August 26, 2022

Aidoc Medical, Ltd.
% John Smith
Partner
Hogan Lovells U.S. LLP
555 Thirteenth Street NW
WASHINGTON DC 20004

Re: K222277
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: July 29, 2022
Received: July 29, 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,

For

Jessica Lamb, Ph.D.
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 below*

510(k) Number *(if known)*

K222277

Device Name

BriefCase

Indications for Use *(Describe)*

BriefCase is a radiological computer aided triage and notification software indicated for use in the analysis of CTPA images in adults or transitional adolescents aged 18 and older. The device is intended to assist hospital networks and appropriately trained medical specialists in workflow triage by flagging and communication of suspected positive findings of Pulmonary Embolism (PE) pathologies.

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 PE 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.

510(k) Summary
Aidoc Medical, Ltd.'s BriefCase
K222277

Submitter:

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Tel-Aviv, Israel

Phone: +972-73-7946870

Contact Person: Amalia Schreier, LLM.

Date Prepared: July 29, 2022

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 (PE triage, K203508)

Device Description

BriefCase is a radiological computer-assisted triage and notification software device. The software system is based on an algorithm programmed component and consists 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/Orchestrator) for image acquisition; (2) Aidoc Cloud Server (ACS) for image processing; and (3) Aidoc Desktop Application for workflow integration.

DICOM images are received, saved, filtered and de-identified before processing. Filtration matches metadata fields with keywords. Series are processed chronologically by running the algorithms on each series to detect suspected cases. The software then flags suspect cases by sending notifications to the desktop application, thereby facilitating triage and prioritization by the user. As the BriefCase software platform incorporates several triage algorithms, the user may opt to filter out notifications by pathology, e.g., a chest radiologist may choose to filter out alerts on ICH cases, and a neuro-radiologist would opt to divert pulmonary embolism ("PE") alerts. Where several medical centers are linked to a shared PACS, a user may read cases for a certain center but not for another, and thus may opt to filter out alerts by center. Activating the filter does not impact the order in which notifications are presented in the Aidoc Desktop Application.

The desktop application feed displays all incoming suspect cases, each notified case in a line. Hovering over a line in the feed pops up a compressed, low-quality, grayscale, unannotated 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 users with worklist prioritization 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 CTPA images in adults or transitional adolescents aged 18 and older. The device is intended to assist hospital networks and appropriately trained medical specialists in workflow triage by flagging and communication of suspected positive findings of Pulmonary Embolism (PE) pathologies.

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 notification for cases with suspected PE 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 BriefCase for PE triage (K203508) are identical in most aspects and differ with respect to their algorithm performance due to training the subject device on a larger data set, the addition of 2 operating points, and ability to process single and dual energy exams.

Both the predicate and subject device are radiological computer-aided triage and notification software programs. Both devices are artificial intelligence, deep-learning algorithms that incorporate software packages for use with DICOM 3.0 compliant CT scanners, PACS, and radiology workstations.

Both devices are intended to aid in triage and prioritization of radiological images and utilize the same design of deep learning algorithms trained on medical images. Both devices are intended to provide specialists with notifications and unannotated low-quality preview images of suspect studies for the purpose of preemptive triage.

The subject and predicate BriefCase devices 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 neither removes cases from the standard of care reading queue nor deprioritizes cases. 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 the primary predicate devices is provided below.

Table 1. Key Feature Comparison

	Predicate Device **Aidoc Briefcase (K203508)**	**Subject Device** **Aidoc Briefcase (K222277)**
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.	BriefCase is a radiological computer aided triage and notification software indicated for use in the analysis of CTPA images in adults or transitional adolescents aged 18 and older. The device is intended to assist hospital networks and appropriately trained medical specialists in workflow triage by flagging and communication of suspected positive findings of Pulmonary Embolism (PE) pathologies. 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 PE 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

	Predicate Device Aidoc Briefcase (K203508)	Subject Device Aidoc Briefcase (K222277)
	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.	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	Hospital networks and appropriately trained medical specialists	Hospital networks and appropriately trained medical specialists
Anatomical Region of Interest	Chest	Chest
Data Acquisition Protocol	CTPA	CTPA
Notification-Only (/notification alerts), Parallel Workflow Tool	Yes	Yes
Images Format	DICOM	DICOM
Interference with Standard Workflow	No. No cases are removed from Worklist or deprioritized.	No. No cases are removed from desktop application or deprioritized.
Inclusion/ Exclusion Criteria for Clinical Performance Testing	Inclusion criteria • CT pulmonary angiogram (CTPA) with a 64-slice scanner or higher; • Slice thickness 0.5 mm – 3.0 mm. • Scans performed on adults/ transitional adults ≥ 18 years of age. Exclusion Criteria • All studies that are technically inadequate, including studies with motion artifacts, severe metal artifacts, sub-optimal bolus timing or an inadequate field of view.	Inclusion criteria • CT pulmonary angiogram (CTPA) with a 64-slice scanner or higher; • Slice thickness 0.5 mm – 3.0 mm. • Scans performed on adults/ transitional adults ≥ 18 years of age. Exclusion Criteria • All studies that are technically inadequate, including studies with motion artifacts, severe metal artifacts, sub-optimal bolus timing or an inadequate field of view.

	Predicate Device Aidoc Briefcase (K203508)	Subject Device Aidoc Briefcase (K222277)
Algorithm	Artificial intelligence algorithm with database of images.	Artificial intelligence algorithm with database of images.
Structure	- AHS module (image acquisition); - ACS module (image processing); - Aidoc Worklist application for workflow integration (worklist and non-diagnostic Image Viewer).	- AHS module (image acquisition); - ACS module (image processing); - Aidoc Desktop Application for workflow integration (Feed/Worklist (alternate names) and non-diagnostic Image Viewer).

Performance Data

Pivotal Study Summary

Aidoc conducted a retrospective, blinded, multicenter, study with the BriefCase software to evaluate the software's performance in identifying CTPA images containing Pulmonary Embolism (PE) in 499 cases from 6 US-based clinical sites, compared to the ground truth as determined by three senior board-certified radiologists. The cases collected for the pivotal dataset were all distinct in time or center from the cases used to train the algorithm.

Primary endpoints were sensitivity and specificity with an 80% performance goal.

Secondary endpoints were BriefCase time-to-notification compared to the predicate device. Positive Predictive Value (PPV), Negative Predictive Value (NPV), Positive Likelihood Ratio (PLR), and Negative Likelihood Ratio (NLR) were also assessed.

Primary Endpoint

Sensitivity and specificity exceeded the 80% performance goal. Sensitivity was 94.86% (95% CI: 90.99%, 97.41%) and specificity was 94.04% (95% CI: 90.62%, 96.49%).

Secondary Endpoint

In addition, the time-to-notification metric observed for the BriefCase software in the 6 medical centers was compared to the equivalent metric of the predicate devices.

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 on a positive suspect case back to the desktop application.

The BriefCase time-to-notification was measured for all True Positive cases (i.e., identified as positive both by the reviewers as well as the BriefCase device) and is given in **Table 2** below. The Table also displays the same metric reported for the predicate BriefCase PE.

The time-to-notification results obtained for the subject BriefCase device show comparability with the primary predicate with regard to time savings to the standard of care review. The BriefCase mean time-to-notification for BriefCase for PE triage was 78.0 seconds (95% CI: 73.6-82.3). The time-to-notification for the predicate PE triage was 234 seconds (95% CI: 222-246).

Table 2. Time-to-notification Comparison for BriefCase Devices

Time -to-notification (in seconds)	Mean Estimate	95% Lower CL	95% Upper CL	Median	IQR
Predicate K203508 Processing Time	234	222	246	234	N/A
BriefCase Time-to-notification	78	73.6	82.3	64.5	53.2

NPV was 99.0% (95% CI: 98.3%- 99.5%) and PPV was 73.7% (95% CI: 63.9%- 81.7%).

PLR was 15.903 (95% CI: 10.019 - 25.242) and NLR was 0.055 (95% CI: 0.031- 0.097).

Thus, the reported similar time-to-notification data demonstrates that when using the subject BriefCase for PE triage the clinician may have the same benefit in time saving as with the predicate BriefCase for PE triage.

As can be seen in **Table 3** the mean age of patients whose scans were reviewed in the study was 62.1 years, with standard deviation of 17.3 years. Gender distribution was 48% male, 51% female and 1% unknown (**Table 4**). Scanner distribution can also be found in **Table 5** below.

Table 3. Descriptive Statistics for Age

	Mean	Std	Min	Median	Max	N
Age (Years)	62.1	17.3	18	64	90	499

Table 4. Frequency Distribution of Gender

Ground Truth Results	Gender				All	
	Male		Female			
	N	%	N	%	N	%
Positive	113	22.6	100	20.0	213	42.7
Negative	127	25.5	154	30.9	281	56.6
All	240	48.1	254	50.9	494	99.0

5 cases (4 negative, 1 positive) did not contain any gender information in the DICOM header and were classified as gender unknown.

Table 5. Frequency Distribution of manufacturer

Manufacturer	N	%
Siemens	201	40.3%
GE	100	20.0%
Canon	99	19.8%
Philips	99	19.8%
Total	499	100%

Clinical subgroups and confounders present in the dataset included the following: Fully negative; Heart & vascular; Chronic lung diseases; Trauma; Inflammatory; Oncology; None of the above.

Additional operating points:

In addition to the default operating point that was selected to maximize both sensitivity and specificity, two additional operating points (AOP) were selected to maximize specificity or sensitivity while maintaining a lower bound 95% confidence interval of 80% for sensitivity and specificity respectively:

AOP1: Sensitivity was 98.60% (95% CI: 95.96%-99.71%) and specificity was 85.26% (95% CI: 80.61%-89.17%).
AOP2: Sensitivity was 86.45% (95% CI: 81.12%-90.73%) and specificity was 98.25% (95% CI: 95.95%-99.43%).

In summary, performance goals were achieved for the default and two additional operating points.

Combined with the comparison results of time-to-notification metric with the predicate device, these data establish the achievement by the subject BriefCase of preemptive triage in the range of several minutes.

Conclusions

The subject BriefCase for PE triage and the predicate BriefCase for PE triage are intended to aid in prioritization and triage of radiological images for the indications for suspected positive findings of Pulmonary Embolism (PE) pathologies. Both devices are software packages with the same technological characteristics and principles of operation, incorporating deep learning AI algorithms that process images, and software to send notifications and display unannotated compressed low-quality preview images. In both devices, the labeling clearly states that the devices are not for diagnostic use and 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, do not remove images from the standard of care FIFO queue and do not de-prioritize cases, thus not disturbing standard interpretation of the images. Both devices notify the radiologist of time-sensitive critical cases within the range of several minutes, and thus contribute similarly to the standard of care workflow turnaround time reduction through preemptive triage.

The subject BriefCase device for PE triage is thus substantially equivalent to the primary predicate BriefCase for PE.