Avicenna.AI
℅ John Smith
Partner
Hogan Lovells, US LLP
555 Thirteenth Street, NW
Washington, District of Columbia 20004

May 31, 2024

Re: K240612
Trade/Device Name: Cina-VCF
Regulation Number: 21 CFR 892.2080
Regulation Name: Radiological computer aided triage and notification software
Regulatory Class: Class II
Product Code: QFM
Dated: March 5, 2024
Received: March 5, 2024

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.
Assistant Director
Imaging Software Team
DHT8B: Division of Radiological Imaging
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Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

Submission Number *(if known)*

K240612

Device Name

CINA-VCF

Indications for Use *(Describe)*

CINA-VCF is a radiological computer aided triage and notification software indicated for use in patients aged 50 years and over undergoing non-enhanced or contrast-enhanced CT scans which include the chest and/or abdomen.

The device is intended to assist hospital networks and appropriately trained medical specialists within the standard-of-care bone health setting in workflow triage by flagging and communication of suspected positive cases of Vertebral Compression Fractures (VCF) findings.

CINA-VCF uses an artificial intelligence algorithm to analyze images and highlight cases with detected findings on a standalone application in parallel to the ongoing standard of care image interpretation. 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-VCF 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)*

☒ 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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510(K) SUMMARY

AVICENNA.AI's CINA-VCF

K240612

Submitter

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Date prepared: May 28, 2024

Device Identification

Name of Device:	CINA-VCF
Classification Name:	Radiological computer-assisted triage and notification software
Regulation No:	21 CFR § 892.2080
Product Code:	QFM
Regulatory Class:	Class II
Classification Panel:	Radiology devices

Predicate Device

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

510(k):	K222692
Trade Name:	BriefCase
Manufacturer:	Aidoc Medical Vision Ltd.
Classification Name:	Radiological computer-assisted triage and notification software
Regulation No:	21 CFR § 892.2080
Product Code:	QFM
Regulatory Class:	Class II

Device Description

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

CINA-VCF runs on a standard “off the shelf” server/workstation and consists of VCF Image Processing Application, which can be integrated, deployed and used with the CINA Platform (cleared under K200855) or other compatible medical image communications devices. CINA-VCF receives non-enhanced or contrast-enhanced CT scans (which include the chest and/or abdomen) 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 Vertebral Compression Fractures (VCF) findings 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.

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 vertebral compressions fracture (VCF).

The device uses deep learning models to detect VCF at the T1-L5 level. The models were trained end-to-end on a dataset of 886 series collected from multiple centers in the USA and France satisfying the device protocol and representing a large distribution of scanner models from Siemens, Philips, GE and Canon (formerly Toshiba), acquisition protocols, spine presentation and fracture location and severity. Additional models, trained on subsets of this dataset, are used to locate the spine, identify the vertebra bodies and exclude vertebra which have been subjected to vertebroplasty or contains orthopedic material.

The Worklist Application displays all incoming suspect cases, each notified case is marked with an icon. In addition, compressed, grayscale, unannotated images that are captioned “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 specialist with worklist prioritization 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 practice alone.

The CINA Platform is an example of medical image communications platform for integrating and deploying the CINA-VCF 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 which receives notifications from the CINA-VCF Image Processing application.

Intended Use / Indications for Use

CINA-VCF is a radiological computer aided triage and notification software indicated for use in patients aged 50 years and over undergoing non-enhanced or contrast-enhanced CT scans which include the chest and/or abdomen.
The device is intended to assist hospital networks and appropriately trained medical specialists within the standard-of-care bone health setting in workflow triage by flagging and communication of suspected positive cases of Vertebral Compression Fractures (VCF) findings.
CINA-VCF uses an artificial intelligence algorithm to analyze images and highlight cases with detected findings on a standalone application in parallel to the ongoing standard of care image interpretation. 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-VCF 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-VCF 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-VCF device as standalone software. CINA-VCF 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-VCF 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-VCF application with the primary endpoint to evaluate the software's performance in identifying vertebral compression fractures (VCF) on non contrast-enhanced/contrast-enhanced Chest and/or Abdominal CT images performed for another clinical indications than for thoraco-lumbar vertebral compression fractures assessments, including at least three (3) consecutive measurable vertebrae in the T1-L5 portion of the spine, in 474 clinical anonymized cases.

The data was provided from multiple US (66.9%) and OUS (33.1%) clinical sites. There were 180 (37.9%) positive cases (CT with VCF) and 294 (62.1%) negative cases included in the analyses. The data was acquired by 4 different scanner makers and 38 different scanner models.

Multiple subgroups of interest were considered in the analysis. Mean age of patients included in the study was 72.1 ± [SD] 10.1 yo (MIN = 50 yo and MAX = 100 yo) and 50.8% were female. Data were acquired from different regions across the US to account for race/ethnicity in the intended US patient population. Additional scanner parameters considered were slice thickness, number of detector rows, and kVp ranges, contrast vs non-contrast, imaging protocol (chest and/or abdomen), reconstruction kernel (soft/standard). Detailed subgroup analysis were reported in the labeling.

Device Area Under the Receiver Operating Characteristic curve (ROC AUC) was computed against the ground truth established by consensus of three US-board-certified expert radiologists, as the primary endpoint, in accordance with the established required technical method under the QFM product code. A case was considered positive if at least one moderate or severe vertebral compression fracture located within the thoracic or lumbar spine was identified by the experts.

Sensitivity, Specificity and Accuracy, were also assessed as additional analyses.

The secondary endpoint was CINA-VCF time-to-notification, which was compared to the predicate device for true positive cases only, as provided by the predicate device - BriefCase (Aidoc Medical - K222692).

The ROC AUC was 0.974 [95% CI: 0.962 - 0.986], which exceeded the 0.95 performance goal, thus, achieving the primary endpoint.

Sensitivity and Specificity were 95.2% [95% CI: 90.7% – 97.9%] and 92.9% [95% CI: 89.4% – 96.5%], respectively. Similarly, the overall agreement (Accuracy) was 93.7% [95% CI: 91.1% - 95.7%], which represents very good predictions.

The CINA-VCF prioritization and triage effectiveness (time-to-notification) was evaluated by the standalone per-case processing time of the device, which corresponds to time between the end of the DICOM reception (made available for VCF image processing) and the end of processing (positive or negative identification). The results are presented below:

Table 1: Time-to-Notification for CINA-VCF Image Processing Application

Time-to-Notification (seconds)	MEAN ± SD	MEDIAN	95% CI	MIN	MAX
CINA-VCF All cases (N = 474)	23.4 ± 8.4	21.0	[22.7 - 24.2]	9.0	60.0
CINA-VCF True Positive cases (N = 158)	21.7 ± 7.5	20.0	[20.5 - 22.8]	9.0	45.0

The mean [95% CI] time-to-notification for all included cases (n = 474) was estimated to be 23.4 [95% CI: 22.7 – 24.2] seconds for CINA-VCF.

When taking into account only true positive cases (n = 158), the mean [95% CI] time-to-notification was 21.7 [95% CI: 20.5 – 22.9] seconds for CINA-VCF and 117.2 [95% CI: 98.64 – 135.85] seconds for BriefCase, the selected predicate device.

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

Substantial Equivalence

The subject CINA-VCF and the predicate BriefCase device are both intended to assist hospital networks and appropriately trained medical specialists within the standard-of-care bone health setting in workflow triage by flagging and communication of suspected positive cases of Vertebral Compression Fractures (VCFx) findings 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-VCF 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. The subject CINA-VCF device and the predicate BriefCase are software packages with substantially 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 both devices, the labeling instructs the user to further evaluate and diagnose based only on the original images in the local PACS.

The subject CINA-VCF 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 (First-in-first-out) queue, thus not disturbing standard interpretation of the images by the attending specialists. The subject and predicate devices achieve time-to-notification performance improvements in a similar range of time and thus contribute similarly to effective triage and early involvement of the specialist in evaluating suspected images of vertebral compression fractures.

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

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

Table 2: Comparison of key features between CINA-VCF and predicate device (Aidoc Medical Vision Ltd)

	Subject device: CINA-VCF Software	**Predicate device: BriefCase Software (K222692)**
Intended Use / Indications for Use	CINA-VCF is a radiological computer aided triage and notification software indicated for use in patients aged 50 years and over undergoing non-enhanced or contrast-enhanced CT scans which include the chest and/or abdomen. The device is intended to assist hospital networks and appropriately trained medical specialists within the standard-of-care bone health setting in workflow triage by flagging and communication of suspected positive cases of Vertebral Compression Fractures (VCF) findings. CINA-VCF uses an artificial intelligence algorithm to analyze images and highlight cases with detected findings on a standalone application in parallel to the ongoing standard of care image interpretation. 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-VCF 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.	BriefCase is a radiological computer aided triage and notification software indicated for use in the analysis of chest and abdominal CT images. The device is intended to assist hospital networks and appropriately trained medical specialists within the standard-of-care bone health setting in workflow triage by flagging and communication of suspected positive cases of Vertebral Compression Fractures (VCFx) findings. BriefCase uses an artificial intelligence algorithm to analyze images and highlight cases with detected findings on a standalone application in parallel to the ongoing standard of care image interpretation. The device does not alter the original medical image and is not intended to be used as a diagnosis 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.
User population	Trained medical specialists within standard-of-care bone health settings	Hospital networks and appropriately trained medical specialists within the standard of-care bone health setting
Anatomical region of interest	Chest and/or abdomen.	Chest and abdomen
Data acquisition protocol	Non-enhanced / contrast-enhanced CT scans of the chest and/or abdomen.	Chest and abdominal CT scans
Passive notification-	Yes	Yes

	Subject device: CINA-VCF Software	**Predicate device: BriefCase Software (K222692)**
only, parallel workflow tool		
Interference with standard workflow	No	No
Algorithm	Artificial intelligence algorithm	Artificial intelligence algorithm
Preview images	Presentation of compressed, grayscale, unannotated images that is marked “not for diagnostic use”	Presentation of compressed, low-quality, grayscale, unannotated 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	-VCF 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 Desktop application for workflow integration (feed and non-diagnostic Image Viewer).

Conclusion

CINA-VCF 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-VCF has the same intended use as the predicate device, i.e., Aidoc Medical Vision Ltd. 's BriefCase, and therefore it may be found substantially equivalent.
- CINA-VCF and the predicate device have very similar indications for use.
- CINA-VCF has similar technological characteristics as the predicate device, i.e., the deployment of an artificial intelligence algorithm with a database of images.

- Standalone performance study demonstrates that the CINA-VCF 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-VCF device is substantially equivalent to the predicate BriefCase device