4Dx Limited
℅ Mr. Terrence Thiel
Principal Consultant
Level 5 Suite 3, 468 St Kilda Rd
Melbourne, Victoria 3004
AUSTRALIA

May 14, 2020

Re: K193293
Trade/Device Name: XV Lung Ventilation Analysis Software System
Regulation Number: 21 CFR 892.1750
Regulation Name: Computed tomography x-ray system
Regulatory Class: Class II
Product Code: JAK
Dated: April 1, 2020
Received: April 17, 2020

Dear Mr. Thiel:

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: 06/30/2020
*See PRA Statement below.*

510(k) Number *(if known)*
K193293

Device Name
XV Lung Ventilation Analysis Software System

Indications for Use *(Describe)*

The XV Ventilation Lung Analysis Software is software-based image processing technology that analyzes cinefluorograph images and a CT (can be a previously acquired CT that is representative of the patient's present lung envelope), to quantify ventilation of pulmonary tissue for use in adult patients.

The XV Ventilation Lung Analysis Software provides reproducible quantification of ventilation for pulmonary tissue, which is essential for providing quantitative support for diagnosis and follow up examinations. For use by referral from a pulmonary specialist or equivalent, the Device can be used to provide the physician with additional clinical data in the diagnosis and documentation of inhomogeneities and defects in pulmonary ventilation. Quantification and statistics are provided in the form of a Report, including:

- The tidal volume (i.e. total lung ventilation), presented as a single value;
- Visualization of lung ventilation with color-defined specific ventilation ranges overlaid on the CT slices;
- The heterogeneity of lung ventilation, presented as three values, which quantifies the regional variability of the ventilation; and
- Ventilation graph/ histogram of the classified lung voxel's relative frequencies showing the frequency distribution of regional specific ventilation measured across the entire lung, including ventilation defect percentage which shows the volume of lung with low ventilation.

The clinical study used to validate the Device was limited to patients selected to undergo Radiation Therapy (most commonly for breast cancer and esophageal cancer). In this study these patients were examined using the Device at four time-points over a 13-month period (twice prior and twice following radiation therapy).

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: XV Lung Ventilation Analysis Software System

## 1. Submitter Information


| | |
|---|---|
| Submitter: | 4Dx Limited<br>Level 5 Suite 3<br>468 St Kilda Rd<br>Melbourne, VIC 3004 AUSTRALIA |
| Primary contact person: | Andreas Fouras<br>e-mail: regulatory@4dx.com |
| Secondary contact person: | Rachael Tenkaten<br>e-mail: rtenkaten@4dx.com |


Date prepared: November 22, 2019

## 2. Subject Device

| | |
|---|---|
| 510(k) number: | K193293 |
| Name of Device: | XV Lung Ventilation Analysis Software System |
| Manufacturer: | 4Dx Limited |
| Regulation Number: | 21 CFR 892.1750 |
| Classification Name: | Computed Tomography X-ray System Class II |
| Classification Class: | JAK |
| Product Code: | |

## 3. Legally Marketed Primary Predicate Device

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|---|---|
| Predicate 510(k) number: | K151919 |
| Name of Device: | Vitra CT Lung Density Analysis Software |
| Manufacturer: | Vital Images, Inc. |
| Regulatory Number: | 21 CFR 892.1750 |
| Classification Name: | Computed Tomography X-ray System |
| Classification Class: | Class II |
| Product Code: | JAK |
| Decision Date: | 10/10/2015 |

## 4. Legally Marketed Secondary Predicate Device

| | |
|---|---|
| Predicate 510(k) number: | K181407 |
| Name of Device: | Artis zee/zeego & Artis Q/Q.zen |
| Manufacturer: | Siemens Medical Solution USA, Inc. |

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|---|---|
| Regulatory Number: | 21 CFR 892.1650 |
| Classification Name: | Image-intensified fluoroscopic X-ray system |
| Classification Class: | Class II |
| Product Code: | OWB, IZI, JAA, JAK |
| Decision Date: | 08/15/2018 |

## 5. Device Description

The **XV Lung Ventilation Analysis Software** is a software-based image processing technology that analyzes cinefluorograph images in combination with a CT image to quantify ventilation of pulmonary tissue, thereby providing support to physicians in their assessment of patients with lung diseases.

The **XV Lung Ventilation Analysis Software** measures the tissue motion of the lung, at all locations throughout the lung, and at all phases of the breath. It uses these motion measurements to calculate the 4-dimensional (4D) ventilation of lung tissues. Quantification and statistics are provided in the form of a Report.

The key outputs are:

- The tidal volume (i.e. total lung ventilation), presented as a single value;
- Visualization of lung ventilation with color-defined specific ventilation ranges;
- The heterogeneity of lung ventilation, presented as three values; and
- Ventilation graph/ histogram of the classified lung voxel's relative frequencies including ventilation defect percentage.

## 6. Indications for use

The **XV Ventilation Lung Analysis Software** is software-based image processing technology that analyzes cinefluorograph images and a CT (can be a previously acquired CT that is representative of the patient's present lung envelope), to quantify ventilation of pulmonary tissue for use in adult patients.

The **XV Ventilation Lung Analysis Software** provides reproducible quantification of ventilation for pulmonary tissue, which is essential for providing quantitative support for diagnosis and follow up examinations. For use by referral from a pulmonary specialist or equivalent, the Device can be used to provide the physician with additional clinical data in the diagnosis and documentation of inhomogeneities and defects in pulmonary ventilation. Quantification and statistics are provided in the form of a Report, including:

- The tidal volume (i.e. total lung ventilation), presented as a single value;
- Visualization of lung ventilation with color-defined specific ventilation ranges overlaid on the CT slices;

- The heterogeneity of lung ventilation, presented as three values, which quantifies the regional variability of the ventilation; and
- Ventilation graph/ histogram of the classified lung voxel's relative frequencies showing the frequency distribution of regional specific ventilation measured across the entire lung, including ventilation defect percentage which shows the volume of lung with low ventilation.

The clinical study used to validate the Device was limited to patients selected to undergo Radiation Therapy (most commonly for breast cancer and esophageal cancer). In this study these patients were examined using the Device at four time-points over a 13-month period (twice prior and twice following radiation therapy).

## 7. Substantial Equivalence

| **Characteristic** | **Subject Device** | **Predicate Device** | **Secondary Predicate Device** | **Comparison and Comments** |
|---|---|---|---|---|
| | **XV Ventilation Lung Analysis Software** | **Vitrea CT Lung Density Analysis Software** | **Artis Q / Q.zen** | |
| Regulatory Comparison | | | | |
| Classification name | Computed Tomography X-ray System | Computed Tomography X-ray System | Image-intensified fluoroscopic X-ray system | Identical (Primary)/ Similar (Secondary)<br>*All three devices are radiology devices.* |
| Regulatory number | 892.1750 | 892.1750 | 892.1650 | |
| Product Code | JAK | JAK | OWB, IZI, JAA, JAK | Identical (Primary)/ Similar (Secondary)<br>*All three devices can be used for CT (JAK), the secondary predicate device is primarily a fluoroscope* |
| Classification | Class II | Class II | Class II | Identical (Primary)/ Identical (Secondary) |
| Review Panel | Radiology | Radiology | Radiology | Identical (Primary)/ Identical (Secondary) |
| | | | | |
| Indications for Use Comparison | | | | |
| **XV Ventilation Lung Analysis Software** | The XV Ventilation Lung Analysis Software is software-based image processing technology that analyzes cinefluorograph images and a CT (can be a previously acquired CT that is representative of the patient's present lung envelope), to quantify ventilation of pulmonary tissue for use in adult patients.<br>The XV Ventilation Lung Analysis Software provides reproducible quantification of ventilation for pulmonary tissue, which is essential for providing quantitative support for diagnosis and follow up examinations. For use by referral from a pulmonary specialist or equivalent, the Device can be used to provide the physician with additional clinical data in the diagnosis and | | | |

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|---|---|
| | documentation of inhomogeneities and defects in pulmonary ventilation. Quantification and statistics are provided in the form of a Report, including:<br>• The tidal volume (i.e. total lung ventilation), presented as a single value;<br>• Visualization of lung ventilation with color-defined specific ventilation ranges overlaid on the CT slices;<br>• The heterogeneity of lung ventilation, presented as three values, which quantifies the regional variability of the ventilation; and<br>• Ventilation graph/ histogram of the classified lung voxel's relative frequencies showing the frequency distribution of regional specific ventilation measured across the entire lung, including ventilation defect percentage which shows the volume of lung with low ventilation. |
| **Vitrea CT Lung Density Analysis Software** | The Vitrea Lung Density Analysis software provides CT values for the pulmonary tissue from CT thoracic datasets. Three-dimensional (3D) segmentation of the left lung and right lung, volumetric analysis, density evaluations and reporting tools are integrated in a specific workflow to offer the physician a quantitative support for diagnosis and follow-up evaluation of lung tissue images. |
| **Artis Q / Q.zen** | Artis is a family of dedicated angiography systems developed for single and biplane diagnostic imaging and interventional procedures.<br>Procedures that can be performed with the Artis family include cardiac angiography, neuro-angiography, general angiography, rotational angiography, multipurpose angiography and whole body radiographic/fluoroscopic procedures as well as procedures next to the table for i.e. patient extremities.<br>The examination table as an integrated part of the system can be used for X-ray imaging, surgery and interventions.<br>Artis can also support the acquisition of position triggered imaging for spatial data synthesis.<br><br>The Artis systems include also the software option DynaCT with following IFU:<br>DynaCT is an x-ray imaging software option, which allows the reconstruction of two-dimensional images acquired with a standard angiographic C-arm device into a three-dimensional image format.<br>DynaCT is intended for imaging both hard and soft tissues as well as other internal body structures for diagnosis, surgical planning, interventional procedures and treatment follow-up. |
| **Comparison and Comments** | Similar (Primary Predicate) / Similar (Secondary Predicate)<br>*These devices are all intended to support physicians in diagnosis and treatment follow-up by providing three-dimensional (3D) information of the lungs.*<br><br>*The primary predicate measures density and the subject device measures ventilation. Ventilation is a commonly used concept in CT-based lung diagnostics, with similarities to the nomenclature of the Device outputs. Pulmonologists often use the concept of controlled ventilation when performing CT scans. Surrogate measurements of ventilation, such as density (which is often referred to as aeration) are routinely used in 3D CT, inspiratory/expiratory CT and V/Q scans, for diagnostic purposes. Measurement of lung density, expressed in Hounsfield Units (HU), is a common output of the predicate device. With the aid of careful calibration, and the knowledge of the relationship between X-ray attenuation and material density, the local lung density can be derived from the voxel intensities. In lung tissue, density is almost universally used as a surrogate of aeration. Similarly, in some CT studies, aeration has been used as a surrogate for ventilation output, ventilation which is output by the subject Device.* |

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|---|---|
| | *The secondary predicate device utilizes fluoroscopy in combination with tomographic reconstruction to generate 3D data, similar to the subject device.* |

| **Characteristic** | **Subject Device** | **Predicate Device** | **Secondary Predicate Device** | **Comparison and Comments** |
|---|---|---|---|---|
| | **XV Ventilation Lung Analysis Software** | **Vitrea CT Lung Density Analysis Software** | **Artis Q / Q.zen** | |
| Intended users | Thoracic Radiologists and Pulmonologists | Thoracic Radiologists and Pulmonologists | Radiologists (including Thoracic Radiologists) and Physicians (including Pulmonologists) | Identical (Primary)/ Similar (Secondary)<br>*All three devices can be used by Thoracic Radiologists, the secondary predicate device also has a wider application (whole body imaging capability).* |
| Patient population | Adult patients with pulmonary diseases and abnormalities | Patients with pulmonary diseases and abnormalities | All patients | Similar (Primary)/ Similar (Secondary)<br>*The subject device will initially have an adult-only patient population. Once 4Dx has completed additional clinical trials (currently under development) 4Dx will add pediatric patients to the IFU in a future submission.* |
| Input images | Cinefluorograph images and CT | CT | 2D cinefluorograph images are acquired by the device. | Similar (Primary)/ Similar (Secondary) |
| Device Description Comparison | | | | |
| Device Description | The Device is a software-based image processing technology that analyzes cinefluorograph images to quantify ventilation of pulmonary tissue, thereby providing support to physicians in their assessment of | Vitrea CT Lung Density Analysis assists in analyzing lung densities and volumes. It semi-automatically segments lung tissues with quantifiable controls and renderings to aid communication with the pulmonologist. | The Artis Modular Angiography systems are specialized angiography systems. In general, they are equipped with C-arm, stand, flat panel detector, x-ray tube, high voltage generator, patient table and image post- | Similar (Primary)/ Similar (Secondary)<br>*The primary predicate utilizes CT input images to provide the end user with 3D measurements of lung function.*<br>*The secondary predicate utilizes* |

| Characteristic | Subject Device | Predicate Device | Secondary Predicate Device | Comparison and Comments |
|---|---|---|---|---|
| | **XV Ventilation Lung Analysis Software** | **Vitrea CT Lung Density Analysis Software** | **Artis Q / Q.zen** | |
| | patients with lung diseases.<br>The Device measures the tissue motion of the lung, at all locations throughout the lung, and at all phases of the breath. It uses these motion measurements to calculate the 4-dimensional ventilation of lung tissues. | | processing software.<br><br>Siemens will provide new software VD11D for both, the Artis zee/zeego and Artis Q/Q.zen systems. The new software VD11D will support the detector Pixium 3040CV (also known as "40HDR") already cleared with Artis Q/Q.zen (K123529). Systems, Artis zee/zeego, and Artis Q/Q.zen use the cleared AEC (Automatic Exposure Control) functionality. | *acquired cinefluorograph images to provide the end user with 3D images.*<br><br>*The subject device utilizes cinefluorograph images and a CT image to provide the end user with 3D measurements of lung function.* |
| Device Output – Lung Volume | The tidal volume (i.e. total lung ventilation), presented as a single value | Semi-automatic right lung, left lung and airway segmentation | NA | *The subject device and predicate device both support Lung Volume measurement.* |
| Device Output – Lung Visualization | Visualization of lung ventilation with color-defined specific ventilation ranges | Visualization of lung density with color-defined Hounsfield Unit (HU) ranges | The systems include a software which allows the reconstruction of 2D images acquired with a standard angiographic C-arm device into a 3D image format. | *The subject device and predicate device both support visualizations of lungs utilizing a color-defined range.*<br>*The subject device and the second predicate both reconstruct cinefluorograph 2D images into 3D images.* |
| Device Output – Lung Analysis | The heterogeneity of lung ventilation, presented as three values. | Lung density result quantification with HU density range, volume | NA | *The subject device and predicate device both support:*<br>• *Region (Voxel by voxel)* |

| Characteristic | Subject Device | Predicate Device | Secondary Predicate Device | Comparison and Comments |
|---|---|---|---|---|
| | **XV Ventilation Lung Analysis Software** | **Vitrea CT Lung Density Analysis Software** | **Artis Q / Q.zen** | |
| | | measurements, lung density index and the PD15% measurement | | *characterization of lung tissue*<br>• *Quantification of pulmonary tissue ventilation*<br>• *Lung analysis; deriving further analysis metrics from the voxel characteristics and frequency distribution histogram characteristics.* |
| Device Output – Lung Voxels | Ventilation graph/ histogram of the classified lung voxel's relative frequencies including ventilation defect percentage. | Density graph/histogram of the classified lung voxels' relative frequencies. | NA | *The subject device and predicate device both support histograms of the classified lung voxels' relative frequencies.* |
| Device Output – Reporting | This data is provided in the form of a Report. | Comparison of upper and lower lung density index ratios.<br>Adjustable density thresholds for refining and optimizing HU ranges.<br>Overlay of density quantification results and density graph histogram for reporting.<br>Export of density values and curves to CSV tables or copy to clipboard for insertion into a report. | NA (does not produce a report) | *All devices support data to the end user, the subject device and primary predicate device support reporting.* |
| Technology Comparison | | | | |

| Characteristic | Subject Device | Predicate Device | Secondary Predicate Device | Comparison and Comments |
|---|---|---|---|---|
| | **XV Ventilation Lung Analysis Software** | **Vitrea CT Lung Density Analysis Software** | **Artis Q / Q.zen** | |
| Modality | Cinefluorograph images and CT | CT | Cinefluorograph images | Substantially equivalent |
| Lung Volume measurement | Measures Tidal Volume. | Measures left and right lung volume | NA | Substantially equivalent |
| Visualization representation | Visualization of lung ventilation with color-defined specific ventilation ranges. | Visualization of lung density with color-defined Hounsfield Unit (HU) ranges. | NA | Substantially equivalent |
| Voxel by voxel measure of lung characteristics | Measures ventilation in each lung voxel. | Measures HU in each lung voxel. | NA | Substantially equivalent |
| Quantification of pulmonary tissue ventilation | Analyzing ventilation at all voxels throughout the lung, and at all phases of the breath. | Analyzing densities and volumes of pulmonary tissue. | NA | Substantially equivalent |
| Lung analysis support | Analyzes voxel characteristics to provide metrics derived from ventilation, i.e. regional ventilation. | Analyzes voxel characteristics to provide metrics derived from density, i.e. density indices as a function of both HU range (low/ medium) and location (right/left/both lungs). | NA | Substantially equivalent |
| Statistical measures derived from voxel characteristics | The heterogeneity of lung ventilation derived from frequency distribution histograms of specific ventilation. | PD15 measurement derived from frequency distribution histograms of HU in a given lung region (15% of voxels have a lower HU unit in right/left/both lungs). | NA | Substantially equivalent |
| Generate frequency distribution histograms | Frequency distribution histograms of specific ventilation. | Frequency distribution histograms of HU. | NA | Substantially equivalent |
| Analyzed data export | Ability to export outputs in a report. | Ability to export outputs to support reporting. | Ability to export 3D data from 2D images. | Substantially equivalent |

| Characteristic | Subject Device | Predicate Device | Secondary Predicate Device | Comparison and Comments |
|---|---|---|---|---|
| | **XV Ventilation Lung Analysis Software** | **Vitrea CT Lung Density Analysis Software** | **Artis Q / Q.zen** | |
| Approximate effective radiation dose | For a patient with an existing thoracic CT scan on file; the radiation dose is approximately 3% the dose of a thoracic CT. | Radiation dose of a thoracic CT. | Radiation dose for 3D image is comparable to a thoracic CT (dose is dependent on procedure) | Significant Improvement<br>*The subject device can use a previously acquired CT and therefore the effective radiation dose is significantly less than both of the predicate devices providing a* ***considerable benefit to the patient****.* |

## 8. General safety and Effectives concerns

The device is designed and manufactured under the Quality System Regulations as outlined in 21 CFR §820. The device labelling contains instructions for use and any necessary cautions and warnings for safe and effective use of the device. Risk management is ensured via a risk analysis, and risk control(s) have been implemented to mitigate identified potential hazards (conforming with "ISO 14971:2007 Medical devices –Application of risk management to medical devices"). Testing for verification and validation of the device supports that all software specifications have met the acceptance criteria.

## 9. Verification

The software level of concern for the **XV Lung Ventilation Analysis Software** is Moderate as per FDA's guidance document "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" issued on May 11, 2005. The performance data demonstrates conformance with "IEC 62304: 2006 Medical device software — Software life cycle processes". Software testing was completed using a combination of automatic testing (unit, integration, coverage and performance) and manual component level testing to ensure the software operates in according to defined requirements.

## 10. Summary of Clinical Study

The clinical performance of the **XV Lung Ventilation Analysis Software** was assessed in a clinical study involving patients undergoing radiation therapy. The clinical study involves the patients using the Device at four timepoints (twice prior and twice following radiation therapy). The cohort typically had breast cancer or esophageal cancer, (i.e. patients at the first two timepoints represent a very broad cross-section of lung health in the community). Data from all four time points was analyzed, with the two timepoints after radiation therapy being used to demonstrate the sensitivity of the Device to changes in the lung over time.

The study validated the consistency of outputs with gold-standard measures (CT and PFT). Based upon:

- consideration of the Device design;
- consideration of the intended clinical usage; and
- a review of the literature on current clinical practice in use of similar devices,

it is considered that the **XV Lung Ventilation Analysis Software** presents no unacceptable clinical risks, is safe for clinical usage as indicated by the manufacturer and meets the manufacturer's intended performance criteria.

## 11. Conclusion as to Substantial Equivalence

The **XV Lung Ventilation Analysis Software** application has the same intended use and similar target patient population, indications for use, principle of operation, and technical characteristics as the legally marketed Vitrea CT Lung Density Analysis Software from Vital Images (K151919). The subject Device and the Artis Q / Q.zen (K181407) share similar functionality of producing 3D data from cinefluorographs.

Based on the close similarities between **XV Lung Ventilation Analysis Software** device and the predicates, the similar technological characteristics and as the proposed Device has no additional considerations impacting safety or effectiveness, it is believed the Vitrea CT Lung software is **substantially equivalent** to the subject Device.