Nines, Inc.   April 21, 2020
℅ John J. Smith, M.D., J.D.
Regulatory Counsel
Hogan Lovells US LLP
555 13th Street, NW
WASHINGTON DC 20004

Re: K193351
      Trade/Device Name: NinesAI
      Regulation Number: 21 CFR 892.2080
      Regulation Name: Radiological computer aided triage and notification software
      Regulatory Class: Class II
      Product Code: QAS
      Dated: March 30, 2020
      Received: March 30, 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

K193351

Device Name

NinesAI

Indications for Use *(Describe)*

NinesAI is a parallel workflow tool indicated for use by hospital networks and trained clinicians to identify images of specific patients to a radiologist, independent of standard of care workflow, to aid in prioritizing and performing the radiological review. NinesAI uses artificial intelligence algorithms to analyze head CT images for findings suggestive of a pre-specified emergent clinical condition.

The software automatically analyzes Digital Imaging and Communications in Medicine (DICOM) images as they arrive in the Picture Archive and Communication System (PACS) using machine learning algorithms. Identification of suspected findings is not for diagnostic use beyond notification. Specifically, the software analyzes head CT images of the brain to assess the suspected presence of intracranial hemorrhage and/or mass effect and identifies images with potential emergent findings in a radiologist's worklist.

NinesAI is intended to be used as a triage tool limited to analysis of imaging data and should not be used in-lieu of full patient evaluation or relied upon to make or confirm a diagnosis. Additionally, preview images displayed to the radiologist outside of the DICOM viewer are non-diagnostic quality and should only be used for informational purposes.

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)

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510(k) SUMMARY
Nines, Inc.'s NinesAI
K193351

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Submitter:

      Nines, Inc.
      329 Alma Street
      Palo Alto, CA 94301

Contact Person:

      Dr. Russell Stewart
      Phone: 650 924 6159
      russell@ninesai.com

Date Prepared: April 17, 2020

Name of Device: NinesAI

Classification Name: Radiological Computer-Assisted Triage and Notification Software

Regulatory Class: Class II

Product Code: QAS

Predicate Device: Aidoc Medical's BriefCase (K180647)

Device Description

NinesAI notifies a radiologist of the presence of a suspected critical abnormality in a radiological image. The software system is a complete package comprised of image analysis software and a workstation module that is used to alert the radiologist. The image analysis can also be configured to send HL7 messages and DICOM secondary series.

The image analysis uses Artificial Intelligence (AI) technology to analyze non contrast CT Head scans for the presence of Intracranial Hemorrhage and/or Mass Effect. More specifically, the device utilizes two machine learning (ML) algorithms to detect each finding respectively.

NinesAI is a software device and does not come into contact with patients. All radiological studies are still reviewed by trained radiologists. NinesAI is meant to be used as an aid for case prioritization.

Intended Use / Indications for Use

NinesAI is a parallel workflow tool indicated for use by hospital networks and trained clinicians to identify images of specific patients to a radiologist, independent of standard of care workflow, to aid in prioritizing and performing the radiological review. NinesAI uses artificial intelligence algorithms to analyze head CT images for findings suggestive of a pre-specified emergent clinical condition.

The software automatically analyzes Digital Imaging and Communications in Medicine (DICOM) images as they arrive in the Picture Archive and Communication System (PACS) using machine learning algorithms. Identification of suspected findings is not for diagnostic use beyond notification. Specifically, the software analyzes head CT images of the brain to assess the suspected presence of intracranial hemorrhage and/or mass effect and identifies images with potential emergent findings in a radiologist's worklist.

NinesAI is intended to be used as a triage tool limited to analysis of imaging data and should not be used in-lieu of full patient evaluation or relied upon to make or confirm a diagnosis. Additionally, preview images displayed to the radiologist outside of the DICOM viewer are non-diagnostic quality and should only be used for informational purposes.

Summary of Technological Characteristics

The NinesAI indications for use differ slightly from the predicate, but the minor differences do not negatively impact the safety and effectiveness of the subject device. In sum, the predicate is indicated for use to analyze images for the presence of ICH. NinesAI is indicated for use to analyze ICH, as well as Mass Effect. The additional potential finding of Mass Effect can be seen concomitantly with ICH cases and the detection of such potential pathology is supported by performance testing. All potential findings covered by the predicate and NinesAI are emergent findings in the head.

Artificial intelligence algorithms are the technological principle for both the subject and predicate devices. The algorithms are trained using a database of radiological images. At a high level, the subject and predicate devices are based on the following same technological elements:

- Artificial Intelligence Algorithm(s);
- Notification Technology.

A table comparing the key features of the subject and predicate devices is provided below.

	NinesAI (K193351)	AIDoc's BriefCase (K180647)
Indications for Use	NinesAI is a parallel workflow tool indicated for use by hospital networks and trained clinicians to identify images of specific patients to a radiologist, independent of standard of care workflow, to aid in prioritizing and performing the radiological review. NinesAI uses artificial intelligence algorithms to analyze head CT images for findings	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,

	NinesAI (K193351)	AIDoc's BriefCase (K180647)
	suggestive of a pre-specified emergent clinical condition. The software automatically analyzes Digital Imaging and Communications in Medicine (DICOM) images as they arrive in the Picture Archive and Communication System (PACS) using machine learning algorithms. Identification of suspected findings is not for diagnostic use beyond notification. Specifically, the software analyzes head CT images of the brain to assess the suspected presence of intracranial hemorrhage and/or mass effect and identifies images with potential emergent findings in a radiologist's worklist. NinesAI is intended to be used as a triage tool limited to analysis of imaging data and should not be used in-lieu of full patient evaluation or relied upon to make or confirm a diagnosis. Additionally, preview images displayed to the radiologist outside of the DICOM viewer are non-diagnostic quality and should only be used for informational purposes.	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 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.
User Population	Radiologists	Radiologists
Technological Characteristics	Artificial Intelligence algorithms detecting emergent findings sending notifications to the workstation.	Artificial Intelligence algorithms detecting emergent findings sending notifications to the workstation.
Components	- Artificial Intelligence Algorithm - Notification Technology	- Artificial Intelligence Algorithm - Notification Technology
Anatomical Region of Interest	Head	Head
Findings Covered	Intracranial Hemorrhage and Mass Effect	Intracranial Hemorrhage
Data Acquisition Protocol	Non contrast CT scan of the head	Non contrast CT scan of the head or neck
View DICOM Data	DICOM information about the patient, study and current image	DICOM information about the patient, study and current image
Preview Images	Presentation of notification and preview of the study for initial assessment not meant for diagnostic purposes. This is done via desktop notification or via DICOM series. The device operates in parallel with the standard of care, which remains	Presentation of notification and preview of the study for initial assessment not meant for diagnostic purposes. This is done via desktop notification. The device operates in parallel with the standard of care, which remains

	NinesAI (K193351)	AIDoc's BriefCase (K180647)
	the default option for all cases	the default option for all cases
Alteration of Original Image	No	No
Removal of Cases from Worklist Queue	No	No
Triage Notification Types	Workstation Application Notification, HL7	Workstation Application Notification

Performance Testing

Nines performed software verification and validation testing that covers the performance of the algorithms, as well as the performance of the software and its components. In all instances, NinesAI functioned as intended and expected.

The NinesAI device underwent performance testing to verify the efficacy and safety of the machine learning algorithms. Both of the algorithms used in NinesAI were evaluated independently from each other to allow for an individual understanding of each algorithm's respective performance. Each algorithm was tested in a retrospective performance trial, with the primary endpoints of each trial being the respective sensitivity and specificity of the algorithm in question. Other endpoints included: Positive Predictive Value, Negative Predictive Value, ROC AUC, time savings relative to standard of care, and agreement rate between labelers who determined ground truth for the test dataset studies. Head CT studies included in each of the test datasets were obtained from over 20 clinical sites and included a minimum of 3 scanner manufacturers and over 20 scanner models, and also reflected broad patient demographics.

The primary endpoints for each algorithm are listed below:

Finding	Sensitivity [95% confidence intervals]	Specificity [95% confidence intervals]
Intracranial Hemorrhage	0.899 [0.837, 0.940]	0.974 [0.994, 0.992]
Mass Effect	0.964 [0.916, 0.987]	0.911 [0.856, 0.948]

A time benefit analysis was performed for each algorithm and showed a time-to-notification that is faster than the similar standard of care metric of time-to-open-dictation. These results are summarized below for each algorithm.

The time-savings data for Intracranial Hemorrhage is listed below:

Metric	Mean (min)	Median (min)
Time-to-open-dictation standard of care	159.4 [67.07, 251.7]	6.0

Metric	Mean (min)	Median (min)
Time-notification of NinesAI	0.23 [0.23, 0.24]	0.24

The time-savings data for Mass Effect is listed below:

Metric	Mean (min)	Median (min)
Time-to-open-dictation standard of care	28.5 [14.1, 42.8]	7.5
Time-notification of NinesAI	0.23 [0.23, 0.24]	0.24

The Intracranial Hemorrhage and Mass Effect algorithms met the performance goal outlined by the predicate device of .80 for both sensitivity and specificity. Additionally, the performance for each algorithm is comparable to the observed performance reported for the predicate device: 93.6% (95% CI: 86.6%-97.6%) sensitivity and 92.3% (95% CI: 85.4%-96.6%) specificity.

Based on the clinical performance as documented in the pivotal clinical study, the subject software has a safety and effectiveness profile that is similar to the predicate device.

Conclusions

NinesAI has the same intended uses and similar indications, technological characteristics, and principles of operation as its predicate device. The minor differences in indication do not alter the intended use of the device and do not affect its safety and effectiveness when used as labeled. In addition, the minor technological differences between the NinesAI and its predicate devices raise no new issues of safety or effectiveness. Performance data demonstrate that NinesAI performs as intended. Thus, NinesAI is substantially equivalent.