

QIBA Profile:

<Title of the Profile> (<Acronym>)

Edition: 2022

Stage: <Stage Name>

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When referencing this document, please use the following format:

QIBA <BC Name> Biomarker Committee. <Title of the Profile> (<Edition>), <Stage Name>. Quantitative Imaging Biomarkers Alliance, Month Day, Year. Available at: <https://qibawiki.rsna.org/index.php/Profiles>

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# 1. Executive Summary

A QIBA Profile is an implementation guide to generate a biomarker with an effective level of performance, mostly by reducing variability and bias in the measurement.

The expected performance is expressed as **Claims** (Section 1.2). To achieve those claims, **Actors** (Scanners, Technologists, Physicists, Radiologists, Reconstruction Software, and Image Analysis Tools) must meet the Checklist **Requirements** (Section 3) covering Periodic QA, Subject Handling, Image Data Acquisition, Image Data Reconstruction, Image QA, and Image Analysis.

This Profile is at the <Stage Name> stage ([qibawiki.rsna.org/index.php/QIBA\_Profile\_Stages](http://qibawiki.rsna.org/index.php/QIBA_Profile_Stages)) so,

* The requirements are believed to be practical by the committee;
* The claim is a hypothesis based on committee assessment of literature and QIBA groundwork

QIBA Profiles for other CT, MRI, PET, and Ultrasound biomarkers can be found at [qibawiki.rsna.org](https://wiki.ihe.net/index.php/Profiles).

## 1.1 Clinical Context

CT Tumor Volume Change is used as a biomarker of disease risk, characterization, progression, and response to treatment.

This involves measuring tumor volumes and assessing longitudinal changes within subjects, based on image processing of CT scans acquired at different timepoints. See Appendix B for a discussion of usage of this biomarker in practice.

## 1.2 Claims

Conformance with this Profile by all relevant staff and equipment supports the following claim(s):

**Change Detection Claim**: A true change in a lung tumor volume has occurred with 95% confidence if the measured change is larger than 24%, 29%, or 39% respectively when the longest in-plane diameter is initially 50-100mm, 35-49mm, or 10-34mm.

**Repeatability Claim**: Tumor volume measurement within-tumor coefficient of variation (wCV), is 0.085, 0.103, and 0.141 respectively for lung tumors with diameters of 50-100mm, 35-49mm, or 10-34mm.

This **claim** holds when:

* the patient is between 20 and 45 years old

The Change Detection Claim is particularly relevant to Clinicians. The Repeatability Claim describes individual measurements and the wCV can be used to compute 95% Confidence Intervals (CI). For example, a tumor measured as 34cm3 (~40mm diam) then 268 cm3 (~80mm) yields a 95% CI for the true volume change of [+189 cm3, +279 cm3]. See Appendix B for more details.

### 1.2.1 Current Performance

To put the above Claims in perspective, consider a site that is not conforming to the requirements in the QIBA Profile or making similar special image acquisition efforts.

Based on the groundwork studies and literature review carried out by the QIBA <BC Name> Biomarker Committee, the use of different radiologists and analysis tools at two timepoints for a given tumor, even when the same scanner is used, might be expected to degrade the minimum detectable change in tumor volume for a 10-34mm tumor to the order of 136%. See Table B-1 in Appendix B.

Of course, without ascertaining site practice and without doing a site-specific analysis, the repeatability and change detectability for any given site is essentially unknown. Important benefits from standardizing a site's biomarker process steps include more predictable and reproducible biomarker technical performance, becoming more comparable across scanners and across sites, and ultimately more reliable decision making and improved clinical performance.

## 1.3 Disclaimers

**Standard of Care**: The requirements are defined to achieve the Claim and do not supersede proper patient management considerations. Requirements that disqualify an exam or lesion mean the performance in the Claims cannot be presumed, but does not preclude clinical use of the measurement at the discretion of the clinician.

**Confirmation of Claims**: The claims are informed by groundwork studies, extensive literature review and expert consensus; they have not yet been fully substantiated by studies that strictly conform to the requirements given here. The QIBA Consensus, Claim Confirmation and Clinical Confirmation Stages will collect data on the actual field performance and appropriate revisions will be made to the Claims and/or the details of the Profile. At that point, this caveat may be removed or re-stated. (<https://qibawiki.rsna.org/index.php/QIBA_Profile_Stages>)

**Scope of Claims**: The quantitative performance values in the claims were derived from analysis of tumor volumetry consisting solely of lung data. Correspondingly, the claims assert that this performance holds for tumors in the lung. Elsewhere, factors like the degree of visual contrast between the tumor and its background, or injected contrast dynamics may affect volumetry performance in ways that have not yet been fully explored and quantified. Despite this, usage of the methods and requirements in this Profile for segmentation and volumetry of tumors in the kidneys, liver, lymph nodes and elsewhere in the thorax is recommended, however the expected performance has not yet been determined and may differ from that stated in the Claim.

**Innovation**: Profile requirements are intended to establish a baseline level of performance. Exceeding the requirements and providing higher performance or advanced capabilities is allowed and encouraged. The Profile does not limit the methods institutions and equipment suppliers use to meet the requirements.

# 2. Conformance

**To conform to this Profile, participating Actors (staff and equipment) shall meet each requirement on their checklist in Section 3.**

* Some requirements reference a specific **assessment procedure** in Section 4 that shall be used to assess conformance to that requirement. For the rest, any reasonable assessment procedure is acceptable.
* Staff must ensure requirements assigned to them are met; however, for the purpose of conforming to the profile, they may delegate a task rather than physically doing it themselves.
* Staff names represent roles in the profile, not formal job titles or certifications. E.g., Site equipment performance requirements are assigned to the Physicist role. The role may be filled by any appropriate person: a staff physicist, a managed contractor, or a vendor provided service.
* If a QIBA Conformance Statement is available for equipment (e.g., published by a scanner vendor), a copy of that statement may be used in lieu of confirming each requirement in that equipment checklist yourself by running the necessary tests.

**To make a formal claim of conformance, the organization responsible for equipment or staff shall publish a QIBA Conformance Statement.**

QIBA Conformance Statements:

* shall follow the current template: (<https://qibawiki.rsna.org/index.php/QIBA_Conformance_Statement_Template>)
* shall include an Appendix containing details recorded by the assessor as stated in requirements or assessment procedures (e.g., acquisition parameters)
* shall describe the test data used for conformance testing or alternatively provide access to it

# 3. Profile Requirement Checklists

The following Checklists are the basis for conforming to this Profile (See Section 2).

Conforms (Y/N) indicates whether conformance to the requirement has been confirmed by the assessor. When responding **N**, it is helpful to include notes explaining why.

Feedback on all aspects of the Profile and associated processes is welcomed. Contact: qiba@rsna.org

## 3.1 Scanner and Reconstruction Software Checklist

Make/Model/Version: Assessment Date: .

| **Parameter** | **Conforms (Y/N)** | **Requirement** |
| --- | --- | --- |
| **Product Validation (see [Section A.1](#_A.2._Product_Validation))** | | |
| Acquisition & Reconstruction Protocol |  | Shall prepare a conformant protocol (see "Protocol Design" on [Radiologist Checklist](#_3.5_Radiologist_Checklist)). |
|  | Shall validate that the protocol achieves an f50 value that is between 0.3 mm-1 and 0.5 mm-1 for both air and soft tissue edges.  See 4.1. Assessment Procedure: In-plane Spatial Resolution |
|  | Shall validate that the protocol achieves a standard deviation < 60HU.  See 4.2. Assessment Procedure: Voxel Noise |
| Image Header |  | Shall record, in the DICOM header, values for tags identified in "Protocol Design" requirements on [Radiologist Checklist](#_3.5_Radiologist_Checklist). |

## 3.2 Image Analysis Tool Checklist

Make/Model/Version: Assessment Date: .

| **Parameter** | **Conforms (Y/N)** | **Requirement** |
| --- | --- | --- |
| **Product Validation (see** [**Section A.1**](#_A.1._Product_Validation)**)** | | |
| Reading Paradigm |  | Shall be able to present the reader with both timepoints side-by-side for comparison when processing the second timepoint. |
| Reading Paradigm |  | Shall be able to re-process the first timepoint (e.g. if it was processed by a different Image Analysis Tool or Radiologist). |
| Tumor Volume Computation |  | Shall be validated to compute volume within 5% of the true volume.  See 4.3 Assessment Procedure: Tumor Volume Computation. |
| Tumor Volume  Repeatability |  | Shall be validated to achieve tumor volume repeatability with:   * an overall repeatability coefficient of less than 0.16 * a small subgroup repeatability coefficient of less than 0.21 * a large subgroup repeatability coefficient of less than 0.21   See 4.4. Assessment Procedure: Tumor Volume Repeatability. |

## 3.3 Physicist Checklist

**Note:** The role of "Physicist" may be played by an in-house medical physicist, a physics consultant or other staff (such as vendor service or specialists) qualified to perform the validations described.

Physicist Name: Assessment Date: .

| **Parameter** | **Conforms (Y/N)** | **Requirement** |
| --- | --- | --- |
| **Protocol Design (see** [**Section A.6**](#_A.4._Protocol_Design)**)** | | |
| In-plane Spatial Resolution |  | Shall validate that the protocol achieves an f50 value between 0.3 mm-1 and 0.5 mm-1 for both air and soft tissue edges.  See 4.1. Assessment Procedure: In-plane Spatial Resolution |
| Voxel Noise |  | Shall validate that the protocol achieves a standard deviation < 60HU.  See 4.2. Assessment Procedure: Voxel Noise |

## 3.4 Technologist Checklist

Technologist Name: Assessment Date: .

| **Parameter** | **Conforms (Y/N)** | **Specification** |
| --- | --- | --- |
| **Subject Handling (see** [**Section A.8**](#_A.8._Subject_Handling)**)** | | |
| Artifact Sources |  | Shall remove or position potential artifact sources (specifically including breast shields, metal-containing clothing, and EKG leads) such that they will not degrade reconstructed CT volumes. |
| Table Height |  | Shall adjust the table height for the mid-axillary plane to pass through the isocenter. |
| **Image Data Acquisition (see** [**Section A.9**](#_A.9._Image_Data)**)** | | |
| Acquisition Protocol |  | Shall select a protocol that has been previously prepared and validated for this purpose. |
| Localizer |  | Shall confirm on the localizer image the absence of artifact sources that could affect the volume acquisitions or the attenuation of lung nodules. |
| Scan Duration for Thorax |  | Shall set parameter values to cover an axial field of view of 35cm in 10 seconds or less. |
| **Image Data Reconstruction (see** [**Section A.10**](#_A.10._Image_Data)**)** | | |
| Reconstruction Protocol |  | Shall select a protocol that has been previously prepared and validated for this purpose. |
| Reconstructed Image Thickness |  | Shall set to between 0.5mm and 2.5mm (inclusive) if not set in the protocol. |
| Reconstructed Image Interval |  | Shall set to less than or equal to the Reconstructed Image Thickness (i.e. no gap, may have overlap) and consistent with baseline. |
| Reconstruction Field of View |  | Shall ensure the Field of View spans at least the full extent of the thoracic and abdominal cavity, but not substantially greater than that. [Reconstruction Field of View (0018,9317)] |

## 3.5 Radiologist Checklist

**Note:** The Radiologist is responsible for the protocol parameters. They may choose to use a protocol provided by the scanner vendor. Working collaboratively with a physicist is recommended as some parameters are system dependent and may require special attention.

Radiologist Name: Assessment Date: .

| **Parameter** | **Conforms (Y/N)** | **Specification** |
| --- | --- | --- |
| **Staff Qualification (see** [**Section A.2**](#_A.2._Staff_Qualification)**)** | | |
| Tumor Volume  Computation Repeatability |  | Shall, if operator interaction is required by the Image Analysis Tool to perform measurements, be validated to achieve tumor volume change repeatability with:   * an overall repeatability coefficient of less than 0.16 * a small subgroup repeatability coefficient of less than 0.21 * a large subgroup repeatability coefficient of less than 0.21   See 4.4. Assessment Procedure: Tumor Volume Change Repeatability. |
| Acquisition Protocol |  | Shall ensure technologists have been trained on the requirements of this Profile. |
| **Protocol Design (see** [**Section A.6**](#_A.4._Protocol_Design)**)** | | |
| Acquisition Protocol |  | Shall prepare a protocol to meet the specifications in this table. |
| Total Collimation Width |  | Shall set to Greater than or equal to 16mm. [Total Collimation Width (0018,9307)] |
| Nominal Tomographic Section Thickness (T) |  | Shall set to Less than or equal to 1.5mm. [Single Collimation Width (0018,9306)] |
| Scan Duration for Thorax |  | Shall set parameter values to cover an axial field of view of 35cm in 10 seconds or less. |
| IEC Pitch |  | Shall set to Less than 1.5. [Spiral Pitch Factor (0018,9311)] |
| Reconstructed Image Thickness |  | Shall set to between 0.5mm and 2.5mm (inclusive). [Slice Thickness (0018,0050)] |
| Reconstructed Image Interval |  | Shall set to less than or equal to the Reconstructed Image Thickness (i.e. no gap, may have overlap). [Spacing Between Slices (0018,0088)] |
| **Subject Handling (see** [**Section A.8**](#_A.8._Subject_Handling)**)** | | |
| Contrast Protocol |  | Shall prescribe a contrast protocol (which may be No Contrast) expected to achieve enhancement consistent with baseline. |
| **Image QA (see** [**Section A.11**](#_A.11._Image_QA)**)** | | |
| Tumor Measurability |  | Shall disqualify any tumor they feel might reasonably degrade the consistency and accuracy of the measurement.  Conversely, if artifacts or attachments are present but the radiologist is confident and prepared to edit the contour to eliminate the impact, then the tumor need not be judged non-conformant to the Profile. |
| Patient Motion Artifacts |  | Shall confirm the images containing the tumor are free from artifact due to patient motion. |
| Dense Object Artifacts |  | Shall confirm the images containing the tumor are free from artifact due to dense objects, materials or anatomic positioning. |
| Clinical Conditions |  | Shall confirm no clinical conditions are affecting the measurability of the tumor. |
| Tumor Margin Conspicuity |  | Shall confirm the tumor margins are sufficiently conspicuous and unattached to other structures of equal density to distinguish the volume of the tumor. |
| Contrast Enhancement |  | Shall confirm the phase of enhancement, if any, and degree of enhancement are consistent with baseline. |
| Patient Positioning Consistency |  | Shall confirm any tumor deformation due to patient positioning is consistent with baseline. |
| Breath Hold Consistency |  | Shall confirm breath hold state and degree of inspiration is consistent with baseline. |
| Reconstructed Image Thickness |  | Shall confirm the reconstructed image thickness is between 0.5mm and 2.5mm, and consistent (e.g. within 0.5mm) with baseline. |
| Field of View |  | Shall confirm the image field of view (FOV) is consistent with baseline. |
| Tumor Size |  | Shall confirm (now or during measurement) each tumor longest in-plane diameter is between 10 mm and 100 mm. (For a spherical tumor, this roughly corresponds to a volume between 0.5 cm3 and 524 cm3.) |
| **Image Analysis (see** [**Section A.13**](#_A.13._Image_Analysis)**)** | | |
| Reading Paradigm |  | Shall re-process the first timepoint if it was processed by a different Image Analysis Tool or Radiologist. |
| Result Verification |  | Shall review & approve the margin contours produced by the tool. |

# 4. Assessment Procedures

Most requirements in Section 3 checklists can be assessed for conformance by direct observation and checked off. Some requirements (e.g., performance metrics) depend on a formalized assessment procedure, in which case that requirement references an Assessment Procedure here in Section 4.

The QIBA-defined procedures that follow are not intended to preclude reasonable alternative methods. Such methods may be submitted to QIBA with evidence that the results produced are equivalent to those here. Upon review by QIBA, the proposed method may be approved as an accepted assessment procedure in this Profile.

## 4.1. Assessment Procedure: In-plane Spatial Resolution

This procedure can be used by a manufacturer or an imaging site to assess the In-plane Spatial Resolution of reconstructed images (for both conventional filtered back-projection and iterative). Resolution is assessed in terms of the f50 value (in mm-1) of the modulation transfer function (MTF).

Loosely speaking, the MTF represents the blur of an infinitely small feature of interest, f50 represents the spatial frequency at which the contrast of the feature has decreased by 50%, and the inverse of the f50 value represents the size of a feature that would be degraded 50%. Thus, for an f50 value of 0.4 mm-1, features that are 2.5mm would have their contrast degraded by 50% (and smaller features would be degraded more).

The assessor shall:

1. Warm up the scanner’s x-ray tube and perform calibration scans (often called air-calibration scans) according to scanner manufacturer recommendations.
2. Select and record acquisition and reconstruction parameters that conform to the Profile (See Protocol Design in the Radiologist Checklist 3.5). Use the same parameters for 4.1 & 4.2, i.e., the noise level during resolution assessment should be that measured during noise assessment.
3. Scan a spatial resolution phantom that has a series of HU-value cylindrical inserts including one with soft-tissue equivalence. E.g., the ACR CT Accreditation Program (CTAP) Phantom module 1 or the AAPM TG233 phantom.
4. Position the phantom with the center of the phantom at isocenter and properly aligned along the z-axis. For details, refer to Section C, Step 3 of the CT Accreditation Testing Instructions: <https://www.acraccreditation.org/~/media/ACRAccreditation/Documents/CT/CT-Accreditation-Testing-Instructions.pdf>
5. Generate an MTF curve, measured as an average of the MTF in the x-y plane along the edge of a target soft-tissue-equivalent insert using AAPM TG233 or equivalent methodology as implemented in manufacturer analysis software, AAPM TG233 software or equivalent.

Note: The AAPM TG233 software provides axial resolution (MTF in the z-direction) in addition to the x-y plane MTF.

1. Determine and record the f50 value, defined as the spatial frequency (in mm-1 units) corresponding to 0.5 MTF on the MTF curve.
2. Generate another MTF curve and determine and record the f50 value using the edge of the "air insert" (i.e. an empty cutout in the phantom). If the phantom does not have a cutout that provides an internal air edge to assess, it is permitted to use the outer edge of the phantom.

The above procedure is provided as a reference method. This reference method, and the method used by the scanner manufacturer for FDA submission of MTF values, are accepted methods for this assessment procedure. The manufacturer may have specific test methods for non-linear reconstruction algorithms.

## 4.2. Assessment Procedure: Voxel Noise

This procedure can be used by a manufacturer or an imaging site to assess the voxel noise of reconstructed images (for both conventional filtered back-projection and iterative). Voxel noise is assessed in terms of the standard deviation of pixel values when imaging a material with uniform density.

Note: This simple assessment is intended to set a reasonable noise limit that is sufficient to avoid degrading segmentation performance. When characterizing reconstruction methods, voxel noise is a limited representation of image noise when noise texture is varied.

The assessor shall:

1. Warm up the scanner’s x-ray tube and perform calibration scans (often called air-calibration scans) according to scanner manufacturer recommendations.
2. Select and record acquisition and reconstruction parameters that conform to the Profile (See Protocol Design in the Radiologist Checklist 3.5). Use the same parameters as used for section 4.1.
3. Place at the isocenter of the scanner a phantom of uniform density that includes a 20 cm diameter cylinder of water equivalent material. E.g. ACR CT Accreditation Program (CTAP) Phantom module 3
4. Scan the phantom and select a single representative slice, likely close to the center, from the uniformity portion of the phantom.
5. Place a region of interest (ROI) of at least 400 mm2 near the center of the slice and record the values reported for the ROI mean and standard deviation.

The assessor is encouraged, but not required, to record and retain images and associated measurement details. Such details support assessment when the voxel noise is close to the acceptable limit.

Note that noise is assessed here in a standard-sized object. In cases of protocols adaptive to the patient body habitus (such as those using Automatic Exposure Control), the qualification of CT scanner noise should include noise as a function of body habitus (using a phantom such as that provisioned in AAPM TG233) if there is any concern that the noise performance may be outside compliance for different body habitus.

The above procedure is provided as a reference method. This reference method and the method used by the scanner manufacturer for FDA submissions are accepted methods for this assessment procedure.

# Appendix A: Activity Requirements

This Appendix organizes Profile requirements according to the sequence of activities involved in generating the biomarker. The requirements here are the same as those in the requirement checklists in Section 3. The step-by-step activity organization can be more conducive to ferreting out sources of variance by the Biomarker Committee and may be helpful for users of the Profile to understand the big picture. The requirement checklist organization in Section 3 is more convenient for the individuals, systems, and organizations checking their conformance to the Profile.

The sequencing of the Activities specified in this Profile are shown in Figure A-1:

activity sequence diagram

Figure A-1: <Title of the Profile> - Activity Sequence

## A.1. Product Validation

This activity evaluates equipment (Scanner, Reconstruction Software, and Image Analysis Tool) prior to their use in the Profile (e.g. at the factory). Product validation includes validations and performance assessments necessary to reliably meet the Profile Claim.

### A.1.1 Discussion

**Tumor Volume Computation** is assessed to confirm that the software is computing the volume correctly and confirm there is a reasonable lack of bias at individual timepoints.

**Tumor Volume Change Repeatability** is assessed to confirm that the software produces sufficiently consistent results over a set of test data. *Repeatability* considers multiple measurements taken under the same conditions (same equipment, parameters, reader, algorithm, etc.) but different subjects, while *reproducibility* considers multiple measurements taken where one or more conditions have changed. So while the Profile Claims address reproducibility, this particular requirement is limited to repeatability. Target repeatability values were chosen based on groundwork [1][2][3][4][5].

**Segmentation** may be performed automatically by software, manually by a human, or semi-automatically with human guidance/intervention, for example to identify a starting seed point, or region, or to edit boundaries. If a human participates in the segmentation, it is suggested that consistent settings be used for conversion of density into display levels (window and level) either by fixing them during the segmentation process or documenting them. When a human operator in involved, product performance assessments should be based on a typical operator (i.e. with standard training and experience).

It is up to products that do not use contours to propose a method for verification by the radiologist.

**Reading Paradigms**, such as the “sequential locked” paradigm here, can reduce variability from inconsistent judgments (such as where to separate an attached tumor) but may also introduce subconscious biases. The Image Analysis Tool is not prohibited from displaying the volume value from the previous timepoint, but if that is determined to be the source of problems, it might be prohibited in future Profile editions.

**Confidence Interval of Result** provides a range of plausible values for the change in tumor volume. Presenting the radiologist with the confidence interval (e.g. [ 2.5 cm3, 4.9 cm3 ]) in addition to, or perhaps instead of, the measured volume (e.g. 3.7 cm3), potentially provides a better decision-making sense of the result by focusing on the range, not a single value.

The Image Analysis tool is encouraged to calculate and make available to the operator the 95% confidence interval for tumor volume change based on the equation:

Where

*Y1* and *Y2* is the volume measured at timepoint 1 and 2,

*wCV1* and *wCV2* is the within-nodule coefficient of variation for *Y1* and *Y2* taken from the following table,

*D1* and *D2* is the longest in-plane diameter of the volume at timepoint 1 and 2:

|  |  |  |  |
| --- | --- | --- | --- |
| ***D1*, *D2*** | **10-34mm** | **35-49mm** | **50-100mm** |
| ***wCV1*, *wCV2*** | 0.141 | 0.103 | 0.085 |

The 95% confidence interval (CI) can be interpreted as follows: If the change in a tumor's volume over two timepoints is measured repeatedly and the CI range is constructed for each measurement, then 95% of those CI ranges would contain the true volume of the tumor.

A reference implementation of a calculator that uses the specified equation is available at: <https://www.accumetra.com/NoduleCalculator.html>

Note: While displaying the 95% CI based on an operator configured wCV would be more convenient for the radiologist than transcribing measured values into a web tool, it is currently unclear whether providing such a calculator constitutes a product claim requiring detailed evidence for the FDA. For this reason, Confidence Interval of Result is a suggestion, not a requirement for conformance to the Profile.

**Assumptions:** The following details were considered safe to reasonably assume, rather than increase the Profile conformance effort by including them as formal requirements. If these assumptions are not met, the staff or equipment are not conformant to the Profile.

* The Image Analysis Tool allows multiple tumors to be measured.
* The Image Analysis Tool correlates each measured tumor across timepoints (manually or automatically). Correlation can be an independent step from segmentation/measurement.

### A.1.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Acquisition & Reconstruction Protocol | Scanner | Shall prepare a protocol conformant with section A.4.2 "Protocol Design Specification". |
| Scanner | Shall validate that the protocol achieves an f50 value that is between 0.3 mm-1 and 0.5 mm-1 for both air and soft tissue edges.  See 4.1. Assessment Procedure: In-plane Spatial Resolution |
| Scanner | Shall validate that the protocol achieves a standard deviation < 60HU.  See 4.2. Assessment Procedure: Voxel Noise |
| Image Header | Reconstruction Software | Shall record in the DICOM header values for tags identified in requirements in A.4.2 "Protocol Design Specification". |
| Reading Paradigm | Image Analysis Tool | Shall be able to present the reader with both timepoints side-by-side for comparison when processing the second timepoint. |
| Reading Paradigm | Image Analysis Tool | Shall be able to re-process the first timepoint (e.g. if it was processed by a different Image Analysis Tool or Radiologist). |
| Tumor Volume Computation | Image Analysis Tool | Shall be validated to compute volume within 5% of the true volume.  See 4.3 Assessment Procedure: Tumor Volume Computation. |
| Tumor Volume  Repeatability | Image Analysis Tool | Shall be validated to achieve tumor volume repeatability with:   * an overall repeatability coefficient of less than 0.16 * a small subgroup repeatability coefficient of less than 0.21 * a large subgroup repeatability coefficient of less than 0.21   See 4.4. Assessment Procedure: Tumor Volume Repeatability. |

## A.2. Staff Qualification

This activity evaluates staff (Radiologist, Physicist, and Technologist) prior to participation in the Profile. Staff Qualification includes training, qualification, or performance assessments necessary to reliably meet the Profile Claim.

### A.2.1 Discussion

If measurement contours are prepared by an Image Analyst but reviewed and edited by a Radiologist, validate the repeatability of the Radiologist. If contours are completely delegated to an Image Analyst, validate the repeatability the Image Analyst.

It is expected that the effect of radiologist volume bias will largely cancel out due to the requirement that the radiologist process both timepoints (see A.9.2), so no Tumor Volume Bias & Linearity validation requirement is placed on the Radiologist.

### A.2.2 Specification

| **Parameter** | **Actor** | **Specification** |
| --- | --- | --- |
| Tumor Volume  Change Repeatability | Radiologist | Shall, if operator interaction is required by the Image Analysis Tool to perform measurements, be validated to achieve tumor volume change repeatability with:   * an overall repeatability coefficient of less than 0.16 * a small subgroup repeatability coefficient of less than 0.21 * a large subgroup repeatability coefficient of less than 0.21   See 4.4. Assessment Procedure: Tumor Volume Repeatability. |
| Acquisition Protocol | Radiologist | Shall ensure technologists have been trained on the requirements of this Profile. |

## A.3. Pre-delivery

This activity describes calibrations, phantom imaging, performance assessments or validations prior to delivery of equipment to a site (e.g. performed at the factory) that are necessary to reliably meet the Profile Claim.

### A.3.1 Discussion

### A.3.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
|  | Acquisition Device |  |
|  |  |
|  |  |  |

## A.4. Installation

This activity describes calibrations, phantom imaging, performance assessments or validations following installation of equipment at the site that are necessary to reliably meet the Profile Claim.

### A.4.1 Discussion

### A.4.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
|  |  |  |
|  |  |
|  |  |  |

## A.5. Periodic QA

This activity involves quality assurance of the scanners that is periodic, not directly associated with a specific subject. Periodic QA includes calibrations, phantom imaging, performance assessments or validations to ensure the scanner is aligned, calibrated, and functioning as needed to reliably meet the Profile Claim. Performance measurements of specific protocols are addressed in Section A.5, not here.

### A.5.1 Discussion

**…**

**Assumptions:** The following details were considered safe to reasonably assume, rather than increase the Profile conformance effort by including them as formal requirements. If these assumptions are not met, the staff or equipment are not conformant to the Profile.

* The Physicist performs relevant quality control procedures as recommended by the manufacturer and records the date/time of QC procedures for auditing.

### A.5.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| PET Calibration Factor | Physicist | Shall assess the current PET Calibration Factor at least quarterly.  See 4.3 Assessment Procedure: PET Calibration Factor.  Shall record the date/time of the calibration for auditing. |
| Acquisition Device | Shall be capable of performing the PET Calibration Factor assessment.  Shall record the most recent PET Calibration Factor for use in subsequent activities. |
| Time sync | Physicist | Shall confirm on a weekly basis that all device clocks are synchronized to within +- 1 minute. |

## A.6. Protocol Design

This activity involves designing and validating image acquisition protocols. Protocol design includes constraints on acquisition and reconstruction parameters necessary to reliably meet the Profile Claim.

### A.6.1 Discussion

Protocol Design is considered to take place at the imaging site; however, sites may choose to make use of protocols developed elsewhere. It is not intended that design and validation be repeated for each subject.

These specifications focus as much as possible on the characteristics of the resulting dataset, rather than a particular technique for achieving those characteristics. This is intended to achieve Profile performance targets while allowing patient-specific adjustments (such as increasing acquisition mAs and reconstruction DFOV for larger patients), and flexibility for product innovation. Technique parameter sets in the QIBA Conformance Statements for Scanners and Reconstruction Software may be helpful for those looking for more guidance. The acquisition parameter constraints here have been selected with scans of the chest, abdomen and pelvis in mind.

Specific constraints are not placed on most acquisition and reconstruction protocol parameters. It is presumed that significant changes to those parameters would result in non-conformant changes in Noise and Resolution. Changes that do not affect the Noise and Resolution are considered insignificant for the purposes of the Profile.

It is not expected that Noise and Resolution be assessed for each subject scan, but rather the Scanner and Reconstruction Software be qualified for the expected acquisition and reconstruction parameters.

**Total Collimation Width** is defined as the total nominal beam width, NxT, where N is the number of detector rows and T is the nominal tomographic section thickness, for example 64x1.25mm. Wider collimation widths can increase coverage and shorten acquisition, but can introduce cone beam artifacts which may degrade image quality. This parameter might not be directly visible in all scanner interfaces.

**Nominal Tomographic Section Thickness** (T), the term preferred by the IEC, is sometimes also called the Single Collimation Width. Thinner slices improve spatial resolution along the subject z-axis and reduce partial volume effects but can increase image noise.

**Scan Duration** is constrained to facilitate acquisition in a single breath-hold, thereby preventing respiratory motion artifacts or anatomic gaps between breath-holds. This requirement is applicable to scanning of the chest and upper abdomen, and is not required for imaging of the head, neck, pelvis, spine, or extremities.

**IEC Pitch** is chosen to ensure sufficient acquisition data sampling for adequate image quality.

…, etc.

X-ray CT uses ionizing radiation. Exposure to radiation can pose risks; however, as the radiation dose is reduced, image quality can be degraded. It is expected that health care professionals will balance the need for good image quality with the risks of radiation exposure on a case-by-case basis. It is not within the scope of this document to describe how these trade-offs should be resolved.

### A.6.2 Specification

**Note:** The Radiologist is responsible for the protocol parameters and for ensuring that the protocol has been validated, which may be done by an in-house medical physicist, a physics consultant or other staff (such as vendor service or specialists) qualified to perform the validations described. Protocol design should be done collaboratively between the physicist and the radiologist with the ultimate responsibility to the radiologist. Some parameters are system dependent and may require special attention from a physicist. They may choose to use a protocol provided by the vendor of the scanner.

| **Parameter** | **Actor** | **Specification** |
| --- | --- | --- |
| Acquisition Protocol | Radiologist | Shall prepare a protocol to meet the specifications in this table. |
| Total Collimation Width | Radiologist | Shall set to Greater than or equal to 16mm. [Total Collimation Width (0018,9307)] |
| Nominal Tomographic Section Thickness (T) | Radiologist | Shall set to Less than or equal to 1.5mm. [Single Collimation Width (0018,9306)] |
| Scan Duration for Thorax | Radiologist | Shall set parameter values to cover an axial field of view of 35cm in 10 seconds or less. |
| IEC Pitch | Radiologist | Shall set to Less than 1.5. [Spiral Pitch Factor (0018,9311)] |
| Reconstructed Image Thickness | Radiologist | Shall set to between 0.5mm and 2.5mm (inclusive). [Slice Thickness (0018,0050)] |
| Reconstructed Image Interval | Radiologist | Shall set to less than or equal to the Reconstructed Image Thickness (i.e. no gap, may have overlap). [Spacing Between Slices (0018,0088)] |
| In-plane Spatial Resolution | Physicist | Shall validate that the protocol achieves an f50 value between 0.3 mm-1 and 0.5 mm-1 for both air and soft tissue edges.  See 4.1. Assessment Procedure: In-plane Spatial Resolution |
| Voxel Noise | Physicist | Shall validate that the protocol achieves a standard deviation < 60HU.  See 4.2. Assessment Procedure: Voxel Noise |

## A.7. Subject Selection

This activity describes criteria and procedures related to the selection of appropriate imaging subjects that are necessary to reliably meet the Profile Claim.

### A.7.1 Discussion

### A.7.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
|  |  |  |
|  |  |
|  |  |  |

## A.8. Subject Handling

This activity involves handling each imaging subject at each timepoint. It includes subject handling details that are necessary to reliably meet the Profile Claim.

### A.8.1 Discussion

**Artifact sources**, in particular metal and other high-density materials, can degrade reconstructed volume data such that it is difficult to determine the true boundary of a tumor. Artifacts can be induced some distance from the artifact source, depending on scan geometry. If feasible, removing artifact sources completely from the patient during the scan is the best solution. Artifacts from residual oral contrast in the esophagus can affect the measurement of nearby small tumors.

**Breath holding** reduces motion that might degrade the image and full inspiration inflates the lungs, which separates structures and makes tumors more conspicuous. Since motion may occur in the first few seconds after full inspiration due to diaphragmatic relaxation, allowing 5 seconds before initiating the acquisition is recommended. A practice round of the breathing instructions is also recommended. This familiarizes the subject with the procedure, allows any difficulties with the instructions to be addressed, and familiarizes the technologist with the subject’s breathing rate.

A single breath-hold acquisition is likely to be more repeatable and avoids problems of tumors on scan boundaries. If two or more breath-holds are needed to fully cover an anatomic region, different tumors may be acquired on different breath-holds. It is still necessary that each tumor be fully included in images acquired within a single breath-hold to avoid discontinuities or gaps that would affect the measurement.

**Assumptions:** The following details were considered safe to reasonably assume, rather than increase the Profile conformance effort by including them as formal requirements. If these assumptions are not met, the staff or equipment are not conformant to the Profile.

* The Technologist positions the subject such that the “sagittal laser line” lies along the sternum (e.g. from the suprasternal notch to the xiphoid process).
* The Technologist instructs the subject in proper breath-hold, and starts image acquisition shortly after full inspiration and visible movement has ceased, accounting for lag time between full inspiration and diaphragmatic relaxation.

### A.8.2 Specification

| **Parameter** | **Actor** | **Specification** |
| --- | --- | --- |
| Artifact Sources | Technologist | Shall remove or position potential artifact sources (specifically including breast shields, metal-containing clothing, and EKG leads) such that they will not degrade reconstructed CT volumes. |
| Table Height | Technologist | Shall adjust the table height for the mid-axillary plane to pass through the isocenter. |
| Contrast Protocol | Radiologist | Shall prescribe a contrast protocol (which may be No Contrast) expected to achieve enhancement consistent with baseline. |

## A.9. Image Data Acquisition

This activity involves acquisition of image data for a subject. It includes details necessary to reliably meet the Profile Claim. This activity applies to every subject. Protocol Design (Section A.6) touches on similar parameters, but addresses details that are not done for each subject, such as designing standard protocols and validating protocol performance with phantoms.

### A.9.1 Discussion

**Acquisition Protocols** are often selected by the Technologist at scan time based on the procedure request in the modality worklist. For measurements to be conformant, the technologist must use a validated protocol (see Section A.4.2). The site could communicate which protocols have been validated using tags in the protocol name, a paper list for the technologist, or a special pick-list on the modality console. Or a site might validate ALL protocols for a given procedure so any selected protocol will have been validated.

There is no requirement to scan phantoms before every subject, or for the technologist to validate the protocol themselves.

### A.9.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Acquisition Protocol | Technologist | Shall select a protocol that has been previously prepared and validated for this purpose. (See A.6.2 "Protocol Design Specification") |
| Localizer | Technologist | Shall confirm on the localizer image the absence of artifact sources that could affect the volume acquisitions or the attenuation of lung nodules. |
| Scan Duration for Thorax | Technologist | Shall set parameter values to cover an axial field of view of 35cm in 10 seconds or less. |

## A.10. Image Data Reconstruction

This activity involves the reconstruction of image data for a subject. It includes criteria and procedures related to producing images from the acquired data that are necessary to reliably meet the Profile Claim. This activity applies to every subject. Protocol Design (Section A.6) touches on similar parameters, but addresses details that are not done for each subject, such as designing standard protocols and validating protocol performance with phantoms.

### A.10.1 Discussion

### A.10.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Reconstruction Protocol | Technologist | Shall select a protocol that has been previously prepared and validated for this purpose. (See A.6.2 "Protocol Design Specification"). |
| Reconstructed Image Thickness | Technologist | Shall set to between 0.5mm and 2.5mm (inclusive) if not set in the protocol. |
| Reconstructed Image Interval | Technologist | Shall set to less than or equal to the Reconstructed Image Thickness (i.e. no gap, may have overlap) and consistent with baseline. |
| Reconstruction Field of View | Technologist | Shall ensure the Field of View spans at least the full extent of the thoracic and abdominal cavity, but not substantially greater than that. [Reconstruction Field of View (0018,9317)] |

## A.11. Image QA

This activity involves evaluating the reconstructed images prior to image analysis. It includes image criteria that are necessary to reliably meet the Profile Claim. This activity applies to every subject. Prior activities, such as Subject Handling (Section A.8), include requirements that attempt to avoid issues mentioned here, but it can still be necessary to confirm during this QA step whether or not those prior activities were successful.

### A.11.1 Discussion

This QA is performed between image generation and analysis. Image content characteristics are checked for conformance with the Profile. It's expected sites perform other QA as part of good imaging practices.

The Radiologist is identified here as ultimately responsible for this activity; however, sites may find it beneficial for technologists to review these details at the time of imaging and identify cases which might require a repeat acquisition and/or reconstruction to address issues with patient motion or artifacts.

Similarly, some or all of these checks may be performed by the radiologist at reporting time to detect whether the technologist was unsuccessful in avoiding them at acquisition time and as a result some or all of the tumor measurements may then be identified as not within the performance target of the Profile.

**Tumor Measurability** is a general evaluation left to the judgement of the radiologist. They oversee segmentation and disqualify tumors with poor measurability or inconsistent segmentation between the two timepoints. If the tumor has varying margin conspicuity on different slices, or is conspicuous but has complex geometry, or the segmentation software is visibly failing, or the background didn't respond to contrast the same way in the two timepoints, the radiologist should disqualify the tumor. Conversely, if the tumor is attached to another structure but the radiologist is confident they can get consistent segmentation over the two timepoints, they may allow a tumor that would be otherwise disqualified.

**Patient motion artifacts** can manifest in a variety of ways, such as a perceptible tram tracking appearance of the bronchioles or blurring of the lung architectural contours with lung windows.

**Dense object artifacts** (both internal and external to the patient) can variably degrade the ability to assess tumor boundaries as discussed in section A.5, resulting in poor change measures and repeatability.

**Clinical conditions** can degrade the ability to assess tumor boundaries, or influence the structure of the tumor itself. For example, atelectasis, pleural effusion, pneumonia and/or pneumothorax can result in architectural changes to the lung surrounding a nodule. Necrosis may complicate tumor extent decisions.

**Tumor Margin Conspicuity** refers to the clarity with which the boundary of the tumor can be discerned from the surroundings which can directly impact the ability to segment the tumor. Conspicuity problems can derive from poor contrast enhancement, from the inherent texture, homogeneity or structure of the tumor, or from attachment of the tumor to other structures.

**Contrast Enhancement** is required to be consistent between the two timepoints. A non-contrast scan at both timepoints satisfies that requirement.

**Tumor Size** can affect the accuracy of measurements. Theoretical assessment and the groundwork projects done by QIBA both indicate that for tumors that are small, errors in measurement represent a greater percentage of the measured size. For tumors that are smaller than the range required here, refer to the QIBA Small Lung Nodule Profile. For tumors that are larger than the range required here, the limitations on measurement are driven more by anatomy than imaging physics. Such tumors are likely to cross anatomical boundaries and abut structures that make consistent segmentation difficult.

### A.11.2 Specification

The Radiologist shall ensure the following has been evaluated for each tumor being measured.

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Tumor Measurability | Radiologist | Shall disqualify any tumor they feel might reasonably degrade the consistency and accuracy of the measurement.  Conversely, if artifacts or attachments are present but the radiologist is confident and prepared to edit the contour to eliminate the impact, then the tumor need not be judged non-conformant to the Profile. |
| Patient Motion Artifacts | Radiologist | Shall confirm the images containing the tumor are free from artifact due to patient motion. |
| Dense Object Artifacts | Radiologist | Shall confirm the images containing the tumor are free from artifact due to dense objects, materials or anatomic positioning. |
| Clinical Conditions | Radiologist | Shall confirm no clinical conditions are affecting the measurability of the tumor. |
| Tumor Margin Conspicuity | Radiologist | Shall confirm the tumor margins are sufficiently conspicuous and unattached to other structures of equal density to distinguish the volume of the tumor. |
| Contrast Enhancement | Radiologist | Shall confirm the phase of enhancement, if any, and degree of enhancement are consistent with baseline. |
| Breath Hold Consistency | Radiologist | Shall confirm the breath hold state and degree of inspiration is consistent with baseline. |
| Reconstructed Image Thickness | Radiologist | Shall confirm the reconstructed image thickness is between 0.5mm and 2.5mm, and consistent (e.g. within 0.5mm) with baseline. |
| Field of View | Radiologist | Shall confirm the image field of view (FOV) is consistent with baseline. |
| Tumor Size | Radiologist | Shall confirm (now or during measurement) each tumor longest in-plane diameter is between 10 mm and 100 mm. (For a spherical tumor, this roughly corresponds to a volume between 0.5 cm3 and 524 cm3.) |

## A.12. Image Distribution

This activity describes criteria and procedures related to distributing images that are necessary to reliably meet the Profile Claim.

### A.12.1 Discussion

### A.12.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
|  |  |  |
|  |  |
|  |  |  |

## A.13. Image Analysis

This activity involves producing the quantitative measurements described in the Profile Claim. This activity applies to every subject. Requirements related to the assessment of the general performance of the tool or operator go in sections A.1 (Product Validation) and A.2 (Staff Qualification) respectively.

### A.13.1 Discussion

The Profile requires that the same Image Analysis Tool and the same Radiologist measure both timepoints of a given tumor. This requirement is due to the variability introduced when a different Image Analysis Tool and/or Radiologist is used between the two timepoints. (See Table 2-1 and the related Discussion)

### A.13.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Reading Paradigm | Radiologist | Shall re-process the first timepoint if it was processed by a different Image Analysis Tool or Radiologist. |
| Result  Verification | Radiologist | Shall review & approve margin contours produced by the tool. |

## A.14. Image Interpretation

This activity describes criteria and procedures related to clinically interpreting the measurements and images that are necessary to reliably meet the Profile Claim.

### 3.14.1 Discussion

### 3.14.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
|  |  |  |
|  |  |
|  |  |  |

# Appendix B: Biomarker Usage

This Appendix discusses concepts and considerations related to the meaning of the Claims and the application of this Biomarker in clinical contexts.

QIBA Claims describe the technical performance of quantitative measurements. The clinical significance and interpretation of those measurements is left to the clinician. Some considerations are presented in the following text.

**Change Confidence Intervals:**

95% Confidence Intervals (CI) help to understand measurement uncertainty. It can be instructive to look at both ends of the 95% CI and consider if a clinical decision would be the same for both values. If so, then the measurement behind that CI may be a good basis for that decision. The 95% confidence interval (CI) for a true change in volume is computed as , where and are the volume measurements at baseline and the subsequent timepoint, and and are the wCV estimates corresponding to these measurements. Consider the following example tumors:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Change Example (Diameter)** | **Baseline Volume** | **Subsequent Volume** | **Volume Change Confidence Interval Calculation** | **95% CI of  True Volume Change** |
| 100mm -> 50mm | **524 cm3** (100mm) | **65 cm3** (50mm) | **-459 cm3 ±** **88 cm3** | **[ -547 cm3, -371 cm3 ]** |
| 40mm -> 80mm | **34 cm3**  (40mm) | **268 cm3**  (80mm) | **234 cm3 ±** **45 cm3** | **[ 189 cm3, 279 cm3 ]** |
| 10mm -> 20mm | **0.5 cm3** (10mm) | **4.2 cm3** (20mm) | **3.7 cm3 ±** **1.2 cm3** | **[ 2.5 cm3, 4.9 cm3 ]** |

Note: The 95% CI in the first example includes a volume reduction of 547 cm3 for a tumor initially measured as 524 cm3 because it accounts for variability in the initial measurement (i.e. the tumor may have initially been larger).

**Change Detection Confidence Thresholds:**

The 95% confidence thresholds (±24%, ±29%, ±39%) in the Change Detection Claim can be thought of as “error bars” or “noise” around the measurement of volume change. If a change is measured to be within this range, it cannot be ascertained that a change has actually occurred. However, if a tumor changes size beyond these limits, it can be ascertained with 95% statistical confidence that there has been a true change in the size of the tumor, and the perceived change is not just measurement variability. Note that this does not address the biological significance of the change, just the likelihood that the measured change is real.

**Clinical Interpretation of Change (progression/response):**

The existence of a true change is described in the Change Detection Claim in terms of the minimum measured change required to be 95% confident a change has occurred. So, to be 95% confident there has been a true increase or decrease in tumor volume, the measured change should be at least 24% for a tumor that had a longest in-plane diameter of between 50mm and 100mm at baseline (and at least 29% or 39% for the next two size categories respectively).

**Clinical interpretation with respect to neurodegenerative cause of symptoms:**

QIBA Profiles do not make claims of the clinical performance of a profiled measurement, such as clinically distinguishing groups of subjects (those with vs. without a particular disease, or those at different stages of disease) based on specific values (i.e., cut-points) of the measured biomarker. However, a study [reference] of profile-conformant measurements has reached the following conclusion.

When assessing patients during initial presentation of Parkinsonian symptoms, SBR measured in the posterior putamen that is either (a) 50% or less than the value in aged-matched controls, or (b) 80% or less than the value in the whole striatum, might be considered diagnostic for a neurodegenerative cause of the symptoms with a sensitivity of at least 85% and specificity of at least 80% [reference].

**Expected performance:**

Profile users can expect to achieve at least the performance described in the claim for any set of actors that meet the profile requirements. If the actors manage to exceed the profile requirements, users may achieve performance better than the claim.

# Appendix C: Acknowledgements and Attributions

This document is proffered by the Radiological Society of North America (RSNA) Quantitative Imaging Biomarker Alliance (QIBA) Volumetric Computed Tomography (CTVol) Biomarker Committee. The committee is composed of representatives from academia, professional societies, scanner manufacturers, image analysis software developers, image analysis laboratories, biopharmaceutical industry, government research organizations and regulatory agencies, among others. All work is considered pre-competitive.

For a description of the committee and its work, see: <https://qibawiki.rsna.org/index.php/Committees>.

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# Bibliography / References

# Open Issues:

These issues are here to capture associated discussion, to focus the attention of reviewers on topics needing feedback, and to track them so they are ultimately resolved. In particular, comments on these issues are highly encouraged during the Public Comment stage.

|  |
| --- |
| **Q.**  A. |
| **Q.**  A. |

# Closed Issues:

These issues have been considered closed by the Biomarker Committee. They are here to forestall discussion of issues that have already been raised and resolved, and to provide a record of the rationale behind the resolution.

|  |
| --- |
| **Q.** Is this template open to further revisions?  A. Yes.  This is an iterative process by nature.  Submit issues and new suggestions/ideas to the QIBA Process Cmte. |
| **Q.**  A. |

# Change Log:

|  |  |
| --- | --- |
| 2015.10.10 | Major cleanup based on comments resolved in the Process Cmte.  Also had to remove a few hundred extraneous paragraph styles. |
| 2015.10.21 | Approved by Process Cmte |
| 2015.11.04 | Incorporating the more refined form of the claim language and referenced a separate claim template.  Added Voxel Noise requirement to show example of the linkage between the requirement and the assessment procedure. |
| 2017.05.12 | Explain profile stages.  Update Claim examples to match guidance.  Add Clinical Interpretation subsection to separate that topic from general discussion of the claims.  Add Discriminatory text example.  Add Section 3 activity requirement subsections with examples for Site Conformance, Staff Qualification, Product Validation, Protocol Design (some of these are to disentangle activities that happen at different times, i.e. product validation, protocol design and patient image acquisition, that were previously entangled  Add Conformance section 5.  Add Checklist appendix with requirements regrouped by actor. |
| 2022.07.05 | Profile Streamlining Initiative:  Language was simplified and streamlined, particularly in the Executive Summary, Clinical Context, Claims, and Disclaimers. Fits on 2 pages.  Checklists were moved forward for easy access to primary users of the profile.  Activity sections (with discussion) were moved to appendix.  Biomarker usage discussion was moved to appendix.  Assessment procedures adopted numbered steps. |