Riverain Technologies, Inc.
℅ Mr. Jonathan Jackson
Director of Regulatory Affairs & Quality Assurance
3020 South Tech Blvd.
MIAMISBURG OH 45342

March 10, 2022

Re: K213566
Trade/Device Name: ClearRead Xray Pneumothorax
Regulation Number: 21 CFR 892.2080
Regulation Name: Radiological computer aided triage and notification software
Regulatory Class: Class II
Product Code: QFM
Dated: February 8, 2022
Received: February 10, 2022

Dear Mr. Jackson:

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 and Part 809); 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)*

K213566

Device Name
ClearRead Xray Pneumothorax

Indications for Use *(Describe)*

ClearRead Xray Pneumothorax is a notification-only triage workflow tool for use by trained professionals to help prioritize chest X-rays. The device operates in parallel to and independent of standard of care image interpretation workflow. Specifically, the device uses an artificial intelligence algorithm to analyze images for features suggestive of a pneumothorax 5 mm or larger; it makes case-level output available to a PACS/workstation for worklist prioritization or triage. Identification of suspected cases of a pneumothorax is not for diagnostic use beyond notification. ClearRead Xray Pneumothorax is limited to analysis of imaging data as a guide to possible urgency of adult chest X-ray image review, and should not be used in lieu of full patient evaluation or relied upon to make or confirm diagnoses. The device does not replace review and diagnosis of the X-rays by trained professionals. The device is not intended to be used with plain film X-ray.

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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5.0 510(K) SUMMARY

Submission Date: March 9, 2022

Submitter Information:

Company Name: Riverain Technologies, Inc.

Company Address: 3020 South Tech Blvd.
Miamisburg, OH 45342-4860

Contact Person: Jonathan Jackson
Director, Regulatory Affairs and Quality Assurance
Riverain Technologies, Inc.
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937.425.6493
jjackson@riveraintech.com

Device Information:

Trade Name: ClearRead Xray Pneumothorax

Regulation Number: 21 CFR §892.2080

Regulation Name: Radiological computer aided triage and notification software

Regulatory Class: Class II

Product Code: QFM

Device Description: **ClearRead Xray Pneumothorax** is comprised of a computer assisted triaging tool, designed to prioritize chest X-rays based on the suspected presence of a pneumothorax (PTX) 5mm or larger. **ClearRead Xray Pneumothorax** requires both lungs to be in the field of view. **ClearRead Xray Pneumothorax** provides adjunctive information and is not intended to be used for diagnosis. **ClearRead Xray Pneumothorax** receives images according to the DICOM® protocol (via a standard IEEE 802.3 network connection), processes the image, and delivers the resulting information through the same DICOM network interface. Image inputs are limited to adult, digital frontal chest radiographs. The output results are sent to facilitate prioritization of chest X-rays for radiologist review on one or more devices that

conform to the **ClearRead Xray Pneumothorax** DICOM Conformance Statement. **ClearRead Xray Pneumothorax** does not support printing or DICOM media.

Indications for Use:

ClearRead Xray Pneumothorax is a notification-only triage workflow tool for use by trained professionals to help prioritize chest X-rays. The device operates in parallel to and independent of standard of care image interpretation workflow. Specifically, the device uses an artificial intelligence algorithm to analyze images for features suggestive of a pneumothorax 5 mm or larger; it makes case-level output available to a PACS/workstation for worklist prioritization or triage. Identification of cases suspected of containing a pneumothorax is not for diagnostic use beyond notification. **ClearRead Xray Pneumothorax** is limited to analysis of imaging data as a guide to possible urgency of adult chest X-ray image review and should not be used in lieu of full patient evaluation or relied upon to make or confirm diagnoses. The device does not replace review and diagnosis of the X-rays by trained professionals. The device is not intended to be used with plain film X-ray.

Predicate Devices:

RADLogics, Inc.

(K193300)

AIMI-Triage CXR PTX

Class II

Comparison to Predicate Device Technical Characteristics:

Riverain Technologies, Inc. is of the opinion that **ClearRead Xray Pneumothorax** is substantially equivalent, both in intended use as well as to the technical characteristics of the listed predicate device. Differences in the design and performance from the cited predicate device does affect either the safety or the effectiveness of **ClearRead Xray Pneumothorax** for its intended use. Table 1 shows the predicate device listed against the subject device for the Product Code and Intended Use.

	Predicate: **AIMI-Triage CXR PTX** (RADLogics, Inc.) K193300	**Subject Device:** **ClearRead Xray Pneumothorax** (Riverain Technologies, Inc.) K213566
Product Code	QFM	QFM
Intended Use	The AIMI-Triage CXR PTX provides a chest X-ray prioritization service for use by radiologists to identify features suggestive of moderate to large sized pneumothorax.	ClearRead Xray Pneumothorax provides a chest X-ray prioritization service for use by radiologists to identify features suggestive of pneumothoraces in a PA/AP chest x-ray scan.
Intended User	Radiologist	Radiologist
Modality	X-ray	X-ray
Anatomical Region	Lungs	Lungs
Clinical Condition	Pneumothorax	Pneumothorax
Notification / Prioritization	Yes, passive	Yes, passive
ROI Segmentation	No	No
Algorithm	Artificial intelligence algorithm with database of images	Machine learning and image processing
Alteration of input images	No	No

Table 1: Predicate Devices vs. Subject Device

Testing Summary:

Non-clinical Testing

Non-clinical tests were conducted during the development process in accordance with the Riverain Technologies Design Control Process, which is compliant with the FDA Quality System Regulations, ISO 13485:2016 with MDSAP and the following standards.

- IEC 62304:2006/AMD1:2015, Medical devices – Software life cycle processes
- EC62366-1:2015, Medical device – Part1: Application of usability engineering to medical devices
- ISO14971:2007, Medical devices – Application of risk management to medical devices (2nd Ed.)

Testing verified the requirements according to the **ClearRead Xray Pneumothorax** device specifications. The Risk Management Plan, Risk Analysis and Risk Management Report were completed, and risk control measures were implemented to mitigate the identified hazards. Documentation required for software with a Moderate Level of Concern is included as part of this submission. Device labeling, together with the results from verification and validation testing demonstrate that the device is safe and effective.

Clinical Performance Testing

Clinical evaluation used an independent dataset, that is data not used for purposes of training or internal validation, to validate that clinical efficacy of **ClearRead Xray Pneumothorax** for workflow prioritization of X-ray images containing a suspected pneumothorax.

The primary objective of this study was to demonstrate that **ClearRead Xray Pneumothorax** meets or exceeds the expected performance on an independent test set. Device performance was measured by the AUC of the ROC curve. The primary endpoint was based on an overall assessment of the possible presence of a PTX, without localization.

Retrospective adult (18 and older) patient images from multiple sources were evaluated, including >400 true positive PTX and >600 true negative PTX cases, with approximately equal representation of male and female studies. Truth was determined by a panel of 3 senior board-certified radiologists with expertise in thoracic radiology.

To assess performance, the **ClearRead Xray Pneumothorax** system was run on all selected images, both true negative and true positives cases. True negative-pneumothorax images that are identified as having a suspected pneumothorax by the system were labeled as “false positives”. True positive detections are true positive-pneumothorax images wherein the machine indicates a suspected pneumothorax is present.

Machine indications were transferred to the statistical analysis team and used as the basis for performance assessment, including the generation of ROC, point estimate of the ROC AUC, sensitivity and specificity estimates and associated 95% confidence intervals, and time-to-notification estimates. Device performance, as measured by the AUC-ROC, sensitivity and specificity, and time-to-notification were demonstrated with statistical significance to meet the study’s primary endpoints. A summary of the results is listed in Table 2.

AUC	0.974
Sensitivity	0.922
Specificity	0.951
Time to Notification	9.73 seconds

Table 2: Clinical Data Summary of Results

Clinical Trial Data

Images used for the clinical study originated from MIMIC-CXR and Georgetown University Medical Center. All data used in the clinical trial was independent data, not used as part of product development.

The MIMIC-CXR dataset is a controlled online dataset of chest x-rays images. A second dataset was collected by Georgetown University Medical Center (GUMC) between 2009-2012, also not used as part of the development process.

The MIMIC-CXR cases were collected from 2011 to 2016 at Beth Israel Deaconess Medical Center. A total of 1028 cases from the MIMIC-CXR dataset were selected for the study based on the pre-established protocol inclusion and exclusion criteria. Of them, there were 419 and 609 with PTX and without PTX, respectively. The remaining cases were provided by Georgetown University and collected between 2002 to 2013. In total, 110 were selected from this dataset. Of them, 40 and 70 were with PTX and without PTX, respectively. Although the header did not contain the manufacturer information for each case for the MIMIC-CXR dataset, it was removed as part of the anonymization process, the administrators of the database did provide a list of the manufacturers, the distribution of the clinical dataset is shown in Table 3.

Data distribution with respect to device characteristics are summarized below:

Manufacturer	**# of cases**
Carestream	782
GE	220
Fuji	117
Kodak	12
Agfa	3
Other	4
Total	**1138**

Table 3: Clinical Data Device Distribution

The data distribution with respect to comorbidities are summarize in Table 4 below. Indications of comorbidities for true positive pneumothorax (PTX) cases and true negative pneumothorax (NoPTX) cases are provided:

	# of cases	
Disease	**PTX**	**No PTX**
Atelectasis	87	108
Cardiomegaly	30	112
Consolidation	23	20
Edema	15	69
Enlarged Cardiomediastinum	9	13
Fracture	23	11
Lung Lesion/mass	21	34
Lung Opacity	43	131
Pleural Effusion	115	114
Pneumonia	5	20

Table 4: Clinical Data Comorbidity Distribution

The data distribution with respect to gender is again provided for true positive pneumothorax (PTX) cases and true negative pneumothorax (NoPTX) cases. The gender of a subset of the cases, identified as Unknown, could not be determined and is shown in Table 5.

	# of cases	
Gender	**PTX**	**No PTX**
Male	227	328
Female	176	319
Unknown	56	32

Table 5: Clinical Data Gender Distribution

All patients were adult, however specific age was not available due to the anonymization process. Additionally, ethnicity could not be determined as this information is not generally available for image data based on DICOM header content.

Clinical Data Case Selection and Ground Truth

Three senior expert radiologists formed the Expert Panel, all of which were board certified radiologists with expertise in thoracic radiology. The expert radiologists validated the label of each image as a true positive image or true negative based on the visual inspection of image data along with available radiology reports, and if a true positive case, annotated the location of the pneumothorax with a bounding box.

The members of the expert panel considered each PA/AP image and associated radiology reports independently as part of their review. The final image label and associated annotations were derived from a majority voting rule, where the associated annotation bounding boxes were replaced with a single box that enclosed all bounding boxes.

Algorithm Development Data

All models used by the **ClearRead Xray Pneumothorax** system were trained with cases that were clinically validated as negative for pneumothorax, and cases labeled as positive via a simulated data construction process. The simulated cases start with negative cases and digitally insert synthetic pneumothoraces. For synthetic data, the ground truth is arrived at via construction. For real cases the ground truth was hand drawn outlines as established by clinical experts. This included the publicly available data from the NIH, as hosted by Kaggle, wherein experts outlined proven pneumothoraces for thousands of images. Importantly, this also included over 7000 confirmed negatives cases.

Two datasets were constructed for the purposes of developing the pneumothorax system. One dataset, labeled the "development set", was used iteratively to validate and judiciously update the simulation engine, which in turn is used to train the system's models. The second dataset, deemed the test set, was 600 cases, 300 negatives and 300 positives, that were selected based on the diversity of location and size, and were not used in anyway in the development of the models.

Factors associated with manufacturers and patient demographics were not available as the data was thoroughly scrubbed for patient privacy. This was not deemed a limitation as the system utilizes two important aspects that mitigate such concerns. First, the system makes use of a normalization component that removes strong device characteristics such as noise, tone scale and contrast detail. Secondly, by forcing the system to strongly detect local patterns of pneumothorax, the final decision is based on clinically meaningful structure, and not spurious information – age, gender, or ethnicity - as might be learned if just image labels were used. Clinical testing confirms this hypothesis where very similar results were achieved using a large independent dataset.

Internal Test Data Benchmarks

Figure 1 below provides the image level performance as captured by a receiver operating characteristic (ROC) curve, the area under curve (AUC) was measured to be 0.975 for the internal validation/test set.

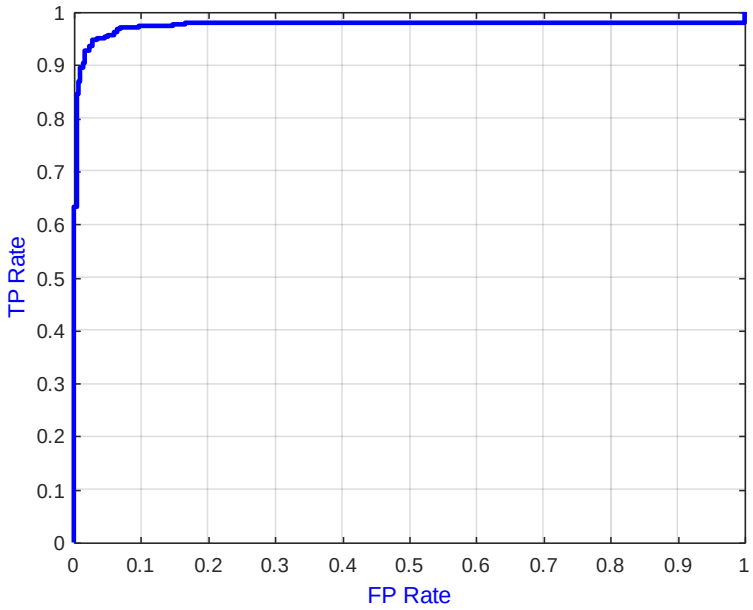

Figure 1: Internal image level pneumothorax detection performance ROC

For an image-level performance assessment, a probability threshold of 0.5 was selected as the operating point. The performance metrics for the test set at this operating point are found below in Table 6.

Image Performance	**TP**	**FP**	**FN**	**Se**	**Sp**
Threshold of 0.50	278	7	22	92.7%	97.7%

Table 6: Image level pneumothorax detection performance indices at the selected operating point

Conclusion

In preparing this 510(k) submission, Riverain Technologies has carefully considered the relevant statutory and regulatory requirements and believes that the information contained within satisfies the requirements for demonstrating substantial equivalence.