Avicenna.ai
% John Smith
Partner
Hogan Lovells US LLP
555 13th Street, NW
WASHINGTON, DISTRICT OF COLUMBIA 20004

November 22, 2022

Re: K221716
Trade/Device Name: Cina
Regulation Number: 21 CFR 892.2080
Regulation Name: Radiological Computer Aided Triage And Notification Software
Regulatory Class: Class II
Product Code: QAS
Dated: October 21, 2022
Received: October 25, 2022

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 (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,

Jessica Lamb,
Assistant Director
Imaging Software Team
DHT8B: Division of Radiological Imaging Devices and Electronic Products
OHT8: Office of Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

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

510(k) Number *K221716*

Device Name
Cina

Indications for Use *(Describe)*

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 angiography 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) head CT angiography for large vessel occlusion (LVO) of the anterior circulation (distal ICA, MCA-M1 or proximal MCA-M2). 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 judgement 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)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

510(k) SUMMARY

AVICENNA.AI's Cina

I. Submitter

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Date prepared: November, 22, 2022

II. Device Identification

Name of Device:	Cina
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 is claimed to be substantially equivalent to Cina (K200855).

IV. Purpose of the Special 510(k) Notice

The modifications to Cina consist in minor software changes and labeling updates.

The main following modification that has been made is to the indications for use of the device within the labeling:

Indications for use have been modified with new information to include:

"*large vessel occlusion (LVO)* ***of the anterior circulation (distal ICA, MCA-M1 or proximal MCA-M2)****."*

V. Intended Use / Indications for Use

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 angiography 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) head CT angiography for large vessel occlusion (LVO) of the anterior circulation (distal ICA, MCA-M1 or proximal MCA-M2).

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 judgement to assist with triage/prioritization of medical images. Notified clinicians are ultimately responsible for reviewing full images per the standard of care.

VI. Device Description

Cina 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 suspicious results of an intracranial hemorrhage (ICH) or a large vessel occlusion (LVO), 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 (ICH or LVO). All the non-enhanced head CT images and head CT angiography studies received by Cina device are displayed in the worklist and those on which the algorithms have detected a suspected finding (ICH or LVO) 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.

VII. Summary of Technological Characteristics

The subject and predicate devices have the same technological characteristics.

Cina runs on a standard “off the shelf” server/workstation and is made of the following software components:

- Cina Image Processing Applications including two applications: ICH and LVO;
- Cina Platform server that includes the Worklist client application in which notifications from the Cina Image Processing applications (ICH and LVO) are received.

Cina receives 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 ICH or LVO 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.

VII.1. Cina Platform

The Cina platform is an example of medical image communications platform for integrating and deploying the Cina ICH and LVO 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 Image Processing applications (ICH and LVO) are received.

VII.2. ICH Application

The ICH application includes the software algorithm responsible for identifying and quantifying image characteristics that are consistent with an ICH. 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 an ICH is detected) compatible with the Cina Platform and with DICOM format.

VII.3. LVO Application

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

VIII. Substantial Equivalence

The subject and predicate devices have a similar intended use, technological characteristics, and principles of operation. The only difference is that the intended use of the subject has been revised to include the vessels (arteries) for which the device was designed and tested to detect LVO (the anterior circulation: distal ICA, MCA-M1 or proximal MCA-M2). Both devices are intended to provide the users with notifications and unannotated preview images of suspect studies for the purpose of preemptive triage, and are therefore substantially equivalent. A table comparing the key features of the subject and predicate devices is provided below.

Table 1: Substantial Equivalence Chart

	Subject device: Cina Software	**Predicate device: Cina software (K200855)**
Intended Use / Indications for Use	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 angiography 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 angiography of the head for large vessel occlusion (LVO) of the anterior circulation (distal ICA, MCA-M1 or proximal MCA-M2). 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.	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 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 Software	**Predicate device: Cina software (K200855)**
User population	Radiologist	Radiologist
Anatomical region of interest	Head	Head
Data acquisition protocol	Non contrast CT scan of the head or neck and CT angiogram images of the brain	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
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 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.	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.
Alteration of original image	No	No
Removal of cases from worklist queue	No	No
Structure	- LVO and ICH image processing applications - Cina Platform (worklist and Image Viewer)	- LVO and ICH image processing applications - Cina Platform (worklist and Image Viewer)

IX. Summary of Performance Data

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

IX.1. Software Verification and Validation Testing

The Cina device has been evaluated and verified in accordance with software specifications and applicable performance standards through 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".

IX. 2. Performance Testing

Avicenna.AI conducted a retrospective, blinded, multicenter, multinational study with the Cina software with the primary endpoint to evaluate the software's performance in 1) non-contrast CT (NCCT) head images pertaining to patient with suspected intracranial hemorrhage (ICH) findings and 2) CT angiography (CTA) head series pertaining to patient with suspected large vessel occlusion (LVO) findings, in 814 and 476 clinical anonymized cases, respectively. The device's Sensitivity and Specificity were analyzed, in addition to time-to-notification.

The data was provided from 3 clinical sources (2 US and 1 OUS). There were 255 (31.3%) positive ICH (images with ICH) and 188 (39.5%) positive LVO (images with LVO) cases included in the analysis. Within the 188 LVO positive cases, 156 (83%) were US and 32 (17%) OUS. Both tested dataset (for ICH and LVO) contained a sufficient number of cases from important cohorts in terms of imaging acquisitions (e.g., scanner makers – GE, Siemens, Philips and Toshiba/Canon; number of detector rows, gantry tilt and slice thickness) and patients' groups (e.g., age, sex and US regions).

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

Sensitivity and Specificity for the "ICH" prioritization and triage application are 91.4% (95% CI: 87.2% – 94.5%) and 97.5% (95% CI: 95.8% – 98.6%), respectively. These findings achieved the 80% performance goal and are the same as those reported for Cina - ICH (K200855, the predicate device.

The ROC curve shows an AUC of 0.94, which is also the same as for the predicate device.

Regarding the "LVO" prioritization and triage application, Sensitivity and Specificity of 97.9% (95% CI: 94.6% – 99.4%) and 97.6% (95% CI: 95.1% – 99%), respectively are observed. These results achieved the 80% performance goal and are the same as the ones reported for Cina - LVO (K200855), the predicate device.

The ROC curve shows an AUC of 0.98, which is also the same as for the predicate device.

The results of the standalone assessment study demonstrated an overall agreement (accuracy) of 95.6% and 97.7% for the "ICH" and "LVO" tested cases, respectively, when compared to the ground truth (operators' visual assessments).

Positive predictive value (PPV) and negative predictive value (NPV) with varying prevalence, for both applications, are presented in **Table 1** below:

Table 1: PPV and NVP values for ICH and LVO image processing applications

Prevalence	Cina - ICH triage application		Cina - LVO triage application	
	PPV (%)	NPV (%)	PPV (%)	NPV (%)
10%	80.2	99.0	81.7	99.8
15%	86.6	98.5	87.7	99.6
20%	90.1	97.8	91.0	99.5
25%	92.4	97.1	93.1	99.3
30%	94.0	96.3	94.5	99.1
35%	95.2	95.5	95.6	98.8

40%	96.1	94.4	96.4	98.6
45%	96.8	93.2	97.1	98.2
50%	97.3	91.9	97.6	97.9

Additionally, both “ICH” and “LVO” 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 ICH and LVO image processing applications

Time-to-Notification	MEAN ± SD (seconds)	MEDIAN (seconds)	Lower 95% CI (seconds)	Upper 95% CI (seconds)	MIN (seconds)	MAX (seconds)
Cina-ICH (N = 814)	13.2 ± 2.9	13.2	13.0	13.4	8.6	39.1
Cina-LVO (N = 476)	25.8 ± 7.0	24.7	25.1	26.4	13.0	55.3

The standalone effectiveness assessment demonstrated a substantial equivalence of the Cina - ICH triage application when compared to the predicate device (Cina-ICH – K200855). Specifically, the Cina’s “ICH” triage mean ± SD “time-to-notification” is estimated to 13.2 ± 2.9 seconds. This is similar to the one reported for the predicate device (Cina-ICH – K200855: 21.6 ± 4.4 seconds).

Regarding Cina - LVO triage application, the mean ± SD “time-to-notification” is estimated to 25.8 ± 7.0 seconds. This demonstrated a substantial equivalence with the predicate device (Cina-LVO – K200855: 34.7 ± 10.7 seconds).

The performance testing of the Cina device establishes that the subject device is as safe and effective as the predicate device. This established that the Cina device meets its intended use statement and is substantially equivalent to the predicate device.

X. Conclusions

The subject Cina device is as safe and effective as the predicate Cina, with the similar intended use, technological characteristics, and principles of operation. Including in the intended use the vessels (arteries) for which the device was designed and tested to detect LVO does not raise new or different questions of safety or effectiveness.