Aidoc Medical, Ltd.
% John J. Smith
Partner
Hogan Lovells US LLP
555 Thirteenth Street, N.W.
WASHINGTON DC 20004

November 18, 2022

Re: K221330
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: October 11, 2022
Received: October 11, 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, 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)*

K221330

Device Name

BriefCase

Indications for Use *(Describe)*

BriefCase is a radiological computer-aided triage and notification software indicated for use in the analysis of frontal chest X-ray (CXR) 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 communicating suspected positive cases of vertically malpositioned endotracheal tube (ETT) in relation to the carina.

Findings are flagged when the ETT distal tip is assessed as being more than 5 cm above the carina, less than 2 cm above the carina, or when it is below the carina (i.e., in the right or left mainstem bronchus).

The device assesses solely the vertical position of the ETT distal tip relative to the carina, does not factor patient positioning, and cannot detect esophageal intubation. The device does not provide results when the carina is not well-visualized on the x-ray image. The device does not discriminate types of ETTs, as such a properly positioned double lumen ETT may trigger a false prioritization alert.

BriefCase uses an artificial intelligence algorithm to analyze images and highlight cases with detected findings on a standalone 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 the user's 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)

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510(k) Summary
Aidoc Medical, Ltd.'s BriefCase
K221330

Submitter: Aidoc Medical, Ltd.
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Tel-Aviv, Israel
Phone: +972-73-7946870

Contact Person: Amalia Schreier, LLM

Date Prepared: November 17, 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)

Primary Predicate Device: BriefCase (for iPE 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 harbors 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 VO cases, and a neuro-radiologist would opt to divert vertically malpositioned ETT in relation to the carina 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 frontal chest X-ray (CXR) 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 communicating suspected positive cases of vertically malpositioned endotracheal tube (ETT) in relation to the carina.

Findings are flagged when the ETT distal tip is assessed as being more than 5 cm above the carina, less than 2 cm above the carina, or when it is below the carina (i.e in the right or left mainstem bronchus).

The device assesses solely the vertical position of the ETT distal tip relative to the carina, does not factor patient positioning, and cannot detect esophageal intubation. The device does not provide results when the carina is not well-visualized on the x-ray image. The device does not discriminate types of ETTs, as such a properly positioned double lumen ETT may trigger a false prioritization alert.

BriefCase uses an artificial intelligence algorithm to analyze images and highlight cases with detected findings on a standalone 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 the user's 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 vertically malpositioned ETT in relation to the carina triage and primary predicate BriefCase for iPE triage (K203508) are identical in all aspects and defer only with respect to the training of the algorithm on vertically malpositioned ETT in relation to the carina vs iPE images.

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 x-ray scanners, PACS, and radiology workstations. The predicate BriefCase for iPE evaluates images from CT scanners and the proposed Briefcase for vertically malpositioned ETT in relation to the carina evaluates images from X-ray scanners.

The proposed device for vertically malpositioned ETT in relation to the carina triage has identical technology and design as the predicate device, and similar indications for use, i.e., both devices are intended to aid in prioritization and triage of time-critical radiological images. 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 deprioritized 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 predicate devices is provided below.

Table 1. Key Feature Comparison

	Predicate Device **Aidoc Briefcase for iPE Triage (K203508)**	**Subject Device** **Aidoc Briefcase for Vertically Malpositioned ETT in Relation to the Carina Triage (K221330)**
Intended Use / Indications for Use	BriefCase is a radiological computer aided triage and notification software indicated for use in the analysis of contrast enhanced chest CTs (but not dedicated CTPA protocol). The device is intended to assist hospital networks and trained medical specialists in workflow triage by flagging and communication of suspect positive cases of incidental Pulmonary Embolism (iPE) pathologies. 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 presented with notifications 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	BriefCase is a radiological computer-aided triage and notification software indicated for use in the analysis of frontal chest X-ray (CXR) 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 communicating suspected positive cases of vertically malpositioned endotracheal tube (ETT) in relation to the carina. Findings are flagged when the ETT distal tip is assessed as being more than 5 cm above the carina, less than 2 cm above the carina, or when it is below the carina (i.e in the right or left mainstem bronchus). The device assesses solely the vertical position of the ETT distal tip relative to the carina, does not factor patient positioning, and cannot detect esophageal intubation. The device does not provide results when the carina is not well-visualized on the x-ray image. The device does not discriminate types of ETTs, as such a properly positioned double lumen ETT may trigger a false prioritization alert. BriefCase uses an artificial intelligence algorithm to analyze images and

	Predicate Device Aidoc Briefcase for iPE Triage (K203508)	Subject Device Aidoc Briefcase for Vertically Malpositioned ETT in Relation to the Carina Triage (K221330)
	viewing full images per the standard of care.	highlight cases with detected findings on a standalone 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 the user's 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	Contrast-enhanced chest CTs (but not dedicated CTPA protocol)	Frontal Chest X-ray (CXR)
Notification-only (/notification alerts), parallel workflow tool	Yes	Yes
Images format	DICOM	DICOM

	Predicate Device **Aidoc Briefcase for iPE Triage (K203508)**	**Subject Device** **Aidoc Briefcase for Vertically Malpositioned ETT in Relation to the Carina Triage (K221330)**
Interference with standard workflow	No. No cases are removed from Worklist or deprioritized.	No. No cases are removed from desktop app or deprioritized
Inclusion/ Exclusion criteria	Inclusion criteria • Contrast-enhanced chest CTs (but not dedicated CTPA protocol. • Single energy exams. • Scans performed with a 64 slice or greater number of detectors. • Scans performed on adults/ transitional adults ≥ 18 years of age. • Slice thickness: 0.5mm – 2.0mm axial. Exclusion Criteria • All studies that are technically inadequate, including studies with motion artifacts, severe metal artifacts, or inadequate field of view.	Inclusion criteria • Frontal Chest X-ray protocol. • Images performed on adults/ transitional adults ≥ 18 years of age. Exclusion Criteria • All x-ray images that have inadequate field of view.The device does not provide results when the carina is not well-visualized on the x-ray image.
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 (orchestrator, image acquisition); • ACS module (image processing); • Aidoc Desktop application for workflow integration (feed 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 chest X-ray (CXR) images of vertically malpositioned endotracheal tube (ETT) in relation to the carina in 921 cases from 5 US-based clinical sites. The software's performance was compared to the ground truth as determined by 2 out of 3 majority voting 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 86.81% (95% CI: 81.02%-91.36%) and Specificity was 92.02% (95% CI: 89.20%-93.87%).

Secondary Endpoint

In addition, the time-to-notification metric observed for the BriefCase software in the five 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 secondary measure of time-to-notification analysis demonstrated that standard of care time-to-exam-open (157.0 minutes: 95% CI: 155.0-159.0; Median: 50.0 IQR: 156.0) was substantially longer than the parallel time-to-notification of the BriefCase for Malpositioned Endotracheal Tube (ETT) device (4.93 minutes, 95% CI: 4.64-5.22; Median: 4.13 IQR: 0.76). The mean difference of 152.07 minutes between these two measures quantifies effective triage by the device.

Table 2. Time Saving Data (Sec)

Time-to-notification	Mean Estimate	N	95% Lower CL	95% Upper CL	Median	IQR
Standard of Care Time-To-Exam-Open	157.0	197	155.0	159.0	50.0	156.0
BriefCase Time-to-notification	4.93	182	4.64	5.22	4.13	0.76

NPV was 98.43% (95% CI: 97.74% - 98.92%), 96.54% (95% CI: 95.05% 97.59%) and 94.21% (95% CI: 91.81% 95.94%) at 10%, 20% and 30% positive prevalence.
PPV was 54.71% (95% CI: 48.45% 60.83%), 73.11% (95% CI: 67.89%- 77.75%) and 82.33% (95% CI: 78.38%- 85.70%) at 10%, 20% and 30% positive prevalence.

PLR was 10.874 (95% CI: 8.458-13.979) and NLR was 0.143 (95% CI: 0.099- 0.208).

Thus, the reported similar time-to-notification data demonstrates that when using the subject BriefCase for vertically malpositioned ETT in relation to the carina triage the radiologists may have the same benefit in time saving as with the BriefCase for iPE triage.

As can be seen in **Table 3** the mean age of patients whose images were reviewed for vertically malpositioned ETT in relation to the carina was 62.5 years, with standard deviation of 17.0 years. Gender distribution was 58.52% male, and 41.37% female (**Table 4**). X-ray scanner distribution can also be found in **Table 5** below.

Table 3. Descriptive Statistics for Age

	Mean	Std	Min	Median	Max	N
Age (Years)	62.5	17.0	18.0	64.0	90	921

Table 4. Frequency Distribution of Gender *

Ground Truth Results	Gender				All	
	Male		Female			
	N	%	N	%	N	%
Positive	112	12.16	70	7.60	182	19.76
Negative	427	46.36	311	33.77	738	80.13
All	439	58.52	381	41.37	920*	100.0

* The gender of 1 case remained unknown due to incomplete DICOM tag information

Table 5. Frequency Distribution of Manufacturer

Manufacturer	N	%
Carestream	358	38.9
Canon	223	24.2
Siemens	186	20.2
Philips	154	16.7
Total	921	100%

Tables 6-8 below detail the distribution of pathologies with and without ETT in negative cases, distribution of ETT in negative cases, distribution of other (no ETT) tubes, lines and life support devices in positive cases.

Table 6. Distribution of Pathologies with and without ETT in Negative Cases

Pathology	N (w/o ETT)	% (w/o ETT)	N (w/ ETT)	% (w/ ETT)
Fully Negative	84	11.4%	0	0.0%
Other (non ETT) tubes,lines and life support devices*	220	29.8%	164	22.2%
Inflammatory	185	25.1%	57	7.7%
Post op	133	18.0%	58	7.9%
Cardiovascular	94	12.7%	45	6.1%
Lung pathologies	46	6.2%	7	0.9%
Pneumothorax	36	4.9%	5	0.7%
Infectious	33	4.5%	6	0.8%
Trauma	14	1.9%	2	0.3%
Neoplastic	13	1.8%	3	0.4%
Chronic diseases	2	0.3%	0	0.0%
None of the above	28	3.8%	7	0.9%

Table 7. Distribution of ETT in Negative Cases

Pathology	N	%
With correctly positioned ETT	199	26.9%
With no ETT	540	73.1%

Table 8. Distribution of Other (no ETT) Tubes, Lines and Life Support Devices in Positive Cases

Pathology	N	%
Other tubes, lines and life support devices	144	60.0%
No other tubes, lines and life support devices	96	40.0%

Other (non-ETT) tubes, lines & life support devices' includes a variety of tubes, lines, catheters, monitoring devices and other life support devices. For example: enteric tube (nasogastric/orogastric), chest tube, mediastinal drains, internal jugular central venous catheter, PICC, ECMO cannula, EKG leads, Mediport, etc.

Clinical Subgroups And Confounders:

- Pathologies present in negative cases: Fully Negative; Other (non ETT) tubes, lines and life support devices; Inflammatory; Post op; Cardiovascular; Lung pathologies; Pneumothorax; Infectious; Trauma; Neoplastic; Chronic diseases; None of the above.

- Tip position sub-types: Too high; Too low (Trachea); Too low (Bronchus); Too low - right mainstem bronchus; Too low - left mainstem bronchus. An additional enriched dataset was collected for Tip position sub-types analysis on 327 positive cases.

Conclusions

The subject BriefCase for vertically malpositioned ETT in relation to the carina triage and the predicate BriefCase for iPE triage are intended to aid in prioritization and triage of radiological images for the indications of malpositioned endotracheal tube and incidental pulmonary embolism, respectively. 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 vertically malpositioned ETT in relation to the carina triage is thus substantially equivalent to the primary predicate BriefCase for iPE triage.