Aidoc Medical, Ltd.
% John J. Smith, M.D., J.D.
Partner
Hogan Lovells US LLP
555 Thirteenth St.
WASHINGTON DC 20004

March 14, 2022

Re: K214043
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: QFM
Dated: February 28, 2022
Received: February 28, 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 Diretor
Division of Radiological Health
OHT7: Office of In Vitro Diagnostics
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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)*
K214043

Device Name

BriefCase

Indications for Use *(Describe)*

BriefCase is a radiological computer aided triage and notification software indicated for use in the analysis of Chest X-Ray 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 suspect positive cases with Pneumothorax (Ptx) findings.

BriefCase uses an artificial intelligence algorithm to analyze images and flag suspect cases on a standalone desktop application in parallel to the ongoing standard of care image interpretation. The user is notified for suspect cases. 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
K214043

Submitter:

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Contact Person: N. Epstein, Ph.D.

Date Prepared: March 2, 2022

Name of Device: BriefCase

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

Regulatory Class: Class II

Product Code: QFM (21.CFR 892.2080)

Predicate Device: K191556 Behold.ai red dot™ device, Behold.AI Technologies Limited

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) for image acquisition; (2) Aidoc Cloud Server (ACS) for image processing; and (3) Aidoc Worklist 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 passive notifications to the Worklist desktop application, thereby facilitating triage and prioritization by the user. As the BriefCase software platform harbors several triage algorithms, the user may opt to filter out notifications by pathology, e.g., a chest radiologist may choose to filter out notifications on LVO cases, and a neuro-radiologist would opt to divert PE notifications. 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 notification by center. Activating the filter does not impact the order in which notifications are presented in the Aidoc worklist application.

The Worklist application displays all incoming suspect cases, each notified case in a line. Hovering over a line in the worklist 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 Chest X-Ray cases 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 suspect positive cases with Pneumothorax (Ptx) findings.

BriefCase uses an artificial intelligence algorithm to analyze images and flag suspect cases on a standalone desktop application in parallel to the ongoing standard of care image interpretation. The user is notified for suspect cases. 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 and the predicate red dot™ device (K191556) are nearly identical, as explained below.

Both devices are radiological computer-aided triage and notification software programs. Both devices are artificial intelligence deep-learning algorithms incorporating 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. Both devices operate in parallel to the standard of care workflow in the sense that they do not change the original image, and do not remove cases from the standard of care queue or de-prioritize them. In addition, performance testing demonstrates that both devices have similar performance.

Thus, the subject and predicate devices raise the same types of safety and effectiveness questions, namely, accurate detection of findings within the processed study. It is important to note again that, like the predicate, the subject device neither removes cases from the standard of care reading queue, nor de-prioritize them and does not modify the image. Both devices operate in parallel to 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 **Behold.ai red dot™ device (K191556)**	**Subject Device** **Aidoc Briefcase (K214043)**
Intended Use / Indications for Use	The red dot™ software platform is a software workflow tool designed to aid the clinical assessment of adult Chest XRay cases with features suggestive of Pneumothorax in the medical care environment. red dot™ analyzes cases using an artificial intelligence algorithm to identify suspected findings. It makes case-level output available to a PACS/ workstation for worklist prioritization or triage. red dot™ is not intended to direct attention to specific portions of an image or to anomalies other than Pneumothorax. Its results are not intended to be used on a stand-alone basis for clinical decision-making nor is it intended to rule out Pneumothorax or otherwise preclude clinical assessment of X-Ray cases.	BriefCase is a radiological computer aided triage and notification software indicated for use in the analysis of Chest X-Ray cases 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 suspect positive cases with Pneumothorax (Ptx) findings. BriefCase uses an artificial intelligence algorithm to analyze images and flag suspect cases on a standalone desktop application in parallel to the ongoing standard of care image interpretation. The user is notified for suspect cases. 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	Trained clinicians	Appropriately trained medical specialists
Anatomical region	Chest	Chest
Data acquisition protocol	Chest X-ray	Chest X-ray
Notification-only, parallel workflow tool	Yes (passive)	Yes
Images format	DICOM	DICOM
Interference with standard workflow	No. No cases are removed from Worklist or de-prioritized.	No. No cases are removed from worklist or de-prioritized
Algorithm	Artificial intelligence algorithm with database of images	Artificial intelligence algorithm with database of images
Structure	- Image input, validation and anonymization - Image Analysis Algorithm - PACS Integration Feature	- AHS module (image acquisition). - ACS module (image processing). - Aidoc Worklist application for workflow integration (worklist and non-diagnostic basic Image Viewer).

Performance Data

Pivotal Study Summary

Performance data were collected on an entirely new data set of Pneumothorax images in a retrospective, blinded, multicenter, multinational study. Cases and reports were selected that have not been previously reviewed using BriefCase. No patient data were reused between the training and the clinical validation datasets. Ground truthing was performed by two radiologists with an additional third radiologist to resolve inconsistencies.

Primary Endpoint

The primary endpoint was to evaluate the software's performance in identifying Pneumothorax in chest X-ray exams, in 619 cases from 5 clinical study sites (4 US-based study sites, 1 OUS, 89% of the cases were collected from the US sites). There were 139 positive reports and 480 negative reports (reports on images with Ptx versus without Ptx) included in the analysis.

The mean age of patients whose scans were reviewed in the study was 59.3 years, with standard deviation of 19.8 years. Gender distribution was 51.3% male, and 48.7% female. Ethnicity distribution within the study data patient population was unavailable. Further, additional characteristics of the data set can be found below:

Table 2. Frequency Distribution of Manufacturer

Manufacturer	N	%
Philips	45	7.3%
FUJIFILM Corporation	94	15.2%
Canon Inc.	97	15.7%
GE Healthcare	33	5.3%
Carestream	285	46.0%
Siemens	65	10.5%
Total	619	100.0%

In addition, to make sure that the Pneumothorax negative cases are representative of the intended-use population, for every Report-negative case ("suspected negative" as defined by the case selector, during the case selection phase), the report was reviewed to identify the existence of other pathologies within the scan.

Table 3. Distribution of Pathologies in Report-Negative Cases

Pathology	N	%
Fully Negative	270	60.8%
Lung Pathologies	117	26.4%
Cardiac Pathologies	15	3.4%
Vascular	14	3.2%
Inflammatory (Pneumonia)	9	2.0%
Other	8	1.8%
Diaphragmatic Pathologies	4	0.9%
Post-Op	3	0.7%
Trauma	2	0.5%
Mechanical	1	0.2%
Neoplastic	1	0.2%

AUC was 0.969 (95% CI: 0.954, 0.985), Sensitivity was 94.2% (95% CI: 89.9%, 97.8%) and Specificity was 90.8% (95% CI: 88.1%, 93.1%). As the AUC exceeded 0.95% and sensitivity and specificity both exceeded 80%, the study's primary endpoints were met.

Three operating points for the BriefCase algorithm were evaluated. Lower confidence limits for AUC, sensitivity and specificity were all above the pre-specified performance goals for all chosen operating points, demonstrating that the pre-specified performance goals were met.

Secondary Endpoint

Briefcase's potential clinical benefit of worklist prioritization for true positive Pneumothorax cases was evaluated by comparing the software's time-to-notification metric to that of the predicate.

The time-to-notification (TTN) metric includes the time to obtain the DICOM exam, de-identify it, upload it to the cloud, analyze and send a notification on a positive suspect case back to the worklist application. The TTN metric was measured for True Positive cases (i.e., identified as positive both by the reviewers as well as the BriefCase device), and the results compared to the predicate are reported in the **Table 4** below.

The BriefCase time-to-notification for Pneumothorax was 13.1 seconds (95% CI: 10.6 -15.7 ; Median 11.8, IQR 15.8), thus shown to be substantially similar to the predicate red dot™ time-to-notification which was reported to be 13.8 seconds (95% CI: 10.9 -13.0 ; Median 14.5, IQR 8.56). Furthermore, the predicate demonstrated the benefit of triage compared to the standard of care for pneumothorax.

Table 4 . TTN Comparison Subject & Predicate

Time-to-notification	Mean estimate	95% Lower CL	95% Upper CL	Median	IQR
BriefCase	13.1	10.6	15.7	11.8	15.8
Red dot™	13.8	10.9	13.0	14.5	8.56

NPV was 99.3% (95% CI: 98.6%-99.6%) and PPV was 53.3 % (95% CI: 46.2%-60.3%).
PLR was 10.28% (95% CI: 7.73%-13.67%) and NLR was 0.06 % (95% CI: 0.03%-0.12%).

Thus, the reported TTN metric data demonstrates that BriefCase users may have the opportunity to be involved in the clinical workflow of true positive Pneumothorax cases on the same timeframe as the predicate. Performance validation data suggest that when using the subject BriefCase, the users may have the same benefit in time saving as with using the red dot.

Conclusion

The subject BriefCase and the predicate red dot™ devices are both intended to aid in prioritization and triage of radiological images for the indications of Pneumothorax. Both devices are software packages with similar technological characteristics and principles of operation, both incorporating deep learning AI algorithms that process images, to triage of radiological images, independent of standard of care workflow.

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 users. In addition, performance testing demonstrates that Briefcase has similar performance compared to the predicate device.

The BriefCase device is thus substantially equivalent to the predicate red dot™.