Technical Performance Assessment of Quantitative Imaging in Device Premarket Submissions

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

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U.S. Department of Health and Human Services
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Preface

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Draft Guidance for Industry and Food and Drug Administration Staff

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I. Introduction

When finalized, this draft guidance document will provide detailed recommendations for manufacturers about the information that should be included in premarket submissions (i.e., premarket approval (PMA) applications, humanitarian device exemption (HDE) applications, premarket notification (510(k)) submissions, investigational device exemption (IDE) applications and De Novo requests) for devices that include quantitative imaging functions. In general, manufacturers preparing premarket submissions for devices that include quantitative imaging functions should provide performance specifications for the quantitative imaging functions, supporting performance data to demonstrate that the quantitative imaging functions meet those performance specifications, and sufficient information for the end user to obtain, understand and interpret the values provided by the quantitative imaging functions.

FDA's guidance documents, including this draft guidance, do not establish legally enforceable responsibilities. Instead, guidance documents describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word “should” in Agency guidance documents means that something is suggested or recommended, but not required.

II. Background

Medical imaging is used routinely in hospitals and clinics to assist with the diagnosis and management of patients with a variety of diseases and conditions. Medical images provide visual

representations of the internal structures of the body that may assist medical professionals in making diagnostic and treatment decisions.

Most medical images are acquired with the intention of qualitative interpretation by a trained physician to identify the presence or absence of a structure or feature. For example, a radiologist may read an x-ray to identify or rule out a fracture or a head CT to look for hemorrhage.

Quantitative imaging extracts additional information from medical images in the form of numerical values. Examples of quantitative imaging values include standard uptake values (SUVs) in nuclear medicine, volumetry measurements in tomographic imaging (magnetic resonance (MR) and computed tomography (CT)), and relaxometry (T1 or T2 values) in MR. Quantitative imaging values are usually subject to both systematic error and random variation. Thus, a quantitative imaging value can often differ from the true value of the measurand (the quantity being estimated). Systematic errors and random variation in quantitative imaging impact the reported outputs and may affect clinical decision making.

The utility of any quantitative imaging value is greatest if the performance of the quantitative imaging function is well characterized and users have sufficient information to understand and interpret the quantitative values being reported. Quantitative imaging functions have a broad range of intended uses, making it difficult to define universal criteria for achieving a "well-characterized" quantitative imaging function and "sufficient user information," but we believe a general approach for developing appropriate technical performance information can be defined.

III. Scope

This guidance document is applicable to all devices that generate quantitative imaging values across a wide range of imaging modalities, intended uses, levels of automation, and complexity of algorithms. This guidance document provides FDA's recommendations on the information, technical performance assessment, and user information that should be included in a premarket submission for devices that include quantitative imaging functions.

The rigor of the technical performance assessment and the breadth/specificity of the information provided to the user in the labeling should ensure that the intended use of the device is adequately supported and consider the benefit-risk profile of the information provided by the quantitative imaging function. Depending on the intended use of a device, assessment of technical performance alone may not be sufficient and clinical validation may be necessary. This document is not intended to provide comprehensive guidance on the types of scientific evidence needed to assess the technical performance for specific intended uses of the device, or the benefit-risk assessment conducted as part of the review of the premarket submission.[1]

[1] For more information on benefit-risk determinations, please see the following guidance documents: "Benefit-Risk Factors to Consider When Determining Substantial Equivalence in Premarket Notifications (510(k)) with Different Technological Characteristics," available at https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM404773.pdf; "Factors to Consider When Making Benefit-Risk Determinations for Medical Device Investigational Device Exemptions," available at

The clinical validation of any quantitative imaging values is also outside the scope of this guidance document. For example, a function that reports a percent stenosis value from the ratio of two vessel diameters would be considered a quantitative imaging function and the technical performance assessment of that quantitative imaging function would be within the scope of this document. However, linking the probability of a cardiac event to the percentage of vessel stenosis would be outside the scope of this guidance document.

IV. Definitions

To ensure consistency throughout this document and in premarket submissions of devices that include quantitative imaging functions, FDA encourages use of the following terminology when describing quantitative imaging functions. The terminology below is derived from Radiological Society of North America's (RSNA) Quantitative Imaging Biomarker Alliance (QIBA),[2,3,4] the BEST (Biomarkers, EndpointS and other Tools) glossary,[5,6] the International Vocabulary of Metrology,[7] and the IMDRF (International Medical Device Regulators Forum) "Software as a Medical Device (SaMD): Clinical Evaluation Guidance" document.[8]

Technical Performance Assessment: Establishing that the technical performance of a quantitative imaging function is acceptable in terms of performance characteristics relevant to the intrinsic properties of the imaging media used by the device. The technical performance assessment of a quantitative imaging device is based on a specified technical protocol, which may include media collection and processing. The concept of analytical validation (that is, accuracy, reliability, and precision) as described in the document entitled "Software as a Medical Device (SaMD): Clinical Evaluation Guidance"[9] can be used in the technical performance assessment of an imaging device.

Bias: The systematic difference between a quantitative imaging value made on the same object and its true value. If the true value is unknown, then bias cannot be evaluated. However, systematic difference between a quantitative imaging value and an accepted value of the measurand (see reference value) may be evaluated. **Percent bias:** Bias divided by the true value in percent.

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https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM451440.pdf; and "Factors to Consider Regarding Benefit-Risk in Medical Device Product Availability, Compliance, and Enforcement Decisions," available at https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm506679.pdf.

[2] Kessler, L.G., et al., "The emerging science of quantitative imaging biomarkers terminology and definitions for scientific studies and regulatory submissions," Stat Meth Med Res 24(1) 9-26 (2015).

[3] Sullivan, D.C., et al., "Metrology standards for quantitative imaging biomarkers," Radiology 277(3) 813-825 (2015).

[4] Joint Committee for Guides in Metrology, "International vocabulary of metrology – Basic and general concepts and associated terms (IVM)," JCGM 200:2012 (2012).

[5] Kessler, L.G., et al. (2015).

[6] BEST (Biomarkers, EndpointS, and other Tools Resource), available at https://www.ncbi.nlm.nih.gov/books/NBK326791/.

[7] International Vocabulary of Metrology – Basic and General Concepts and Associated Terms (VIM 3rd edition) JCGM 200, available at https://www.bipm.org/en/publications/guides/vim.html 2012.

[8] Available at http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-170921-samd-n41-clinical-evaluation_1.pdf.

[9] *Ibid.*

Characterization: Description and documentation of the performance of the quantitative imaging function. That is, what values does the function consistently produce under defined conditions?

Clinical Validation: The assessment and analysis of clinical data pertaining to a medical device to verify the clinical safety, performance, and effectiveness of the device when used as intended by the manufacturer. [Note: Clinical validation is outside the scope of this guidance document. See Software as a Medical Device (SaMD): Clinical Evaluation Guidance[10] document for FDA's current thinking on clinical validation.]

Limits of quantitation: The lower and upper values of the measurand that can be reliably detected under specified experimental conditions and quantitatively determined with stated precision and stated bias.

Linearity: The ability to provide measured quantity values that are directly proportional to the value of the measurand.

Measurand: The quantity intended to be measured.

Measurement: The process of experimentally obtaining one or more quantity values that can reasonably be attributed to a quantity.

Precision: The closeness of agreement between measured quantity values obtained by replicate measurements under specified conditions.

Quantitative Imaging: Measurement of quantities from medical images.

Quantitative Imaging Function: A medical device, or a component or part of a medical device, that produces quantitative imaging values.

Quantitative Imaging Value: An objective, physical characteristic derived from a medical image measured on a ratio or interval scale. Types of quantitative imaging values include:

Ratio variable: A variable such that the difference between any two values is meaningful and any two values have a meaningful ratio, making the operations of multiplication and division meaningful. A ratio variable possesses a meaningful (unique and non-arbitrary) zero value (e.g., tumor volume).
Interval variable: A variable for which the difference between two values is meaningful, but the ratio of two values is not (e.g., CT Hounsfield units).

Ordinal and nominal variables are not considered quantitative imaging values:

Ordinal variable: A magnitude is assigned and ordering of values has meaning, but differences and ratios of values have no meaning (e.g., BIRADS score).

[10] Available at http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-170921-samd-n41-clinical-evaluation_1.pdf.

Nominal variable: Numbers arbitrarily assigned to categories. Neither ordering nor arithmetic operations on the numbers have real meaning (e.g., a classifier).

Quantity: A property that has a magnitude which can be expressed as a number and a reference. The reference can be a measurement unit, a measurement procedure, a reference material, or a combination.

Reference material: Material with known properties that can be used as a reference to confirm measurement of specific properties.

Reference phantom: A specially designed physical object that is scanned or imaged to evaluate, analyze, or otherwise assess the performance of imaging devices. Reference phantoms typically contain reference materials.

Reference value: The true **or** accepted value of the measurand. A reference value can be a theoretical or established value based on scientific principles, an assigned value based on experimental work of some national or international organization, or a consensus value based on collaborative experimental work.

Repeatability: Measurement precision under the same set of conditions over a short period of time.

Reproducibility: Measurement precision under different conditions.

Sensitivity Analysis: A systematic analysis of how independent variable(s) impact a dependent variable under a given set of conditions/assumptions.

Uncertainty: A nonnegative parameter characterizing the dispersion of the quantity values being attributed to a measurand.

Verification: Evidence that defined acceptance criteria have been met.

V. Potential Sources of Measurement Error

Quantitative imaging values derived from medical images may be affected by multiple sources of error. Quantitative imaging values are usually subject to both systematic error and random variation. Thus, a quantitative imaging value can, and usually does, differ from the true value of the measurand. Errors may come from the acquisition of the medical images, patient characteristics, and the image processing algorithm. An understanding of the sources of error, especially those with the largest impact on the measurand and the quantitative imaging values produced by your quantitative imaging function is important for characterizing the performance of your quantitative imaging function. A sensitivity analysis is one technique that may be used to determine the magnitude of impact on the output of any particular source of variability.

Some typical sources of error in quantitative imaging values include:

- Patient Characteristics

- Demographic (e.g., patient age, gender, race, etc.)
- Physiological (e.g., weight, heart rate, body temperature, etc.)
- Temporal variability in the measurand (e.g., lesion shape, size, location, blood oxygenation, etc.)
- Spatial heterogeneity of tissue (melanin content)
- Spatial and temporal variability in surrounding tissue (e.g., respiratory motion, breast density, calcification adjacent to lesion, etc.)
- Disease state, comorbidities, or exogenous material present (related or unrelated to quantitative imaging function, e.g., implanted devices present on MRI or tattoos in optical imaging)

- Image acquisition
  - Patient positioning and preparation during image acquisition
  - Imaging hardware (manufacturer, model, software version) of the imaging device
  - Image acquisition protocol (e.g., MR sequence and timings, x-ray dose, amount and type of contrast media used, cardiac or respiratory gating, etc.)
  - Image data noise
  - Presence of image artifacts
  - User interaction in image data acquisition (e.g., transducer position during ultrasound)
  - Image reconstruction algorithm
  - Imaging device motion/vibration

- Image Processing
  - Algorithm specifics (e.g., filtering, software version, database selection)
  - User interaction (e.g., manual segmentation, seed point selection)
  - Non-deterministic algorithm (e.g., curve fitting for dynamic contrast enhanced MRI exams)

VI. Information to Include in a Premarket Submission

FDA recommends that the premarket submission for your device that incorporates quantitative imaging function(s) include the information described below.

A. Function Description

Your premarket submission should include a technical description of the quantitative imaging function(s) included in your device at a level of detail sufficient for the Agency to understand the functionality. In some instances, a more general description of the measurement process may be sufficient; however, you should provide a more detailed description of the processes for more complex quantitative imaging functions, to ensure FDA's understanding of your device. FDA recommends including the following information when describing your quantitative imaging function(s):

- A description of the quantitative imaging function, such as:

- Description of the measurand;
- Name, version, and relevant characteristics of the software platform;
- A detailed description of the algorithm employed, including algorithm inputs and outputs;
- For algorithms derived from physical processes (e.g., fluence correction, tomographic image reconstruction), the assumed underlying physics and its relationship to the mathematical components of the algorithm;
- Level of automation (e.g., manual, automatic, or semi-automatic); and
- If applicable, a brief summary of your algorithm training paradigm (e.g., how algorithm parameters and thresholds were established).

- Information about input images:

  - Target population, including patient population, organs of interest, and diseases/conditions/abnormalities of interest;
  - Restrictions on input images, such as imaging modalities, as applicable, (e.g., computed tomography, magnetic resonance), make, model, and specific trade name for each modality/system, specific image acquisition parameter ranges (e.g., kVp range, slice thickness) or specific imaging protocol(s) (e.g., oral contrast studies, magnetic resonance angiography (MRA) sequence); or
  - Specific limitations including diseases/conditions/abnormalities or imaging conditions for which your quantitative imaging function has been found ineffective and should not be used, as applicable.

- Image acceptance activities (e.g., how your device ensures that input images/preprocessing are acceptable for processing with your algorithm) and whether these are performed manually by a trained user or automatically by your algorithm;

- Information presented to the user (including units); and

- The level of user interaction needed for your device to be used as intended, and if applicable, instructions for users (preprocessing image steps, selecting seed points, applying algorithm, and verifying resulting measurement for a lesion sizing tool).

B. Technical Performance Assessment

Your premarket submission should include performance specifications for your quantitative imaging function(s). In general, quantitative imaging functions should have quantitative performance specifications that correspond to the claims and uncertainty associated with the quantitative imaging function described in the device labeling. The appropriate performance specifications will depend on the intended use of the quantitative imaging function, the complexity of the measurement algorithm, and the availability of reference values. Additionally, performance specifications may change throughout the operating range of the quantitative imaging function. For example, the reproducibility of a volumetric measurement tool may depend on the size of the structure being measured, or the error associated with T1 values from magnetic resonance imaging may depend on the inversion time.

Supporting performance data should demonstrate that your quantitative imaging function meets the predefined performance specifications. The assessment should consider the factors that can impact the performance of your quantitative imaging function (see the Potential Sources of Measurement Error in Section V of this guidance). We recommend that you use performance specifications that incorporate objective reference values, if available, as this enables objective comparison between the subject and predicate device performance. For example, a quantitative lesion size measurement for magnetic resonance images may set a performance specification of bias less than 10% over the range of 3 – 20 mm lesions and compare measured lesion sizes to reference values from widely accepted phantoms.

Best practices for the technical performance assessment of a quantitative imaging function of your device include the following steps:

1. Define the quantitative imaging function, its relationship to the measurand, and the use conditions. For example, if the input to your algorithm is required to have a pixel size of < 1 mm, you would not be expected to evaluate the performance of your algorithm for pixels > 1 mm.

2. Determine the performance metrics applicable to your device. Bias, precision, limits of detection, limits of quantitation, linearity, sensitivity, and uncertainty should generally be considered as applicable.

3. Characterize the performance of the quantitative imaging function under the conditions defined in the device labeling.

4. Define the experimental unit (e.g., per lesion or per patient).

5. Define the appropriate statistical estimates of performance (e.g., limits of agreement vs. total deviation index).

6. Define acceptance criteria (performance targets or goals) based on clinical utility and other restrictions/limitations (such as minimum image quality requirements).

7. Specify the elements of the statistical design, the data requirements (e.g., patient population, type of images), and the statistical analysis plan.

8. Collect the relevant data.

9. Perform the statistical analysis.

10. Compare the analysis results to the pre-defined acceptance criteria.

Uncertainty (see Definition section above) should be included in the performance specifications for all quantitative imaging functions. The most appropriate uncertainty metric will depend on your quantitative imaging function. Uncertainty information should cover the entire operating range of your quantitative imaging function, as the uncertainty associated with a measurand may change

throughout the operating range. Uncertainty information should be presented in units of the measurand whenever possible.

Any claims regarding the performance of the quantitative imaging function should be supported by studies with pre-defined acceptance criteria.

In general, FDA believes that quantitative imaging functions that generate outputs without the opportunity for user correction (i.e., fully automated devices) should include more robust analytical validation and more information describing the uncertainty associated with the output than manual quantitative imaging functions or quantitative imaging functions for which users review and correct outputs (i.e., semi-automated devices). For fully automated functions, it is also generally appropriate to help users understand the situations under which the quantitative imaging function will generate an output that is incorrect, but where the error may not be easily identifiable. Automated devices that make claims of improved accuracy and reproducibility compared to manual methods should be supported by studies comparing quantitative imaging values produced by the device to those of expert users.

C. Labeling (User Instructions)

Your premarket submission must include labeling in sufficient detail to satisfy any applicable requirements for your type of premarket submission (e.g., 21 CFR 807.87(e) or 21 CFR 814.20(b)(10)). In addition, device labeling must satisfy all applicable FDA labeling requirements, including, but not limited to, 21 CFR part 801. Your device labeling should include sufficient information for the end user to obtain, understand, and interpret the values provided by the quantitative imaging function. Generally, this information should include:

a) A description of the measurand.

b) A description of the algorithm inputs, including any restrictions on input images.

c) Performance specifications, including uncertainty information, that cover the entire operating range of the quantitative imaging function. The performance specification or claims in the labeling should correspond to device design requirements or specifications.

   Uncertainty information should facilitate interpretation of results and should be provided in units of the measurand whenever possible. On-screen display of uncertainty information is preferred whenever possible.

   Quantitative imaging functions that are not able to provide specific performance metrics for uncertainty should include information on the primary sources of variability affecting the quantitative imaging output (e.g., pixel size, image signal-to-noise-ratio (SNR), patient anatomy).

d) Instructions for image acceptance or quality assurance activities to be performed by the user. If the performance of the quantitative imaging function is dependent on quality assurance by the user (e.g., ensuring that SNR is acceptable, slice thickness is within a given range, or that

the image is free of artifacts), the device labeling should include quality assurance protocols (e.g., what characteristics to test for, how to execute test methods and calculate metrics), as well as clear instructions on actions to be taken when quality assurance fails. A detailed description of all necessary phantoms and/or instructions on how to obtain phantoms should be included.

e) Quantitative imaging functions that provide a comparison to a reference database should include information about the composition of the reference database. If the database is well known and publicly available, we recommend you include a reference or a hyperlink to the publicly available reference in your labeling. For in-house developed reference databases, information on patient composition (e.g., number of patients, patient demographics, disease conditions, etc.) should be provided.

Examples

The purpose of these examples is to illustrate the range of possibilities that exist for a single type of quantitative imaging function, in this case a vessel stenosis measurement tool. The examples are not intended to describe any particular device, but rather, to illustrate how the validation and labeling for a quantitative imaging function can vary based on the design and outputs of the quantitative imaging function. As stated previously, the appropriate validation and labeling for any particular device will depend on the device's intended use, the device functionality, and the performance claims.

Example 1 - Manual Quantitative Imaging Function

Guiding Principles: Making a quantitative measurement using a fully manual function should be a transparent process. Manual quantitative imaging functions are often used for a variety of clinical tasks, and users should have sufficient information to determine whether the performance of the quantitative imaging function will meet their clinical needs. A simple, fully-manual quantitative imaging function may not have been clinically validated for any specific task, and this should also be made clear to the end user. Alternately, if performance criteria were pre-specified and validated, this important information should also be clearly communicated to the end user.

Function Description

The device description should clearly describe the functionality of the quantitative imaging function, including inputs, outputs, limitations on patient population, or input images (e.g., imaging modalities and acquisition techniques). Any algorithms implemented by the quantitative imaging function should be clearly specified.

Technical Performance Assessment

The premarket submission should include documentation of software verification activities demonstrating that the algorithm underlying the quantitative imaging function has been correctly implemented. This should include confirmation that measurement and user interface functions in the software have been implemented correctly. Software verification could be achieved using a software phantom with simple geometric features and test objects spanning the range of relevant clinical scenarios whenever possible.

It may not be possible to generate pre-specified clinical performance criteria for a quantitative imaging function that relies heavily on user input. However, depending on your device's intended use, it may be appropriate to characterize the performance of the quantitative imaging function as part of your validation for a range of different users expected in clinical use. A quantitative imaging function of this type may or may not include performance claims: any performance claims should be adequately supported.

Labeling (User Instructions)

The labeling should clearly describe the functionality of the quantitative imaging function by addressing labeling elements VI.C.a – VI.C.e, discussed above, including specifying how the quantitative imaging function calculates output values, and providing the geometric formulas employed to generate those results.

If pre-specified performance criteria were defined, those performance specifications should be clearly communicated to the user. If performance specifications are unavailable, the user should be clearly notified that the performance of the quantitative imaging function under any specific clinical use scenario is unknown. It may be appropriate to identify the sources of variability that most impact the output value.

Any limitations on input images (e.g., imaging modalities and acquisition techniques) should be clearly specified, including delineation of which quality control activities the user is expected to perform versus the activities performed automatically by the quantitative imaging function.

Example 2 – Semi-automated Quantitative Imaging Function

Guiding Principles: Making a measurement using a semi-automated quantitative imaging function may involve some "black box" steps that are not transparent even to an expert user. Risks of gross errors due to the performance of the quantitative imaging function are still reasonably mitigated by the expertise of the user, since users are generally expected to inspect and concur with generated results. Modest errors or small biases in function, however, may not be readily detected, making a more thorough evaluation of the performance of the quantitative imaging function advisable compared with a manual measurement tool.

Function Description

The device description should clearly describe the functionality of the quantitative imaging function, including inputs, outputs, limitations on patient population, or input images (e.g., imaging modalities and acquisition techniques), and operations expected to be performed by the user versus functions implemented by the quantitative imaging function. Any algorithms implemented by the quantitative imaging function should be clearly specified.

Technical Performance Assessment

In addition to the verification and validation activities outlined above for the fully-manual quantitative imaging function, supporting performance data for a semi-automated quantitative imaging function should verify that the performance specifications for the quantitative imaging function have been met when the measurement tool is used as intended. This assessment may be performed on phantom data, clinical images, or both; however, it may be difficult to characterize accuracy based only on measurements of clinical images. The following points should be considered when choosing the test method:

- If relying only on phantom data to validate the tool, you should include a rationale as to why the semi-automated tool is expected to perform similar to or consistent with a manual tool on clinical images; and

- Testing should evaluate the quantitative imaging values produced when the tool is used as intended, including any editing steps; however, the testing should also capture performance of the automated steps sufficient to demonstrate the automation performs as intended.

Any claims that the quantitative imaging function improves accuracy and reproducibility over manual methods should be adequately supported with studies involving multiple clinicians and a range of clinical use scenarios. It is important to keep in mind that improvements in reproducibility may not reflect improvements in accuracy and vice versa.

Labeling (User Instructions)

The labeling should clearly describe the functionality of the quantitative imaging function by addressing labeling elements VI.C.a – VI.C.e, discussed above, including tasks performed by the quantitative imaging function versus tasks that are the responsibility of the end user. The user instructions should summarize the testing that was performed to demonstrate that the quantitative imaging function met its pre-specified performance criteria. Known and potential sources of substantial measurement error should be listed, and their potential impact discussed. If applicable, common failure modes, known and potential sources of substantial error, and known limitations of the quantitative imaging function should be communicated to the user. Any performance claims made in the labeling should be consistent with the device specifications and adequately supported by performance data.

Example 3 – Fully Automated Quantitative Imaging Function

Guiding Principles: A fully automated quantitative imaging function may bypass important evaluation steps that would normally be performed by an expert user. A fully automated quantitative imaging function may not have the same opportunities for clinicians to identify and mitigate risks due to gross errors associated with imaging issues or major performance failures of the quantitative imaging function. Therefore, in addition to characterizing performance, the performance testing should demonstrate that the likelihood of unintended performance has been adequately validated across the variety of expected use cases.

Function Description

The device description should clearly describe the functionality of the quantitative imaging function, including inputs, outputs, limitations on patient population, or input images (e.g., imaging modalities and acquisition techniques). Any algorithms implemented by the quantitative imaging function should be clearly specified.

Technical Performance Assessment

A fully automated quantitative imaging function should have pre-specified performance criteria and be tested on clinical data that represent the variety of expected uses cases, including cases that are expected to challenge the algorithm. Depending on intended use, these use cases may need to include a variety of imaging modalities (and manufacturers, models, etc., depending on the device indications for use), a range of clinically relevant settings, and an appropriately diverse patient data set. For a fully automated quantitative imaging function, phantom data may be useful but likely cannot completely replace the need for clinical data because phantoms may be an incomplete representation of clinical data.

Labeling (User Instructions)

The labeling should clearly describe the functionality of the quantitative imaging function by addressing labeling elements VI.C.a – VI.C.e, discussed above. The user instructions should clearly summarize the pre-specified performance specifications for the quantitative imaging function and summarize the testing that was conducted to verify that the quantitative imaging function met these performance specifications. Known and potential sources of substantial measurement error should be listed, and their potential impact discussed. Common failure modes, known and potential sources of substantial error, and known limitations of the quantitative imaging function should be communicated to the user. Any performance claims made in the labeling should be consistent with the device specifications and adequately supported.