Imvaria, Inc
% Dulciana Chan
Principal Consultant
Rqm+
2790 Mosside Blvd
Monroeville, Pennsylvania 15146

January 10, 2025

Re: K241891
Trade/Device Name: ScreenDx
Regulation Number: 21 CFR 892.2085
Regulation Name: Radiology software for referral of findings related to fibrotic lung disease
Regulatory Class: Class II
Product Code: QWO
Dated: December 12, 2024
Received: December 12, 2024

Dear Dulciana Chan:

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 (the 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 available 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.

FDA's substantial equivalence determination also included the review and clearance of your Predetermined Change Control Plan (PCCP). Under section 515C(b)(1) of the Act, a new premarket notification is not required for a change to a device cleared under section 510(k) of the Act, if such change is consistent with an established PCCP granted pursuant to section 515C(b)(2) of the Act. Under 21 CFR 807.81(a)(3), a new

premarket notification is required if there is a major change or modification in the intended use of a device, or if there is a change or modification in a device that could significantly affect the safety or effectiveness of the device, e.g., a significant change or modification in design, material, chemical composition, energy source, or manufacturing process. Accordingly, if deviations from the established PCCP result in a major change or modification in the intended use of the device, or result in a change or modification in the device that could significantly affect the safety or effectiveness of the device, then a new premarket notification would be required consistent with section 515C(b)(1) of the Act and 21 CFR 807.81(a)(3). Failure to submit such a premarket submission would constitute adulteration and misbranding under sections 501(f)(1)(B) and 502(o) of the Act, respectively.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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
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Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

# Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
*See PRA Statement below.*

510(k) Number *(if known)*
K241891

Device Name
ScreenDx

Indications for Use *(Describe)*
ScreenDx is a software-only device that receives and analyzes lung computed tomography (CT) imaging data in order to assess for interstitial lung findings compatible with interstitial lung disease. The device supplements the standard-of-care workflow by providing a qualitative output of imaging findings based on pattern recognition, in order to provide adjunctive information as part of a referral pathway to an appropriately qualified clinician. Patients with positively identified patterns may undergo assessment for lung fibrosis, but ScreenDx does not replace the current standard of care methods for diagnosis of lung fibrosis and the results of the device are not intended to rule-out or rule-in lung fibrosis. The results of ScreenDx are intended to be used only by clinicians qualified in the care of lung disease, in conjunction with the patient's clinical history, symptoms, and other diagnostic tests, as well as the clinician's professional judgment.

The input to ScreenDx is a DICOM-compliant lung CT scan. Clinical case eligibility includes the following criteria:
• Age > 22 years old.

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
**K241891**

**DATE PREPARED**
January 9, 2025

**MANUFACTURER AND 510(k) OWNER**
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**DEVICE INFORMATION**

| | |
|---|---|
| Proprietary Name/Trade Name: | ScreenDx |
| Common Name: | Radiology software for referral of findings related to fibrotic lung disease |
| Regulation Number: | 21 CFR 892.2085 |
| Class: | II |
| Product Code: | QWO |
| Review Panel: | Radiology |

**PREDICATE DEVICE IDENTIFICATION**
ScreenDx is substantially equivalent to the following predicate:

| 510(k) Number | Device/Manufacturer | Predicate/Reference |
|---|---|---|
| DEN220040 | Fibresolve / Imvaria, Inc | Predicate |

**DEVICE DESCRIPTION**
ScreenDx is a computer-assisted analysis software device. The software analyzes lung computed tomography (CT) imaging data to provide a qualitative output assessing for interstitial lung findings compatible with interstitial lung disease. The software system is based on a software algorithm component and connection Application Programing Interface (API) to enable image transfer and notifications. The device consists of the following 3 components:

(1) Image Receiver API for image acquisition;
(2) Ingestion Pipeline and Analysis System for image processing; and
(3) Output API for notification transmission.

(1) The Image Receiver API is accessed via any technologically compliant system (e.g., DICOM, PACS). The case is submitted to the device through the API directly. The API passes the data to the Ingestion Pipeline and Analysis System.

(2) The Ingestion Pipeline and Analysis System accepts the images, selects cases appropriate for processing, processes the images for analyses, analyzes the images, and stores the images. This system includes the analysis algorithm that identifies lung abnormalities in the case. No diagnostic information is generated from the software.

(3) The Output API transmits the result of interstitial lung findings compatible with interstitial lung disease to an assigned set of users in the hospital or clinic, specialists who will then review the case. The Output API is integrated into the hospital or clinic notification software (e.g., EHR, messaging system).

The Analysis System is composed of a 3-D deep learning algorithm trained to identify interstitial lung findings compatible with interstitial lung disease. The training dataset included >3,000 lung CT cases from five different data sources from numerous clinical facilities. The algorithm takes in the ingested CT scan, runs it through the locked model, and classifies whether interstitial lung findings compatible with interstitial lung disease appear to be present. The average patient age was 63 years with male and females representing 51.5% and 48.5% of the patient population respectively. All major CT manufacturers were included, and prevalence of positive cases was 24%.

The software output is a binary Positive (Suggestive of ILD)/Negative result for interstitial lung findings compatible with interstitial lung disease. The output is stored for all cases run. Workflow for managing the output is customizable and under the control of the hospital or clinic making use of the device. For example, one workflow can include configuring the output to list Positive cases in a worklist for clinician review (e.g. a dedicated clinician within the pulmonary clinic environment). Another workflow may include integration with dedicated 3rd party software for workflow management of Positive cases. Regardless of method for case list management, cases with a Positive result will be reviewed for consideration of whether additional work-up is clinically indicated.

No analyzed images or other visually assessed features are output by the device. No regions of interest are either input or provided as an output. Additionally, the software does not provide localization information and there is no filtering, post processing, or annotations. The device is designed to not interrupt standard workflows and operates only in parallel, identifying patients

who may benefit from additional follow-up for possible lung fibrosis, based on interstitial lung findings compatible with interstitial lung disease.

**INDICATIONS FOR USE**

ScreenDx is a software-only device that receives and analyzes lung computed tomography (CT) imaging data in order to assess for interstitial lung findings compatible with interstitial lung disease. The device supplements the standard-of-care workflow by providing a qualitative output of imaging findings based on pattern recognition, in order to provide adjunctive information as part of a referral pathway to an appropriately qualified clinician. Patients with positively identified patterns may undergo assessment for lung fibrosis, but ScreenDx does not replace the current standard of care methods for diagnosis of lung fibrosis and the results of the device are not intended to rule-out or rule-in lung fibrosis. The results of ScreenDx are intended to be used only by clinicians qualified in the care of lung disease, in conjunction with the patient's clinical history, symptoms, and other diagnostic tests, as well as the clinician's professional judgment.

The input to ScreenDx is a DICOM-compliant lung CT scan. Clinical case eligibility includes the following criteria:

- Age > 22 years old.

**COMPARISON OF TECHNOLOGICAL CHARACTERISTICS**

ScreenDx is substantially equivalent to the predicate device based on the information summarized here:

The subject and predicate devices have the same intended use which is to receive and analyze lung computed tomography (CT) imaging data to provide a qualitative output of imaging findings based on pattern recognition. Both devices are also used to serve as an adjunct in the assessment of lung disease prior to invasive testing. Both devices have similar technologies which use artificial intelligence or machine learning algorithms to analyze lung computed tomography (CT) imaging data using pattern recognition. The intended clinical users of the device are the same. Both devices supplement the standard-of-care workflow to provide adjunctive information as part of a referral pathway to an appropriate Multidisciplinary Discussion (MDD) or as part of an MDD.

While both the subject and predicate devices use artificial intelligence or machine learning algorithms with a database of images using pattern recognition, there are differences in their software and algorithms. The pattern recognition algorithm for the subject device is for interstitial lung abnormalities among a more general population of lung CT cases while the pattern recognition for the predicate device is for differentiation within cases of interstitial lung disease and idiopathic pulmonary fibrosis. The technological characteristics of the subject device have undergone testing to ensure the device is as safe and effective as the predicate.

A table comparing the key features of the subject and predicate device is provided below.

| | Subject Device | Predicate Device | Comparison |
|---|---|---|---|
| | ScreenDx | Fibresolve<br>DEN220040 | - |
| Indications for Use | ScreenDx is a software-only device that receives and analyzes lung computed tomography (CT) imaging data in order to assess for interstitial lung findings compatible with interstitial lung disease. The device supplements the standard-of-care workflow by providing a qualitative output of imaging findings based on pattern recognition, in order to provide adjunctive information as part of a referral pathway to an appropriately qualified clinician. Patients with positively identified patterns may undergo assessment for lung fibrosis, but ScreenDx does not replace the current standard of care methods for diagnosis of lung fibrosis and the results of the device are not intended to rule-out or rule-in lung fibrosis. The results of ScreenDx are intended to be used only by clinicians qualified in the care of lung disease, in conjunction with the patient's clinical history, symptoms, and other diagnostic tests, as well as the clinician's professional judgment.<br>The input to ScreenDx is a DICOM-compliant lung CT scan. Clinical case eligibility includes the following criteria:<br>Age > 22 years old. | Fibresolve is a software-only device that receives and analyzes lung computed tomography (CT) imaging data in order to provide a diagnostic subtype classification in suspected cases of interstitial lung disease (ILD). The device supplements the standard-of-care workflow by providing a qualitative, diagnostic classification output of imaging findings based on machine learning pattern recognition, in order to provide adjunctive information as part of a referral pathway to an appropriate Multidisciplinary Discussion (MDD) or as part of an MDD. Specifically, the tool is used to serve as an adjunct in the diagnosis of idiopathic pulmonary fibrosis (IPF) prior to invasive testing. The results of Fibresolve are intended to be used only by clinicians qualified in the care of lung disease, specifically in caring for patients with ILD, in conjunction with the patient's clinical history, symptoms, and other diagnostic tests, as well as the clinician's professional judgment.<br>The input to Fibresolve is a DICOM-compliant lung CT scan. Clinical case eligibility includes the following criteria:<br>Age > 22 years old. | Similar |

| | | | |
|---|---|---|---|
| | | Pulmonary symptoms suggestive of possible ILD including IPF. | |
| User population | Clinicians qualified in the care of lung disease | Clinicians qualified in the care of lung disease, specifically in caring for patients with ILD | Same |
| Target Population | Age > 22 years old. | Age > 22 years old. | Same |
| Anatomical region of interest | Chest | Chest | Same |
| Data input | CT scans acquired in general assessment of thoracic conditions | CT scans acquired in the work-up of patients with suspected ILD and IPF | Similar |
| Scan type and protocol | DICOM-compliant lung CT scan | DICOM-compliant lung CT scan | Same |
| Segmentation of region of interest | No; device does not mark, annotate, or direct users' attention to a specific location in the original image | No; device does not mark, annotate, or direct users' attention to a specific location in the original image | Same |
| Algorithm | Machine learning pattern recognition | Machine learning pattern recognition | Same |
| Alteration of original image | No | No | Same |
| Data Displayed | Qualitative classification output of imaging findings | Qualitative classification output of imaging findings | Same |
| Summarized Use in Workflow | Process a wide array of input images to flag cases for possible follow-up by a specialist | Specifically ordered by a specialist to gather additional discriminatory information | Different |

**SUMMARY OF NON-CLINICAL TESTING**

Software Verification and Validation (per IEC 62304) were performed to demonstrate safety based on current industry standards. The results of these tests indicate that the subject device is equivalent to the predicate device.

**SUMMARY OF CLINICAL TESTING**

To evaluate the performance of the device, a retrospective, multicenter study was performed using ScreenDx software with the primary endpoint to evaluate the software's performance in CT chest cases containing interstitial lung findings compatible with interstitial lung disease versus those without such patterns. Data checks were completed to ensure that there was no overlap between patients from data training to data test set.

The presence or absence of the pattern was intended to correlate with a clinical diagnosis that included lung fibrosis, so could include patients with idiopathic pulmonary fibrosis (IPF), fibrotic nonspecific interstitial pneumonia (NSIP), and other related diagnoses. Negatives were cases without such diagnoses. Positives and negatives were assigned via clinical diagnosis derived directly from the data sources. Methodologies for clinical diagnosis were via combined clinical, radiological, laboratory, and/or pathological assessments, and diagnostic information had been recorded independently for each case.

*Pivotal Study*

Multiple datasets were collated to combine for 3,018 cases from unique patients from multiple clinical sites. The dataset was enriched to a 23.0% positive rate, to enhance statistical analyses for discriminatory performance of the device. Patient demographics, diagnostic distributions, and technical characteristics are summarized below.

| Demographic Distribution of Patients | | | |
|---|---|---|---|
| | | Full Dataset | |
| | | % | n |
| **Age*** | <=40 | 3.9 | 117 |
| - | 41-50 | 3.2 | 96 |
| - | 51-60 | 22.4 | 677 |
| - | 61-70 | 29.8 | 901 |
| - | >70 | 25.7 | 779 |
| **Sex*** | Female | 34.8 | 1054 |
| - | Male | 55.4 | 1678 |
| **Ethnicity†** | Hispanic or Latino | 4.4 | 73 |
| - | Not Hispanic or Latino | 95.6 | 1586 |
| **Race†** | White | 85.8 | 1411 |
| - | Black or African American | 9.2 | 152 |
| - | Asian | 2.9 | 48 |
| - | Multi-race | 1.4 | 23 |
| - | Native Hawaiian or other Pacific Islander | 0.5 | 8 |
| - | American Indian | 0.2 | 3 |

*Age and sex information absent for 10-15% of patients due to data source deidentification processes.†Race and ethnicity information present only for a limited subset of ~40% of patients due to data source deidentification.

| Final Patient Diagnosis Distribution | | | |
|---|---|---|---|
| | | **Full Dataset** | |
| | | % | n |
| **Lung fibrosis** | **Lung fibrosis** | 23.0 | 694 |
| All cases | - | 100.0 | 3018 |
| - | Normal / Screening | 35.5 | 1072 |
| - | IPF | 18.6 | 562 |
| - | Cancer | 14.2 | 429 |
| - | COVID-19 | 12.3 | 371 |
| - | Emphysema | 6.8 | 204 |
| - | Other ILD* | 6.4 | 193 |
| - | Pneumonia | 1.7 | 52 |
| - | Granulomatous disease | 1.4 | 42 |
| - | Other | 3.1 | 93 |

*Other ILD includes pneumoconiosis, bronchiolitis, chronic hypersensitivity pneumonitis, cryptogenic organizing pneumonia, connective tissue disease associated ILD, desquamative interstitial pneumonia, eosinophilic granulomatosis with polyangiitis, nonspecific interstitial pneumonia, sarcoidosis, and vasculitis.

| CT Scan Technical Characteristics | | | |
|---|---|---|---|
| | | **Full Dataset** | |
| | | % | n |
| **CT Manufacturer** | Siemens | 46.8 | 1413 |
| - | Philips | 13.7 | 414 |
| - | GE | 26.0 | 785 |
| - | Toshiba | 7.1 | 214 |
| - | Other* | 0.2 | 6 |
| **Slice Thickness (mm)** | ≤1.5 | 32.9 | 995 |
| - | >1.5, <3 | 48.3 | 1459 |
| - | 3-4 | 8.5 | 258 |
| - | 5 | 10.1 | 305 |

A total of 40 different CT scan protocols (kernels) were used across the various CT manufacturers and sites. CT manufacturer was missing for 186 patients. Slice thickness was missing for 1 patient.

Pre-specified endpoints of 80% sensitivity and 80% specificity were selected based on preliminary performance during device development, as well as planned statistical powering, and were partially derived from related FDA-cleared devices in incidental disease detection via CT imaging.

Sensitivity and specificity both exceeded the 80% performance goal. Specifically, sensitivity was observed to be 91.4% (89.0 - 93.3%) and specificity was observed to be 95.2% (CI: 94.3 - 96.1%).

| **Pivotal Study Performance** | |
|---|---|
| - | **Performance** |
| **Sensitivity** | 91.4% [CI: 89.0-93.3%] |
| **Specificity** | 95.2% [CI: 94.3-96.1%] |
| **LR+** | 19.1 [CI: 18.3-20.0] |
| **LR-** | 0.091 [CI: 0.085-0.098] |
| **OR** | 210.7 [CI: 152.0-291.9] |
| **PPV** | 85.1% [CI: 82.3-87.6%] |
| **NPV** | 97.4% [CI: 96.6-98.0%] |

Relatively fewer patients were in younger age cohorts, as expected for a population of patients undergoing CT thorax examinations. A total of 107 patients ages 22-40 were included, with a lung fibrosis prevalence of 0.9%. Sensitivity was 100.0% [CI: 0.01-100.0%] and specificity was 98.1% [CI: 93.4-99.8%] in this cohort. Positive and negative predictive values were also estimated for various prevalences expected to be encountered by the device.

Smoking history is a relevant risk factor in patients with lung fibrosis, as well as other lung diseases. Results were analyzed within smoking subgroups.

| **Device performance in smoking cohorts** | | | | |
|---|---|---|---|---|
| **Group** | **n** | **Disease Prevalence** | **Sensitivity** | **Specificity** |
| **Positive smoking history** | 1811 | 23.3% | 91.9% [CI: 89.0-94.4%] | 94.2% [CI: 92.8-95.3%] |
| **Negative smoking history** | 262 | 57.3% | 87.3% [CI: 80.9-92.2%] | 91.1% [CI: 84.2-95.6%] |
| **Unknown smoking history** | 945 | 12.9% | 94.3 [CI: 88.9-97.7%] | 97.6% [CI: 96.3-98.5%] |

| **Device Performance by CT Slice Thickness** | | | | |
|---|---|---|---|---|
| **Group** | **N** | **Disease Prevalence** | **Sensitivity** | **Specificity** |
| **<=1.5 mm** | 995 | 56.8% | 94.7% [CI: 92.5-96.4%] | 86.7% [CI: 83.4-90.0%] |
| **>1.5, <3 mm** | 1459 | 2.7% | 90.% [CI: 76.3-97.2%] | 97.7% [CI: 96.7-98.4%] |
| **3-4 mm** | 258 | 7.0% | 72.2% [CI: 46.5-90.3%] | 95.0% [CI: 91.4-97.4%] |
| **5 mm** | 305 | 22.6% | 70.0% [CI: 57.3-80.1%] | 95.8% [CI: 92.3-97.9%] |

| **Device Performance by CT Type** | | | | |
|---|---|---|---|---|
| **Group** | **N** | **Disease Prevalence** | **Sensitivity** | **Specificity** |
| **HRCT** | 854 | 37.6% | 84.7% [CI: 80.3-88.4%] | 87.8% [CI: 84.7-90.5%] |
| **LDCT** | 999 | 1.0% | 60.0% [CI: 26.2-87.8%] | 96.8% [CI: 95.5-97.8%] |
| **Routine CT** | 1165 | 31.2% | 98.1% [CI: 96.1-99.2%] | 98.3% [CI: 97.1-99.0%] |

*Additional Independent Validation Study*

A separate independent validation study was also completed in an additional dataset of 2,482 cases. This dataset had been collected prospectively by an independent organization, with a focus on chronic obstructive pulmonary disease. ILD was initially intended as an exclusion, but some (a total of 39) cases of ILD were ultimately found among the patient population. As a test of the device in a low prevalence population, CT scans from patients at the entry time point of the study were assessed to determine whether the device was able to identify positive cases.

| **Additional Validation Study Performance** | |
|---|---|
| **Study Results** | |
| | (n=2482) |
| Age (years) | Q1: 49, Q3: 63 |
| Sex (% Female) | 50% |
| CT Scanner Manufacturer | |
| GE | 870 (35%) |
| Siemens | 1486 (60%) |
| Philips | 126 (5%) |
| Disease Presence/Absence | |
| Positive | 39 (1.6%) |
| Negative | 2443 (98.4%) |
| Device Sensitivity | 87% [CI: 85.8-88.5%] |
| Device Specificity | 98% [CI: 97.5-98.5%] |

**PREDETERMINED CHANGE CONTROL PLAN**

The device includes a predetermined change control plan (PCCP), detailing the specific modifications (SaMD Pre-Specifications (SPS)) that may be made to the device and the specific methods in place to achieve and appropriately control the risks of the anticipated types of modifications (Algorithm Change Protocol (ACP)). The ACP outlines the process for data management, model re-training, performance evaluation, and update procedures associated with the change. The plan allows for modifications and updates to the underlying Analysis Algorithm within a limited scope of changes, specifically adjustment or updates to the model architecture and changes to the cut-off value for determining positive/negative results.

Changes are evaluated via pre-specified statistical analyses in-line with those as part of the original device testing, to ensure, at minimum, non-inferior absolute performance, and potential improvements in performance, training data, or generalizability. The PCCP lists anticipated software modifications, rationale, testing methods, and impact assessment used to implement the software modifications in a controlled manner and safety and effectiveness of software updates including algorithm changes. These modifications are briefly summarized below.

| Modification | Rationale | Testing Methods | Impact Assessment |
|---|---|---|---|
| Update model architecture or training data | With additional real-world data and ongoing assessments of real-world performance of the model, re-training a new model allows for potential improvements in generalizability which provides greater clinical value. | Substantial equivalence as compared to the prior version. Statistical assessments following same standards used in original device clearance. | Revised generalizability or accuracy metrics for the system.<br><br>*Benefit-Risk Analysis:*<br>Benefit: Enhanced performance; generalizability.<br>Risk: Reduction in clinical performance or generalizability.<br><br>*Risk Mitigation:*<br>Evaluate device model on Test dataset metrics. Execute unit and integration tests for the product code. |
| Updated model threshold selection | With additional real-world data and ongoing assessments of real-world performance of the model, a change in optimized threshold targeting may provide a better balance of sensitivity and specificity for the appropriate populations. | Substantial equivalence as compared to the prior version. Statistical assessments following same standards used in original device clearance. | Revised relative performance of sensitivity, specificity, PPV, and NPV for real-world use.<br><br>*Benefit-Risk Analysis:*<br>Benefit: Enhanced performance; generalizability.<br>Risk: Reduction in clinical performance or generalizability.<br><br>*Risk Mitigation:*<br>Evaluate device model on Test dataset metrics. Execute unit and integration tests for the product code. |

The benefit/risk of the above modifications have been assessed and are favorable for allowing continued device improvement with time while limiting potential for harm.

**CONCLUSION**

The subject device and predicate devices are both intended to provide a qualitative output of imaging findings based on pattern recognition. Both devices supplement the standard-of-care workflow as part of a referral pathway in the assessment of lung disease. The devices are not for diagnostic use and are to be used in parallel to standard-of-care workflow only. The differences in software and algorithms between the devices have been properly evaluated through software verification and validation testing and clinical validation testing. The performance data demonstrate that the device performs as intended in the specified use conditions and do not present any new issues of safety or effectiveness. Thus, ScreenDx is determined to be substantially equivalent to the predicate device.