Annalise-AI Pty Ltd.
℅ Eric Qin
Principal RAQA Advisor
Level 21, 60 Margaret Street
SYDNEY, NSW 2000
AUSTRALIA

February 24, 2022

Re: K213941
Trade/Device Name: Annalise Enterprise CXR Triage Pneumothorax
Regulation Number: 21 CFR 892.2080
Regulation Name: Radiological computer aided triage and notification software
Regulatory Class: Class II
Product Code: QFM
Dated: December 16, 2021
Received: December 16, 2021

Dear Eric Qin:

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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*

K213941

Device Name
Annalise Enterprise CXR Triage Pneumothorax

Indications for Use *(Describe)*
The device is designed to aid the clinical assessment of adult chest x-ray cases with features suggestive of pneumothorax and tension pneumothorax in the medical care environment. The device analyses cases using an artificial intelligence algorithm to identify findings. It makes case-level output available to a PACS or RIS for worklist prioritization or triage. The device is intended to be used by trained clinicians who are qualified to interpret chest X-rays as part of their scope of practice. The device is not intended to direct attention to specific portions of an image or to anomalies other than pneumothorax and tension pneumothorax. Its results are not intended to be used on a standalone basis for clinical decision making nor it is intended to rule out pneumothorax or tension pneumothorax, or otherwise preclude clinical assessment of X-ray cases.

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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

annalise.ai

510(k) Summary
K213941

I. SUBMITTER

Company Name	Annalise-AI Pty Ltd
Address	Level 21, 60 Margaret Street Sydney, NSW 2000 Australia
Phone Number	+61 2 7204 0817
Contact Person	Michele Houldsworth
Date Prepared	December 16, 2021

II. DEVICE

Device Name	Annalise Enterprise CXR Triage Pneumothorax
Classification Name	Radiological computer aided triage and notification software (21CFR892.2080)
Regulatory Class	Class II
Product Code	QFM

III. PREDICATE DEVICE

Manufacturer Name	Behold.AI Technologies Limited
Device Name	Red Dot
510(k) reference	K191556
Classification Name	Radiological computer aided triage and notification software (21CFR892.2080)
Regulatory Class	II
Product Code	QFM

This predicate has not been subject to a design-related recall. No reference devices were used in this submission.

IV. DEVICE DESCRIPTION

Annalise Enterprise CXR Triage Pneumothorax is a software workflow tool that interfaces with RIS and PACS to obtain chest x-ray images to process. The artificial intelligence algorithm within the device uses deep learning techniques to identify the presence of pneumothorax and tension pneumothorax.

The AI algorithm used in the device is a convolutional neural network trained using deep learning techniques. The training dataset included over 1,500,000 chest x-ray images sourced from datasets across three continents from different x-ray manufacturers, machines and a range of patient demographics. Cases in the training dataset were labeled by at least three qualified radiologists for the presence or absence of radiographic features suggestive of pneumothorax or tension pneumothorax.

The AI results output from the device are sent to the reporting worklist software to enable AI assisted triage of the reporting worklist. The exact functionality available depends on the worklist software being used (RIS, PACS).

This triage functionality uses the findings detected in each study by the AI model to provide information into the worklist software enabling the prioritization of the reporting worklist. Each organization can specify which findings will result in triage and the priority of each finding.
It is important to note that the device will never decrease a study's existing priority in the worklist. This ensures that worklist items will never have their priorities downgraded by the AI software.

V. INDICATIONS FOR USE

The Indications For Use statement is as follows;
The device is designed to aid the clinical assessment of adult chest x-ray cases with features suggestive of pneumothorax and tension pneumothorax in the medical care environment. The device analyses cases using an artificial intelligence algorithm to identify findings. It makes case-level output available to a PACS or RIS for worklist prioritization or triage.
The device is intended to be used by trained clinicians who are qualified to interpret chest X-rays as part of their scope of practice.
The device is not intended to direct attention to specific portions of an image or to anomalies other than pneumothorax and tension pneumothorax. Its results are not intended to be used on a standalone basis for clinical decision making nor it is intended to rule out pneumothorax or tension pneumothorax, or otherwise preclude clinical assessment of X-ray cases.

The Indications for Use statement for the subject device is not identical to the predicate device, in that the subject device can identify and triage Pneumothorax and Tension Pneumothorax. The differences, however, do not alter the intended use of the device nor do they affect the safety and effectiveness of the device, as compared to the predicate. Both devices have the same intended use to assist with worklist triage by providing notification of pneumothorax findings.

VI. COMPARISON OF TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

The subject and predicate devices are both Radiological Computer-Assisted Prioritization Software intended to assist with worklist triage by providing notification of pneumothorax findings in adults to trained clinicians. The technologies use AI techniques to analyze radiological images. The devices establish effective triage within a clinician's queue based on high sensitivity and specificity.

At a high level, the subject and predicate devices share similar technological characteristics as follows:

- Target population
- Technical method for notification and prioritization
- Anatomical site and modality
- Intended user and use environment
- Image protocol (input)
- Means of notification to user (output)
- System components
- Prioritization relationship to the standard of care workflow
- Standalone performance level and associated study methods
- Triage effectiveness (turnaround time)

The subject and predicate devices also share equivalent technological characteristics. These characteristics exhibit minor differences, however, do not raise new questions of safety and effectiveness. The equivalent technological characteristics include:

- Capability of the subject device to identify and triage tension pneumothorax
- Results are not delivered to an Electronic Patient Record (EPR)
- Use of multiple operating points

Therefore, by examination of the device intended use and technological attributes, substantial equivalence is supported.

VII. PERFORMANCE DATA

The following performance data have been provided to support evaluation of substantial equivalence.

A. Software Verification and Validation Testing

Software verification and validation testing was conducted, and documentation was provided as recommended by FDA's Guidance for Industry and FDA Staff, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices", May 11, 2005.
The software for this device was considered as posing moderate level of concern, since prior to mitigation of hazards, a failure of the software device could result in minor injury.

B. Performance Testing

Performance of the subject device was assessed in two studies to satisfy requirements set forth in Special Controls per 21CFR892.2080. These included:

- Standalone Performance Assessment (accuracy); and
- Triage Effectiveness Assessment (turn-around time).

Standalone performance was assessed via a retrospective, anonymized study of adult patient, DICOM-compliant CXR cases. The test dataset analyzed included a total of 949 CXR cases (positive pneumothorax n=413 (including tension pneumothorax n=123 as a subset) and negative n=536) from unique patients. To obtain this cohort, eligible chest x-ray cases were collected consecutively from 4 US hospital network sites by manual review (for pneumothorax) or natural language processing analysis (for tension pneumothorax) of the original radiology reports associated with each case. No data had previously been collected from these sites for training or testing of the device's AI algorithm. That is, the test dataset applied during the standalone performance evaluation was newly acquired and independent from the training dataset.

The cohort collected for this evaluation included chest x-ray cases taken using a range of radiographic imaging protocols, including different patient positions (erect and supine), view positions (anteroposterior, posteroanterior and lateral) and x-ray imaging equipment, including different equipment manufacturers (n=10) and equipment models (n=22). Within this cohort, 427 patients were female (45%) and 522 patients were male (55%), with the mean patient age of 62.3 years (SD=17.5, range 22-99 years old). A range of clinical confounders were also present across the cohort, including various clinical conditions and other radiographic findings. The ethnicity breakdown for the cohort was 7.7% Hispanic, 86.7% Not Hispanic (the remaining proportion of the cohort was either unavailable or declined to declare). The race breakdown for the cohort was 0.3% Two or more races, 3.3% Asian, 4.8% Other, 5.5% African American, 83% White (the remaining proportion of the cohort was either unavailable or declined to declare).

To determine the ground truth, each deidentified CXR case was annotated in a blinded fashion by at least two American Board of Radiology (ABR)-certified and protocol-trained radiologists (ground truthers), with consensus determined by two ground truthers and a third ground truther in the event of disagreement.

The results included an AUC of 0.979 (95% CI: 0.970-0.986) and 0.988 (95% CI: 0.981-0.993) for pneumothorax and tension pneumothorax respectively, thus meeting the AUC>0.95 requirement for product code QFM. The sensitivity and specificity of the device was reported for three operating points and shown to meet >80% requirement for product code QFM. The default "balanced sensitivity and specificity" operating point demonstrated sensitivity of 93.9% (95% CI: 91.8, 96.1) and specificity of 92.2% (95% CI: 89.9, 94.4) for pneumothorax and sensitivity of 94.3% (95% CI: 90.2, 98.4) and specificity of 95.8% (95% CI: 94.3, 97.1) for tension pneumothorax. The "optimized for sensitivity" operating point demonstrated sensitivity of 96.6% (95% CI: 94.7, 98.3) and specificity of 84.1% (95% CI: 82.1, 87.1) for pneumothorax and sensitivity of 95.9% (95% CI: 91.9, 99.2) and specificity of 94.9% (95% CI: 93.3, 96.4) for tension pneumothorax. The "optimized for specificity" operating point demonstrated sensitivity of 89.1% (95% CI: 86.2, 92.0) and specificity of 95.7% (95% CI: 94.0, 97.4) for pneumothorax and sensitivity of 83.7% (95% CI: 76.4, 90.2) and specificity of 97.8% (95% CI: 96.7, 98.7) for tension pneumothorax.

The results demonstrate the subject device establishes effective triage within a clinician's queue based on high sensitivity and specificity. Further, these results are substantially equivalent to those of the predicate device.

Triage effectiveness (turn-around time) was assessed by an internal bench study using a dataset of n=621 cases positive for pneumothorax and/or tension pneumothorax eligible for prioritization. These cases were collected from multiple data sources spanning a variety of geographical locations, patient demographics and technical characteristics. The results demonstrated an average triage turn-around time of 20.57 seconds, (95% CI: 19.90-21.24), which is substantially equivalent to the total performance time published for the predicate device.

Therefore, the subject device has been shown to satisfy the performance requirements per 21 CFR 892.2080, for radiological triage and notification software, by providing clinically effective triage for chest x-ray studies containing features suggestive of pneumothorax and tension pneumothorax. This data demonstrates the subject device is as safe, as effective, and performs as well as or better than the legally marketed predicate device.

VIII. CONCLUSIONS

The subject and predicate devices are both software-only devices intended to assist with worklist triage by providing notification of pneumothorax findings in adults to trained clinicians. The labelling of both devices is limited to worklist triage and are not to be used in-lieu of full patient evaluation or relied upon to provide direct diagnosis. The devices both operate by passive notification of suspected cases parallel to the standard of care workflow. The evaluation demonstrates that minor differences between the subject and predicate devices do not raise new questions of safety and effectiveness. In addition, the performance testing conducted demonstrates the subject device performs as intended, that it is as safe, as effective and performs comparably to the predicate device. Therefore, the subject device is substantially equivalent to the predicate device.