Aidoc Medical, Ltd.
% John J. Smith, M.D., J.D.
Regulatory Counsel
Hogan Lovells US LLP
555 Thirteenth Street, NW
WASHINGTON DC 20004

April 15, 2019

Re: K190072
Trade/Device Name: BriefCase
Regulation Number: 21 CFR 892.2080
Regulation Name: Radiological computer aided triage and notification software
Regulatory Class: Class II
Product Code: QAS
Dated: January 15, 2019
Received: January 15, 2019

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/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). 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 (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Michael D. O'Hara For

Thalia T. Mills, Ph.D.
Director
Division of Radiological Health
Office of In Vitro Diagnostics
and Radiological Health
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)*

K190072

Device Name

BriefCase

Indications for Use *(Describe)*

BriefCase is a radiological computer aided triage and notification software indicated for use in the analysis of non-enhanced head CT and CTPA images. The device is intended to assist hospital networks and trained radiologists in workflow triage by flagging and communication of suspected positive findings of Intracranial Hemorrhage (ICH) and Pulmonary Embolism (PE) pathologies. For the PE pathology, the software is only intended to be used on single-energy exams.

BriefCase uses an artificial intelligence algorithm to analyze images and highlight cases with detected findings 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 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 their professional judgment, to assist with triage/prioritization of medical images. Notified clinicians are responsible for viewing 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
Aidoc Medical, Ltd.'s BriefCase (K190072)

Submitter:

Aidoc Medical, Ltd.
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Phone: +972-73-7946870

Contact Person: N. Epstein, Ph.D.

Date Prepared: April 4th, 2019

Name of Device: BriefCase

Classification Name: Radiological computer-assisted triage and notification software device

Regulatory Class: Class II

Product Code: QAS (21 C.F.R. 892.2080)

Predicate Device: BriefCase (K180647, for ICH triage)

Device Description

BriefCase is a radiological computer-assisted triage and notification software device. The software system is based on an algorithm programmed component and is comprised of a standard off-the-shelf operating system, the Microsoft Windows server 2012 64bit, and additional applications, which include PostgreSQL, DICOM module and the BriefCase Image Processing Application. The device consists of the following three modules: (1) Aidoc Hospital Server (AHS); (2) Aidoc Cloud Server (ACS); and (3) Aidoc Worklist Application that is installed on the radiologist' desktop and provides the user interface in which notifications from the BriefCase software are received.

DICOM images are received, saved, filtered and de-identified before processing. Series are processed chronologically by running an algorithm on each series to detect suspected findings and then notifications on flagged series are sent to the Worklist desktop application, thereby prompting preemptive triage and prioritization.

The Worklist Application displays the pop-up text notifications of new studies with suspected findings when they come in. Notifications are in the form of a small pop-up containing patient name, accession number and the relevant pathology (e.g., PE). A list of all incoming cases with suspected findings is also displayed. Hovering over a notification or a case in the worklist pops up a compressed, small black and white, unmarked image that is captioned "not for diagnostic use" and 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 prompting the user to assess the relevant original images in the PACS. Thus, the suspect case receives attention earlier than would have been the case in the standard of care practice alone.

Intended Use / Indications for Use

BriefCase is a radiological computer aided triage and notification software indicated for use in the analysis of non-enhanced head CT and CTPA images. The device is intended to assist hospital networks and trained radiologists in workflow triage by flagging and communication of Intracranial Hemorrhage (ICH) and Pulmonary Embolism (PE) pathologies. For the PE pathology, the software is only intended to be used on single-energy exams.

BriefCase uses an artificial intelligence algorithm to analyze images and highlight cases with detected findings 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 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 their professional judgment, to assist with triage/prioritization of medical images. Notified clinicians are responsible for viewing full images per the standard of care.

Comparison of Technological Characteristics

The subject BriefCase for PE triage and predicate device BriefCase for ICH triage (K180647) are identical in all aspects and defer only with respect to the training of the algorithm on PE and ICH images, respectively.

Both devices are radiological computer-aided triage and notification software programs. Both devices are artificial intelligence algorithms incorporated software packages for use with CT scanners, PACS, and radiology workstations. As noted above, both devices are intended to aid in triage and prioritization of radiological images. The predicate device processes head CTs and is indicated for intracranial hemorrhage triage, while the subject device also processes CTPA images and is indicated for Pulmonary Embolism triage. Both devices are intended to provide radiologists with notifications and unannotated preview images of suspect studies for the purpose of preemptive triage.

In addition, both software devices notify the attending radiologist of the availability of time sensitive radiological medical images for review based on computer aided image analysis. Both devices send notifications and compressed previews to the radiology workstations' desktop. Notifications are meant to prompt the radiologist to start preemptive triage of a flagged case, upon which he may decide after observing the unannotated, low quality preview on his desktop, to turn to the local PACS to perform evaluation of the original series earlier than would have been the case without BriefCase.

Thus, the subject and predicate BriefCase raise the same types of safety and effectiveness questions, namely, accurate detection of findings within the processed study. It is important to note that, like the predicate, the subject device does not remove cases from the standard of care reading queue. Both devices operate in parallel with the standard of care, which remains the default option for all cases.

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

Table 1. Key feature comparison

	Predicate Device **Aidoc Briefcase for ICH triage (K180647)**	**Subject Device** **Aidoc Briefcase for ICH and PE triage**
Intended Use / Indications for Use	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 preview images that are meant for informational purposes only and not intended for diagnostic use eyond 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.	BriefCase is a radiological computer aided triage and notification software indicated for use in the analysis of non-enhanced head CT and CTPA images. The device is intended to assist hospital networks and trained radiologists in workflow triage by flagging and communication of suspected positive findings of Intracranial Hemorrhage (ICH) and Pulmonary Embolism (PE) pathologies. For the PE pathology, the software is only intended to be used on single-energy exams. BriefCase uses an artificial intelligence algorithm to analyze images and highlight cases with detected findings 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 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 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	Radiologist	Radiologist
Anatomical region of interest	Head	Head and chest
Data acquisition protocol	Non-contrast head CT scan	Non-contrast head CT scan and CTPA (single energy exams only)
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, annotate, or direct users' attention to a specific location in the original image	No; device does not mark, annotate, 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 small, compressed, black and white preview image that is labeled "Not for diagnostic use"; 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"; 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

Performance Data

Pilot Study Summary
The company conducted a retrospective evaluation of 2,803 CT pulmonary angiogram (CTPA) exams of patients with suspected PE, from a single center. The goal of this study was primarily to demonstrate that the BriefCase software can identify PE with high accuracy. Ground truth was determined by a review of a single radiologist and the radiology report. Another radiologist was used to break ties between the report and the reviewer.

Performance Endpoints: Specificity and sensitivity.

Pilot Study Results
Sensitivity was 93.0% (95% CI: 90.2%-95.1%). Specificity was 93.7% (95% CI: 92.7%-94.6%).

Pivotal Study Summary
Aidoc conducted a retrospective, blinded, multicenter, multinational study with the BriefCase software with the primary endpoint to evaluate the software's performance in identifying CTPAs containing pulmonary embolism in 184 cases from 3 clinical sites (2 US and 1 OUS). There were approximately an equal number of positive and negative cases (images with PE versus without PE) included in the analysis.

Sensitivity and specificity exceeded the 80% performance goal. Specifically, sensitivity was observed to be 90.6% (95% CI: 82.2%-95.9%) and specificity was observed to be 89.9% (95% CI: 82.2%-95.1%).

In addition, a secondary endpoint measure was Briefcase's potential clinical benefit of worklist prioritization for true positive PE cases. For that purpose, in two medical centers, one in Israel and one in the US, Aidoc compared the standard-of-care metric of time-to-exam-open to the software's time-to-notification metric for PE cases.

The BriefCase time-to-notification includes the time to get the DICOM exam, de-identify it, upload it to the cloud, analyze and send a notification back to the worklist application. The standard of care time-to-open-exam consisted of the time from the initial scan of the patient to when the radiologist first opened the exam for review.

The standard of care time-to-exam-open was compared to the BriefCase time-to-notification for 51 True Positive cases (i.e. identified as positive both by the reviewers as well as the BriefCase device), and the results are reported in the **Table 2** below.

The BriefCase time-to-notification for PE was 3.9 minutes (95% CI: 3.7-4.1). In contrast, standard

of care time-to-exam-open was much longer (64.1 minutes: 95% CI 36.6-91.5). The mean difference of 60.2 minutes (95% CI 32.7-87.6) for these two metrics is statistically significant and assuming the radiologist receives a notification on a true positive PE case and acts on it immediately, it can on average save 60.2 minutes (95% CI 32.7-87.6) compared to the time-to-exam-open in a FIFO reading queue. The value of 60.2 is based on the study of 51 cases, taken from 2 medical centers (1 US, 1 OUS), and may vary in practice.

Table 2. Time saving data

Parameter	N	Mean estimate	Lower Confidence Limit	Upper Confidence Limit	Median	P-value
Time-to-open-exam in the standard of care	51	64.1	36.6	91.5	49.0	
Time-to-notification of BriefCase PE	51	3.9	3.7	4.1	3.9	
Difference	51	60.2	32.7	87.6	45.2	<0.0001

Thus, the reported time savings data demonstrates that radiologists may have the opportunity to be involved in the clinical workflow substantially earlier thanks to the notifications from the BriefCase device.

In summary, performance validation data, combined with real-world evidence, establish the achievement of effective preemptive triage by the BriefCase image analysis algorithm as well as effective notification functionality of the BriefCase application, as compared to the standard of care for improved time-to-exam-open of a notified case.

Conclusions

The subject BriefCase for PE triage and the predicate BriefCase for ICH triage devices are both intended to aid in prioritization and triage of radiological medical images for the indications of Pulmonary Embolism and Intracranial Hemorrhage, respectively. The labeling of both devices clearly states that the devices are not for diagnostic use. Both devices are software packages with similar technological characteristics and principles of operation, incorporating deep learning AI algorithms that process images, and software to send notifications and unannotated compressed preview images to the radiologists' workstation. In both devices, the labeling instructs the user to further evaluate and diagnose based only on the original images in the local PACS.

Both 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. Both devices achieve reduction of the standard of care time-to-open-exam to several minutes, which is the BriefCase' time-to-notification, and thus contribute similarly to the standard of care workflow turnaround time reduction through preemptive triage.

The BriefCase device for PE triage is thus substantially equivalent to the BriefCase for ICH triage.