINA Platform or other compatible medical image communications device, processes them using algorithmic methods involving execution of multiple computational steps to identify suspected presence of PE or AD and generates results files to be transferred by CINA Platform or a similar medical image communications device for output to a PACS system or workstation for worklist prioritization. Each of these components is briefly described below.

VI.1. CINA Platform

The CINA platform is an example of medical image communications platform for integrating and deploying the CINA CHEST PE and AD image processing applications. It provides the necessary requirements for interoperability based on the standardized DICOM protocol and services to communicate with existing systems in the hospital radiology department such as CT modalities or other DICOM nodes (DICOM router or PACS for example). It is responsible for transferring, storing, converting formats, notifying of suspected findings and displaying medical device data such as radiological data. The CINA Platform server includes the Worklist client application in which notifications from the CINA CHEST Image Processing applications (PE and AD) are received. The CINA Platform and base functions were cleared in the reference device (K200855).

VI.2. PE Application

The PE application includes the software algorithm responsible for identifying and quantifying image characteristics that are consistent with a Pulmonary Embolism (PE). This application reads provided DICOM files, checks the DICOM properties to verify the compatibility with the recommended acquisition protocol, launches the algorithm and provides notification results (when a PE is detected) compatible with the CINA Platform and with DICOM format.

VI.3. AD Application

The AD application includes the software algorithm responsible for identifying and quantifying image characteristics that are consistent with an Aortic Dissection (AD). This application reads provided DICOM files, checks the DICOM properties to verify the compatibility with the recommended acquisition protocol, launches the algorithm part and provides notification results (when an AD is detected) compatible with the CINA Platform and with DICOM format.

VII. Summary of Performance Data

The following performance data were provided in support of the substantial equivalence determination.

VII.1. Software Verification and Validation Testing

The CINA CHEST device has been evaluated and verified in accordance with software specifications and applicable performance standards through a Software Development and Validation & Verification Process to ensure performance according to specifications, User Requirements and Federal Regulations and Guidance documents, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices".

The mutual compatibility with the CINA Platform has been verified through the V&V activities that have been conducted at the system level to ensure the safe and proper use of the system. Special attention has been paid to:

- DICOM analysis,
- Processing pipeline,
- Front-end interface, and
- Notifications for suspected findings performances.

VII.2. Performance Testing

Avicenna.AI conducted a retrospective, multicenter and blinded study with the CINA CHEST software with the primary endpoint to evaluate the software's performance in 1) Chest CT angiography (CTA) images pertaining to patient with suspected Pulmonary Embolism (PE) findings and 2) Chest or Thoraco-abdominal CT angiography (CTA) images series pertaining to patient with suspected Aortic Dissection (AD) findings, in 396 and 298 clinical anonymized cases, respectively.

The data was provided from multiple US clinical sites: 230 and 200 US cities, for PE and AD, respectively. There were 190 (48%) positive PE (images with PE) cases and 137 (46%) positive AD (images with AD) cases included in the analyses.

Device sensitivities and specificities were compared to ground truth established by concurrence of several US-board-certified radiologist readers.

Sensitivity and Specificity for the "PE" prioritization and triage application were found to be 91.1% [95% CI: 86.1% – 94.7 %] and 91.8% [95% CI: 87.1% – 95.1%], respectively.

Regarding the "AD" prioritization and triage application, Sensitivity and Specificity of 96.4% [95% CI: 91.7% – 98.8%] and 97.5% [95% CI: 93.8% – 99.3%], respectively, were obtained.

All these findings achieved the 80% performance goal and are similar to the results reported for the predicate device BriefCase (Aidoc Medical): Sensitivity and Specificity of 90.6% [95% CI: 82.2% – 95.9%] and 89.9% [95% CI: 82.2% – 95.1%], respectively.

The results of the standalone assessment study demonstrated an overall agreement (Accuracy) of 91.4% and 97% for the "PE" and "AD" tested cases, respectively, when compared to the ground truth (operators' visual assessments).

Regarding Matthews correlation coefficient (MCC), the found values were 0.83 and 0.94, which represent very good predictions.

Additionally, both "PE" and "AD" prioritization and triage effectiveness were evaluated by the standalone per-case processing time of the device (time-to-notification), with the results are presented in **Table 1** below:

Table 1: Time-to-Notification for PE and AD Image Processing Applications

Time-to-Notification	MEAN ± SD (seconds)	MEDIAN (seconds)	Lower Confidence Limit (seconds)	Upper Confidence Limit (seconds)	MIN (seconds)	MAX (seconds)
CINA CHEST – PE (N = 396)	63 ± 16.1	60.8	61.5	64.6	36.6	122.7
CINA CHEST – AD (N = 298)	36.5 ± 9.1	34.1	35.4	37.5	17.8	90.5

The standalone triage effectiveness assessment demonstrated substantial equivalence of the CINA CHEST triage applications when compared to the predicate (BriefCase) and reference (CINA) devices. Specifically, mean "time-to-notification" were estimated to be 63 [95% CI: 61.5 – 64.6] seconds and 36.5 [95% CI: 35.4 – 37.5] seconds for CINA CHEST – PE and CINA CHEST – AD, respectively. This is similar to the times reported by the predicate BriefCase device (mean 3.9 [95% CI: 3.7 – 4.1] minutes) and the reference CINA device (21.6 ± 4.4 seconds and 34.7 ± 10.7 seconds, for ICH and LVO, respectively).

The performance testing of the CINA CHEST device establishes that the subject device is as safe and effective as the predicate and reference devices. This establishes that the CINA CHEST device meets its intended use and is substantially equivalent to the predicate and reference devices.

VIII. Substantial Equivalence

The subject CINA CHEST for PE and AD prioritization and triage and the predicate device BriefCase device for PE triage are both intended to aid in prioritization and triage of radiological images of time sensitive findings for patient detection and diagnosis (i.e. Pulmonary Embolism and Aortic Dissection) based on the analysis of medical images acquired from radiological signal acquisition systems. The CINA reference device provides the CINA Platform in which the subject CINA CHEST PE and AD prioritization and triage applications can be integrated, deployed and used. The labeling of the subject and the predicate devices clearly states that the devices are not for diagnostic use. All devices are

software packages with similar technological characteristics and principles of operation, and incorporate deep learning AI algorithms that process images, and software to send notifications and to display unannotated preview images. In all three devices, the labeling instructs the user to further evaluate and diagnose based only on the original images in the local PACS.

The subject CINA CHEST, the predicate device BriefCase and the reference device CINA operate in parallel to the standard of care workflow in the sense that they do not change the original image, do not provide any marking on the output preview, and do not remove images from the standard of care FIFO queue, thus not disturbing standard interpretation of the images by the attending radiologists. The subject, predicate and reference devices achieve performance of the time-to-notification metric in similar ranges of time, and thus contribute similarly to effective triage and early involvement of the radiologist in evaluating suspected images of PE and/or AD.

The standalone performance and effectiveness assessment studies demonstrated that the CINA CHEST device performs as intended is therefore substantially equivalent to the BriefCase predicate and CINA reference devices.

Table 2 compares the key features of the subject and the predicate and reference devices.

Table 2: Comparison of Key Features between CINA CHEST and Predicate Device (Aidoc BriefCase) and Reference Device (Avicenna.AI CINA)

	Subject device: CINA CHEST Software	Predicate device: Aidoc BriefCase Software (K190072)	Reference device: Avicenna.AI CINA software (K200855)
Intended Use / Indications for Use	CINA CHEST is a radiological computer aided triage and notification software indicated for use in the analysis of Chest and Thoraco-abdominal CT angiography. The device is intended to assist hospital networks and trained radiologists in workflow triage by flagging and communicating suspected positive findings of (1) Chest CT angiography for Pulmonary Embolism (PE) and (2) Chest or Thoraco-abdominal CT	BriefCase is a radiological computer aided triage and notification software indicated for use in the analysis of non-enhanced head CT and CTPA images. The device is intended to assist hospital networks and trained radiologists in workflow triage by flagging and communication of suspected positive findings of Intracranial Hemorrhage (ICH) and Pulmonary Embolism (PE) pathologies. For the PE pathology, the	CINA is a radiological computer aided triage and notification software indicated for use in the analysis of (1) non-enhanced head CT images and (2) CT angiographies of the head. The device is intended to assist hospital networks and trained radiologists in workflow triage by flagging and communicating suspected positive findings of (1) head CT images for Intracranial Hemorrhage (ICH) and (2) CT angiographies of

	Subject device: CINA CHEST Software	Predicate device: Aidoc BriefCase Software (K190072)	Reference device: Avicenna.AI CINA software (K200855)
	angiography for Aortic Dissection (AD). CINA CHEST uses an artificial intelligence algorithm to analyze images and highlight cases with detected PE and AD on a standalone Web application in parallel to the ongoing standard of care image interpretation. The user is presented with notifications for cases with suspected PE or AD findings. Notifications include compressed preview images that are meant for informational purposes only, and are not intended for diagnostic use beyond notification. The device does not alter the original medical image, and it is not intended to be used as a diagnostic device. The results of CINA CHEST are intended to be used in conjunction with other patient information and based on professional judgment to assist with triage/prioritization of medical images. Notified clinicians are ultimately responsible for reviewing	software is only intended to be used on single-energy exam. BriefCase uses an artificial intelligence algorithm to analyze images and highlight cases with detected findings on a standalone desktop application in parallel to the ongoing standard of care image interpretation. The user is presented with notifications for cases with suspected findings. Notifications include compressed preview images that are meant for informational purposes only and not intended for diagnostic use beyond notification. The device does not alter the original medical image and is not intended to be used as a diagnostic device. The results of BriefCase are intended to be used in conjunction with other patient information and based on professional judgment, to assist with triage/prioritization of medical images. Notified clinicians are responsible for viewing full images per the standard of care.	the head for large vessel occlusion (LVO). CINA uses an artificial intelligence algorithm to analyze images and highlight cases with detected (1) ICH or (2) LVO on a standalone Web application in parallel to the ongoing standard of care image interpretation. The user is presented with notifications for cases with suspected ICH or LVO findings. Notifications include compressed preview images that are meant for informational purposes only, and are not intended for diagnostic use beyond notification. The device does not alter the original medical image, and it is not intended to be used as a diagnostic device. The results of CINA are intended to be used in conjunction with other patient information and based on professional judgment to assist with triage/prioritization of medical images. Notified clinicians are ultimately responsible for reviewing full images per the standard of care.

	Subject device: CINA CHEST Software	Predicate device: Aidoc BriefCase Software (K190072)	Reference device: Avicenna.AI CINA software (K200855)
	full images per the standard of care.		
User population	Radiologist	Radiologist	Radiologist
Anatomical region of interest	Chest	Head and chest	Head
Data acquisition protocol	Chest and Thoraco-abdominal CT angiography	Non contrast head CT scan and CTPA (single energy exams only)	Non contrast CT scan of the head or neck and CT angiogram images of the brain
View DICOM data	DICOM information about the patient, study and current image	DICOM information about the patient, study and current image	DICOM information about the patient, study and current image
Segmentation of region of interest	No; device does not mark, highlight, or direct users' attention to a specific location in the original image	No; device does not mark, highlight, or direct users' attention to a specific location in the original image	No; device does not mark, highlight, or direct users' attention to a specific location in the original image
Algorithm	Artificial intelligence algorithm with database of images	Artificial intelligence algorithm with database of images	Artificial intelligence algorithm
Notification / Prioritization	Yes	Yes	Yes
Preview images	Presentation of a small, compressed, black and white preview image that is labeled "not for diagnostic use"; The device operates in parallel with the standard of care, which remains the default option for all	Presentation of a small, compressed, black and white preview image that is labeled "not for diagnostic use"; The device operates in parallel with the standard of care, which remains the default option for all	Presentation of a preview of the study for initial assessment not meant for diagnostic purposes. The device operates in parallel with the standard of care, which remains the default option for all cases.

	Subject device: CINA CHEST Software	Predicate device: Aidoc BriefCase Software (K190072)	Reference device: Avicenna.AI CINA software (K200855)
	cases.	cases.	
Alteration of original image	No	No	No
Removal of cases from worklist queue	No	No	No
Structure	- PE and AD image processing applications - Compatibility of use with the CINA Platform reference device (worklist and Image Viewer)	- AHS module (image acquisition), - ACS module (image processing), - Aidoc Worklist application for workflow integration (worklist and non-diagnostic basic Image Viewer).	- LVO and ICH image processing applications - CINA Platform (worklist and Image Viewer)