Avicenna.AI
℅ John Smith
Partner
Hogan Lovells US LLP
555 13th St. NW
Washington, District of Columbia 20005

March 13, 2024

Re: K233968
Trade/Device Name: CINA-iPE
Regulation Number: 21 CFR 892.2080
Regulation Name: Radiological computer aided triage and notification software
Regulatory Class: Class II
Product Code: QAS
Dated: December 15, 2023
Received: December 15, 2023

Dear John 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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

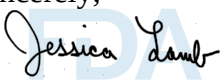
Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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,



Jessica Lamb, Ph.D.
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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)*
K233968

Device Name
CINA-iPE

Indications for Use *(Describe)*

CINA-iPE is a radiological computer-aided triage and notification software indicated for use in patients undergoing contrast-enhanced CT scans (not dedicated CTPA protocol) for other clinical indications than pulmonary embolism suspicion, including at least a part of the lung. The device is intended to assist hospital networks and appropriately trained radiologists in workflow triage by flagging and communicating suspected positive findings for incidental Pulmonary Embolism (iPE). The device is indicated for adults and transitional adolescents (18 to 21 years old but treated as adults).

CINA-iPE uses an artificial intelligence algorithm to analyze images and highlight cases with detected incidental PE on a standalone application in parallel to the ongoing standard of care image interpretation. The user is presented with notifications for cases with suspected incidental PE findings.The device is not designed to detect PE in subsegmental arteries.

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-iPE are intended to be used in conjunction with other patient information and based on their 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)*

☒ 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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K233968

510(K) SUMMARY

AVICENNA.AI's CINA-IPE

Submitter

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Date prepared: March 12, 2024

Device Identification

Name of Device:	CINA-iPE
Classification Name:	Radiological computer aided triage and notification software
Regulation No:	21 CFR § 892.2080
Product Code:	QAS
Regulatory Class:	Class II
Classification Panel:	Radiology

Predicate Device

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

510(k):	K213886
Trade Name:	BriefCase
Manufacturer:	Aidoc Medical, Ltd.
Classification Name:	Radiological computer aided triage and notification software
Regulation No:	21 CFR § 892.2080
Product Code:	QAS
Regulatory Class:	Class II

Device Description

CINA-iPE is a radiological computer aided triage and notification software device.

CINA-iPE runs on a standard “off the shelf” server/workstation and consists of an Image Processing Application, which can be integrated, deployed, and used with the CINA Platform (cleared under K200855) or other medical image communications devices. CINA-iPE receives contrast-enhanced CT scans (not dedicated CTPA protocol) including at least a part of the lung identified by the CINA Platform or other medical image communications device, processes them using deep learning algorithms involving the execution of multiple computational steps to identify the suspected presence of an incidental pulmonary embolism 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.

To identify the suspected presence of pulmonary embolisms, the device uses a deep learning model trained end-to-end on 5,429 cases acquired from US and France, representing a distribution of PE sizes, locations and acquisition protocols, including multiple scanner models from Siemens, Philips, GE and Canon/Toshiba. Additional models are used to locate the aorta and main pulmonary artery, enabling assessment of the contrast timing. The lung’s parenchyma is segmented to evaluate both the presence of the lungs in the field of view and to limit the region of interest for detecting the presence of pulmonary embolisms.

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 an incidental Pulmonary Embolism (iPE), then active notifications on the flagged series are sent to the Worklist Application.

The Worklist Application displays the active notification of new studies with suspected findings when they come in. All the contrast-enhanced CT studies received by CINA-iPE device are displayed in the worklist and those on which the algorithms have detected a suspected finding are marked with an icon (i.e., passive notification). In addition, a compressed, grayscale, unannotated 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 diagnostic use beyond notification.

Presenting the radiologist with notification facilitates earlier triage by allowing prioritization of images in the PACS. Thus, the suspect case receives attention earlier than would have been the case in the standard of care image interpretation practice alone.

The CINA platform is an example of medical image communications platform for integrating and deploying the CINA-iPE image processing application. The medical image communications device (i.e., the technical platform) 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 medical image communications server includes the Worklist client application in which notifications from the CINA-iPE Image Processing application are received.

Intended Use / Indications for Use

CINA-iPE is a radiological computer-aided triage and notification software indicated for use in patients undergoing contrast-enhanced CT scans (not dedicated CTPA protocol) for other clinical indications than pulmonary embolism suspicion, including at least a part of the lung. The device is intended to assist hospital networks and trained radiologists in workflow triage by flagging and communicating suspected positive findings for incidental Pulmonary Embolism (iPE). The device is indicated for adults and transitional adolescents (18 to 21 years old but treated as adults).

CINA-iPE uses an artificial intelligence algorithm to analyze images and highlight cases with detected incidental PE on a standalone application in parallel to the ongoing standard of care image interpretation. The user is presented with notifications for cases with suspected incidental PE findings. The device is not designed to detect PE in subsegmental arteries.

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-iPE 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.

Summary of Performance Data

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

Software Verification and Validation Testing

CINA-IPE complies with DICOM (Digital Imaging and Communications in Medicine) – Developed by the American College of Radiology and the National Electrical Manufacturers Association. NEMA PS 3.1 - 3.20.

Avicenna.AI conducted extensive performance validation testing and software verification and validation testing of the CINA-IPE device as standalone software. CINA-IPE is tested against its user needs and intended use by the successful execution of planned software verification and validation testing included in this submission.

Software performance, validation and verification testing demonstrated that the CINA-IPE met all design requirements and specifications associated with the intended use of the software.

Standalone Performance Testing

Avicenna.AI conducted a retrospective, multicenter, multinational and blinded study with the CINA-iPE application with the primary endpoint to evaluate the software's performance in identifying incidental pulmonary embolisms (iPE) on contrast-enhanced CT images performed for another clinical indication than for pulmonary embolism (PE) evaluation (i.e. not dedicated CTPA protocol), in 381 clinical anonymized cases. The dataset included 53.5% Male and 46.7% Female. Mean ± SD age of patients included in the study was 64.5 ± 15.8 yo (range: 18 - 99 yo).

Multiple subgroups of interest were considered in the analysis. In fact, the validation data was acquired from different regions across the U.S. to account for race/ethnicity in the intended U.S. patient population. Additional scanner parameters considered were slice thickness, number of detector rows, and kVp ranges. Detailed subgroup analysis were reported in the labeling.

The data was provided from multiple U.S. and OUS clinical sites, with 56.4% (215) cases coming from U.S. clinical sources. The independence of the standalone validation dataset from the training data was ensured using data from independent sites and different time periods. There were 181 (47.5%) positive iPE (images with PE) cases and 200 (52.5%) negative iPE cases included in the analyses. The data was acquired primarily by 4 different scanner makers (GE-31.5%, Philips-28.3%, Siemens-26%, and Canon-13.9%) and 39 different scanner models.

Device Sensitivity [95% CI] and Specificity [95% CI] were computed against the groundtruth established by consensus of three US-board-certified expert radiologists.

As a primary endpoint, the global Sensitivity and Specificity were found to be 87.8% [95%CI: 82.2% - 92.2%] and 92.0% [95%CI: 87.3% - 95.4%], respectively. These findings achieved the 80% performance goal of the study and are similar to the results reported for the predicate BriefCase device (Aidoc Medical) which demonstrated Sensitivity and Specificity of 89.7% [95%CI: 80.8% - 95.5%] and 90.1% [95%CI: 81.5% - 95.6%], respectively.

Additionally, subgroup analysis was reported in terms of sensitivity [95%CI] for each lesion location (main, interlobar, lobar and segmental) as presented in the following Table:

Table 1: Stratified statistical analysis (Sensitivity [95%CI]) regarding arterial segments.

Arterial Segment	Sensitivity [95% CI]
Main (N = 55)	96.3% [87.5% - 99.6%]
Interlobar (N = 73)	94.5% [86.6% - 98.5%]
Lobar (N = 127)	92.9% [87.0% - 96.7%]
Segmental (N = 179)	88.3% [82.6% - 92.6%]

Please note that cases with more than one PE location were included in more than one category (e.g., a case with a main and a lobar PE was included in the “main” category and in the “lobar” category)
Finally, the CINA-iPE prioritization and triage effectiveness were evaluated by the standalone per-case processing time of the device (time-to-notification). The results are presented in Table 2 below:

Table 2: Time-to-Notification for CINA-iPE Image Processing Applications

Time-to-Notification (minutes)	MEAN ± SD	MEDIAN	95% CI	MIN	MAX
CINA-iPE All cases (N = 381)	1.5 ± 0.5	1.4	[1.4 - 1.5]	0.3	2.7
CINA-iPE True Positive cases (N = 159)	1.5 ± 0.4	1.5	[1.4 - 1.6]	0.7	3.1

The mean [95% CI] time-to-notification for all included cases (n = 381) was estimated to be 1.5 [95% CI: 1.4 – 1.5] minutes for CINA-iPE. When taking into account only true positive cases (n = 159), the mean [95% CI] time-to-notification was 1.5 [95% CI: 1.4 – 1.6] minutes for CINA-iPE and 4.7 [95% CI: 4.4 – 5.1] minutes for the predicate device.

The performance testing of the CINA-iPE device establishes that the subject device is as safe and effective as the predicate device and compatible with the same clinical use, since the performance demonstrated the clinical effectiveness of the subject device and its ability to provide effective prioritization and triage that was substantially equivalent to that of the predicate device. This establishes that the CINA-iPE device achieves its intended use and is substantially equivalent to the predicate BriefCase device.

Substantial Equivalence

The subject CINA-iPE and the predicate BriefCase device are both intended to aid in prioritization and triage of radiological images of time sensitive findings for patient detection and diagnosis (i.e., incidental Pulmonary Embolism) based on the analysis of medical images acquired from radiological signal acquisition systems. The CINA device provides the CINA Platform in which the subject CINA-iPE prioritization and triage application 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-iPE and the predicate BriefCase device 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 and predicate 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 incidental pulmonary embolism.
The standalone performance and effectiveness assessment studies demonstrated that the CINA-iPE device performs as intended and substantially equivalent to the BriefCase predicate device.

The table below compares the key features of the subject and the predicate devices.

Table 3: Comparison of key features between CINA-iPE and the predicate device (Aidoc Medical Ltd)

	Subject device: CINA-iPE Software	**Predicate device: BriefCase Software (K213886)**
Intended Use / Indications for Use	CINA-iPE is a radiological computer-aided triage and notification software indicated for use in patients undergoing contrast-enhanced CT scans (not dedicated CTPA protocol) for other clinical indications than pulmonary embolism suspicion, including at least a part of the lung. The device is intended to assist hospital networks and trained radiologists in workflow triage by flagging and communicating suspected positive findings for incidental Pulmonary Embolism (iPE). The device is indicated for adults and transitional adolescents (18 to 21 years old but treated as adults). CINA-iPE uses an artificial intelligence algorithm to analyze images and highlight cases with detected incidental PE on a standalone application in parallel to the ongoing standard of care image interpretation. The user is presented with notifications for cases with suspected incidental PE findings. The device is not designed to detect PE in subsegmental arteries. 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-iPE are intended to be used in conjunction with other patient information and based on professional judgment to assist with triage/prioritization of medical	BriefCase is a radiological computer aided triage and notification software indicated for use in the analysis of contrast-enhanced chest CTs (not dedicated CTPA protocol) in adults or transitional adolescents age 18 and older. The device is intended to assist hospital networks and appropriately trained medical specialists in workflow triage by flagging and communication of suspect cases of incidental Pulmonary Embolism (iPE) pathologies. The device is intended to be used on single energy exams only. BriefCase uses an artificial intelligence algorithm to analyze images and flag suspect cases on a standalone desktop application in parallel to the ongoing standard of care image interpretation. The user is presented with notifications for suspect cases. 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 their professional judgment, to assist with triage/prioritization of medical images. Notified clinicians are responsible for viewing full images per the standard of care.

	Subject device: CINA-iPE Software	Predicate device: BriefCase Software (K213886)
	images. Notified clinicians are ultimately responsible for reviewing full images per the standard of care.	
User population	Radiologist	Appropriately trained medical specialists
Anatomical region of interest	Chest or exams including at least a part of the lung	Chest
Data acquisition protocol	Contrast-enhanced CT scans (not dedicated CTPA protocol) containing at least a part of the lung	Contrast-enhanced chest CTs (but not dedicated CTPA protocol)
View DICOM data	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
Algorithm	Artificial intelligence algorithm with database of images	Artificial intelligence algorithm with database of images
Notification / Prioritization	Yes	Yes
Preview images	Presentation of a compressed, grayscale, unannotated image that is marked "not for diagnostic use" is displayed as a preview function.	Presentation of a low-quality, compressed grayscale preview image that is captioned "Not for diagnostic use".
Alteration of original image	No	No
Removal of cases from worklist queue	No. The device operates in parallel with the standard of care, which remains the default option for all cases.	No. The device operates in parallel with the standard of care, which remains the default option for all cases.
Structure	-iPE image processing application - Compatibility of use with the CINA Platform device (worklist and Image Viewer) or other medical image communications device,	-AHS module/Orchestrator (image acquisition). - ACS module (image processing). - Aidoc Worklist application for workflow integration (worklist and non-diagnostic basic Image Viewer).

Conclusion

CINA-iPE and BriefCase have the same intended use and substantially similar indications, technological characteristics, and principles of operation. The following is a summary of the substantial equivalence comparison:

- The predicate device is legally marketed.
- CINA-iPE has the same intended use as the predicate device, i.e., Aidoc Medical, Ltd.'s BriefCase, and therefore it may be found substantially equivalent.
- CINA-iPE and the predicate device have very similar indications for use.
- CINA-iPE has similar technological characteristics as the predicate and reference devices, i.e., the deployment of an artificial intelligence algorithm with a database of images.
- Standalone performance study demonstrates that the CINA-iPE and the predicate BriefCase raise the same types of safety and effectiveness questions, namely, accurate detection of findings within the processed study.

Accordingly, the subject CINA-iPE device is substantially equivalent to the predicate BriefCase device.