AVICENNA.AI
% John J. Smith, M.D., J.D.
Partner
Hogan Lovells US LLP
555 Thirteenth Street, NW
WASHINGTON DC 20004

June 24, 2020

Re: K200855
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: March 31, 2020
Received: March 31, 2020

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); 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: 06/30/2020
See PRA Statement below

510(k) Number *(if known)*

K200855

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 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.

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

I. Submitter

Applicant:
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Date prepared: March 31, 2020

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 device is substantially equivalent to the following FDA cleared predicate device with regard to indications for use, performance, and technological characteristics:

510(k):	K180647
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 Viz.ai's ContaCT (DEN170073), which is a Class II device under the same regulation and product code as above.

IV. 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 angiographies 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.

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 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.

VI. Summary of 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.

Each of these components is briefly described below.

VI.1. CINA Platform

The CINA platform is the technical platform for integrating and deploying CINA image processing applications. It provides the necessary requirements for interoperability 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 display medical device data such as radiological data.

VI.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.

VI.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.

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 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”.

VII.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.

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 were observed to be 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 similar to the results reported for the predicate device BriefCase (Aidoc Medical): Sensitivity and specificity of 93.6% (95% CI: 86.6% - 97.6%) and 92.3% (95% CI: 85.4% - 96.6%), respectively. ROC curve showed an AUC of 0.94.

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 were observed. These results achieved the 80% performance goal and are similar to the ones reported by the reference device ContaCT (Viz.AI): Sensitivity was 87.8% (95% CI: 81.2% – 92.5%) and specificity was 89.6% (95% CI: 83.7% – 93.9%). ROC curve showed an AUC of 0.98.

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)	MIN (seconds)	MAX (seconds)
CINA - ICH	21.6 ± 4.4	20.4	14.4	53.3
CINA - LVO	34.7 ± 10.7	33.4	14.3	63.3

The standalone effectiveness assessment demonstrated a substantial equivalence of the CINA - ICH triage application when compared to the predicate device (BriefCase). Specifically, the CINA’s “ICH” triage mean “time-to-notification” was estimated to be 21.6 seconds. This is similar to the one reported by the predicate BriefCase device (mean: 4.46 minutes).

Regarding CINA - “LVO” triage application, the mean “time-to-notification” was estimated to be 34.7 seconds. This demonstrated a substantial equivalence of the CINA - LVO triage application effectiveness when compared to the reference ContaCT device (mean: 7.32 minutes).

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

VIII. Substantial Equivalence

The subject CINA for ICH and LVO prioritization and triage, the predicate device BriefCase device for ICH triage and the reference Viz.AI for LVO triage are all intended to aid in prioritization and triage of radiological images for ICH and/or LVO. 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.

All three devices 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 ICH and/or LVO.

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

Table 3 compares the key features of the subject and the predicate and reference devices.

Table 3: Comparison of key features between CINA and predicate device (Aidoc BriefCase) and reference device (Viz.AI ContaCT)

	Subject device: CINA Software	**Predicate device: Aidoc BriefCase Software (K180647)**	**Reference device: Viz.AI ContaCT software (DEN170073)**
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 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	BriefCase is a radiological computer aided triage and notification software indicated for use in the analysis of non-enhanced head CT images. The device is intended to assist hospital networks and trained radiologists in workflow triage by flagging and communication of suspected positive findings of pathologies in head CT images, namely Intracranial Hemorrhage (ICH). BriefCase uses an artificial intelligence algorithm to analyze images and highlight cases with detected ICH 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 ICH findings. Notifications include compressed	ContaCT is a notification-only, parallel workflow tool for use by hospital networks and trained clinicians to identify and communicate images of specific patients to a specialist, independent of standard of care workflow. ContaCT uses an artificial intelligence algorithm to analyze images for findings suggestive of a pre-specified clinical condition and to notify an appropriate medical specialist of these findings in parallel to standard of care image interpretation. Identification of suspected findings is not for diagnostic use beyond notification. Specifically, the device analyzes CT angiogram images of the brain acquired in the acute setting and sends notifications to a neurovascular specialist that a suspected large vessel occlusion has been identified and recommends review of those images. Images can

	Subject device: CINA Software	**Predicate device: Aidoc BriefCase Software (K180647)**	**Reference device: Viz.AI ContaCT software (DEN170073)**
	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.	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.	be previewed through a mobile application. Images that are previewed through the mobile application are compressed and are for informational purposes only and not intended for diagnostic use beyond notification. Notified clinicians are responsible for viewing non-compressed images on a diagnostic viewer and engaging in appropriate patient evaluation and relevant discussion with a treating physician before making care-related decisions or requests. ContaCT is limited to analysis of imaging data and should not be used in-lieu of full patient evaluation or relied upon to make or confirm diagnosis.
User population	Radiologist	Radiologist	Clinician (e.g., neurovascular specialist)
Anatomical region of interest	Head	Head	Head
Data acquisition protocol	Non contrast CT scan of the head or neck and CT angiogram images of	Non contrast CT scan of the head or neck	CT angiogram images of the brain

	Subject device: CINA Software	**Predicate device: Aidoc BriefCase Software (K180647)**	**Reference device: Viz.AI ContaCT software (DEN170073)**
	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 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.	Presentation of a small, compressed, black and white preview image that is labeled "Not for diagnostic use".
Alteration of original image	No	No	No
Removal of cases from worklist queue	No	No	No
Structure	- LVO and ICH image processing	- AHS module (image acquisition),	- Image Forwarding Software

	Subject device: CINA Software	**Predicate device: Aidoc BriefCase Software (K180647)**	**Reference device: Viz.AI ContaCT software (DEN170073)**
	applications - CINA Platform (worklist and Image Viewer)	- ACS module (image processing), - Aidoc Worklist application for workflow integration (worklist and Image Viewer).	- Image Processing and Analysis Software - Non-diagnostic DICOM viewing mobile application