Leica Biosystems Imaging, Inc.
Tamatha Melton
Senior Principal Regulatory Affairs
1360 Park Center Dr.
Vista, CA 92081

August 7, 2026

Re: K253561
Trade/Device Name: Aperio iQC DX Software
Regulation Number: 21 CFR 864.3700
Regulation Name: Whole slide imaging system
Regulatory Class: Class II
Product Code: SIX
Dated: November 14, 2025
Received: November 17, 2025

Dear Tamatha Melton:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

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

Your device is also subject to, among other requirements, the Quality Management System Regulation (QMSR) (21 CFR Part 820), which includes, but is not limited to, ISO 13485 clause 7.3 (Design controls), ISO 13484 clause 8.3 (Nonconforming product), and ISO 13485 clause 8.5 (Corrective and preventative action). Please note that regardless of whether a change requires premarket review, the QMSR requires device manufacturers to review and approve changes to device design and production (ISO 13485 clause 7.3 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the Quality Management System Regulation (QMSR) (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

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

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

SHYAM KALAVAR -S

Shyam Kalavar
Deputy Branch Chief
Division of Molecular Genetics and Pathology
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

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

510(k) Number *(if known)*
K253561

Device Name
Aperio iQC DX Software

Indications for Use *(Describe)*

Aperio iQC DX Software is an artificial intelligence-based software intended to be used as an aid in the identification of artifacts in scanned whole slide images (WSIs) of hematoxylin and eosin (H&E) and immunohistochemistry (IHC) stained, formalin-fixed paraffin embedded (FFPE) tissue that should undergo further evaluation for image quality prior to diagnostic review of the images by pathologists. Aperio iQC DX Software identifies the following artifacts:

- Digital artifacts: out of focus, image striping, missing and clipped tissue
- Slide preparation artifact: air bubbles
- Other artifact: pen marks

Aperio iQC DX Software outputs the following:

- Binary 'artifact detected' or 'no artifact detected' for air bubbles, image striping, missing and clipped tissue, out of focus, and pen marks,
- Overlays highlighting the location of air bubbles and out of focus artifacts only, and
- Bounding boxes for missing and clipped tissue artifacts.

Aperio iQC DX Software is intended to be used in conjunction with the complete in-house laboratory image quality control workflow. It is the responsibility of a qualified pathologist to employ appropriate procedures and safeguards to assure the validity of the interpretation of images when using the Aperio iQC DX Software. Aperio iQC DX Software is not intended to be used for diagnosis, prognosis, or prediction of disease.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

510(k) Summary

Aperio iQC DX Software

Preparation date:
08/06/2026

Submitter:
Leica Biosystems Imaging, Inc.

Contact Person:
Tamatha Melton
Leica Biosystems Imaging, Inc.
1360 Park Center Drive
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Device Information:
Trade or Proprietary Name: Aperio iQC DX Software
Software Version: 1.0
Device Classification: Class II
Product Code: SIX
Classification Regulation: 21 CFR 864.3700
Classification Name: Whole Slide Imaging System
Classification Panel: Pathology
510(k) Premarket Notification Number: K253561

Predicate Device:
Device Trade Name: Aperio GT 450 DX System
Device Classification: Class II
Product Code: PSY
Classification Regulation: 21 CFR 864.3700
Classification Name: Whole Slide Imaging System
Classification Panel: Pathology
Premarket Notification Number: K253554

I. Intended Use/Indications for Use

Aperio iQC DX Software is an artificial intelligence-based software intended to be used as an aid in the identification of artifacts in scanned whole slide images (WSIs) of hematoxylin and eosin (H&E) and immunohistochemistry (IHC) stained, formalin-fixed paraffin embedded (FFPE) tissue that should undergo further evaluation for image quality prior to diagnostic review of the images by pathologists. Aperio iQC DX Software identifies the following artifacts:

- Digital artifacts: out of focus, image striping, missing and clipped tissue
- Slide preparation artifact: air bubbles
- Other artifact: pen marks

Aperio iQC DX Software outputs the following:

- Binary ‘artifact detected’ or ‘no artifact detected’ for air bubbles, image striping, missing and clipped tissue, out of focus, and pen marks,

- Overlays highlighting the location of air bubbles and out of focus artifacts only, and
- Bounding boxes for missing and clipped tissue artifacts.

Aperio iQC DX Software is intended to be used in conjunction with the complete in-house laboratory image quality control workflow. It is the responsibility of a qualified pathologist to employ appropriate procedures and safeguards to assure the validity of the interpretation of images when using the Aperio iQC DX Software. Aperio iQC DX Software is not intended to be used for diagnosis, prognosis, or prediction of disease.

II. Device Description

Aperio iQC DX Software, version 1.0, utilizes scanned whole slide images (WSIs) as inputs from Aperio GT 450 DX and GT 180 DX scanners to identify the following digital artifacts (missing and clipped tissue, out of focus, image striping); slide preparation artifacts (air bubbles), and other artifacts (pen marks) on WSIs to augment the initial quality review performed by laboratory personnel prior to making the WSI available to the pathologist for diagnostic review. The final determination of whether the WSIs are sufficient for diagnostic review remains the responsibility of the pathologist and occurs outside of Aperio iQC DX Software.

For each WSI, Aperio iQC DX automatically analyzes the image using four (4) Artificial Intelligence (AI) models derived from deep learning convolutional neural networks. These AI models have been developed and trained on WSIs of H&E and DAB (3,3′-diaminobenzidine) chromogen based IHC stained tissue slides originating from formalin-fixed paraffin-embedded (FFPE) tissue sections.

Aperio iQC DX Software outputs the following:

- Binary ‘artifact detected’ or ‘no artifact detected’ for air bubbles, image striping, missing and clipped tissue, out of focus, and pen marks,
- Overlays highlighting the location of air bubbles and out of focus artifacts only, and
- Bounding boxes for missing and clipped tissue artifacts.

These outputs are displayed to the user in the Aperio iQC DX Dashboard (a browser-based user interface).

Aperio iQC DX Software requires the use of Aperio GT platform system components identified in **Table 1**.

Table 1: Intended Use Components

Component
Aperio GT 450 DX Scanner and/or Aperio GT 180 DX Scanner
Aperio SAM DX Software

Computer Environment/System Requirements for the Aperio iQC DX Software device are identified in **Table 2** below.

Table 2: Customer Environment/System Requirements

Workstation Component	**Specification**
Computer System	RAM: 64 GB per scanner CPU: Intel Core i7 or higher, or AMD EPYC 9004 and 8004Series
Web Browser	Google Chrome: 126 or later Microsoft Edge: 126 or later Firefox: 127 or later
Operating System	Linux Ubuntu 24.04 LTS or higher
Network	Internet access At least 100 Mbps upload speed

Aperio iQC DX Software is operated as follows:

1. Copies of WSIs are sent to the customers dedicated image storage by the connected WSI system.
2. Once available, Aperio iQC DX Software automatically executes AI algorithms on the copies of the WSIs from the customer's dedicated image storage.
3. For WSI, Aperio iQC DX Software outputs 'artifact detected' or 'no artifact detected' for each artifact. In addition, whenever out of focus or air bubble artifacts are detected, overlays indicating the presence of the artifact are available. For missing and clipped tissue, a bounding box is provided.
4. All findings are displayed to the user in the Aperio iQC DX Dashboard where the user will perform image quality review and 'accept' or 'reject' the image and include comments for any rejection.

Algorithm development: Aperio iQC DX Software development was performed on training, tuning, and test datasets. Each dataset contained slides from unique patients ensuring that training, tuning and test datasets do not have any WSIs in common. WSIs were labeled as artifact present or 'none'. These datasets were completely independent from the validation dataset.

Table 3: Data Split for Training, Tuning and Test Sets

Algorithm Development		
Training Dataset	**Tuning Dataset**	**Test Dataset**
De-identified slides were procured from external vendors or prepared at an internal site and scanned with Aperio GT 450 scanners. Number of slide images: 12, 278 (5158 H&E WSIs, 7127 IHC WSIs)	De-identified slides were procured from external vendors or prepared at an internal site and scanned with Aperio GT 450 scanners. Number of slide images: 2,450 (1455 H&E WSIs, 995 IHC WSIs)	De-identified slides were procured from external vendors or prepared at an internal site and scanned with Aperio GT 450 scanners. Number of slide images: 4,752 (1828 H&E WSIs, 2924 IHC WSIs)

Demographics and geographic considerations were not observed as the regional variation in tissue morphology was not expected to influence artifact presence or detection.

III. Comparison with Predicate

Similarities and differences between Aperio iQC DX Software and the predicate device Aperio GT 450 DX are summarized in the table below.

Technological Characteristics	**Aperio iQC DX Software (K253561) Subject Device**	**Aperio GT 450 DX (K253554) Predicate Device**
Indications for Use	Aperio iQC DX Software is an artificial intelligence-based software intended to be used as an aid in the identification of artifacts in scanned whole slide images (WSIs) of hematoxylin and eosin (H&E) and immunohistochemistry (IHC) stained, formalin-fixed paraffin embedded (FFPE) tissue that should undergo further evaluation for image quality prior to diagnostic review of the images by pathologists. Aperio iQC DX Software identifies the following artifacts: • Digital artifacts: out of focus, image striping, missing clipped tissue • Slide preparation artifact: air bubbles • Other artifact: pen marks	The Aperio GT 450 DX is an automated digital slide creation and viewing system. The Aperio GT 450 DX is intended for in vitro diagnostic use as an aid to the pathologist to review and interpret digital images of surgical pathology slides prepared from formalin-fixed paraffin embedded (FFPE) tissue. The Aperio GT 450 DX is for creation and viewing of digital images of scanned glass slides that would otherwise be appropriate for manual visualization by conventional light microscopy. The Aperio GT 450 DX is not intended for use with frozen section, cytology, or non-FFPE hematopathology specimens. It is the responsibility of a qualified pathologist to employ appropriate procedures and safeguards to assure the validity of the interpretation of images obtained using the Aperio GT 450 DX.

Technological Characteristics	Aperio iQC DX Software (K253561) Subject Device	Aperio GT 450 DX (K253554) Predicate Device
	Aperio iQC DX Software outputs the following: • Binary 'artifact detected' or 'no artifact detected' for air bubbles, image striping, missing and clipped tissue, out of focus, and pen marks, • Overlays highlighting the location of air bubbles and out of focus artifacts only, and • Bounding boxes for missing and clipped tissue artifacts. Aperio iQC DX Software in conjunction with their complete in-house laboratory image quality control workflow. It is the responsibility of a qualified pathologist to employ appropriate procedures and safeguards to assure the validity of the interpretation of images when using the Aperio iQC DX Software. Aperio iQC DX Software is not intended to be used for diagnosis, prognosis, or prediction of disease.	

Technological Characteristics	Aperio iQC DX Software (K253561) Subject Device	Aperio GT 450 DX (K253554) Predicate Device
Principle of Operation	In a parallel workflow to that of the WSI system, Aperio iQC DX retrieves copies of WSIs from the user-provided image storage. Aperio iQC DX executes AI algorithms to detect digital (image striping, out of focus, missing and clipped tissue) and histological (pen marks, air bubbles) artifacts and notifies the clinical user through the Aperio iQC DX Dashboard. The clinical user can open and review the images for quality in the Aperio iQC DX Dashboard. The clinical user can then reprocess the slide or manually rescan the image using the WSI system.	The Aperio GT 450 DX is a WSI system. The technician places the slides into the Aperio GT 450 DX scanner. The Aperio GT 450 DX scanner automatically loads the slides, takes the micro images, finds the tissues, and scans the slides. The scanner also automatically performs quality control (QC) and notifies the user of any image quality issue during the image acquisition. The image data is sent to end- user-provided image storage attached to the local network. During the review, the pathologist opens WSI images acquired with the WSI scanner from the image storage, performs further QC, and reads WSI images of the slides to make a diagnosis.
Device Type	Artificial intelligence-based software application (Convolution Neural Networks)	Whole Slide Image
Specimen Type	Formalin-Fixed Paraffin-Embedded (FFPE) specimen	Same
Tissue Finding	Automatic	Same
Auto QC during scanning	No	Yes
Viewer	N/A; images are viewed within the Aperio iQC DX dashboard (not for diagnostic purposes).	Aperio WebViewer DX
Compatible Display (Monitor)	Off-the-Shelf Monitor (not for diagnostic purposes)	Aperio WebViewer DX is intended for use with specific validated monitors as described in the instructions for use for Aperio GT 450 DX and Aperio GT 180 DX.
Image Manipulation Functions	Panning/Zooming (non-continuous)	Aperio WebViewer DX permits continuous panning/zooming, ability to compare images, annotations, digital bookmarks, measurements (distance), gamma function

Technological Characteristics	Aperio iQC DX Software (K253561) Subject Device	Aperio GT 450 DX (K253554) Predicate Device
Operational Mode	Image QC; not to be used to diagnose disease	Diagnostic device
Hardware Inputs	Aperio GT 450 DX and Aperio GT 180 DX • Bounding Box • Macro image • Scan data • Scanner configurations (rack position, rescan capability, scanner identifiers) • Hash files	Tissue finder receives the following from the scanner: • Config Values • Macro Image • Dirt Image
Output	• Binary artifact detected or no artifact detected • Overlays (air bubbles, out of focus) • Bounding Box (missing and clipped tissue)	Whole Slide Image
Ground truth for model training	Positive cases: annotated/categorized WSIs containing digital and histological artifacts (naturally occurring and manufactured). Negative cases: categorized WSIs	Uses traditional image processing; no training required. (Tissue Finder)
Performance	Performance has been established utilizing ground truth as the clinical reference standard.	Performance has been established using technical, analytical and clinical studies
Image Storage	Images stored in the end-user-provided image storage on the local network.	Same

Aperio iQC DX Software has similar indications for use and intended use as the predicate. The differences in technological characteristics do not raise new questions of safety and effectiveness.

IV. Analytical Performance

Analytical Performance included: 1) algorithm accuracy, 2) algorithm localization, and 3) precision

A. Algorithm Accuracy

Evaluation Method: Algorithm accuracy for Aperio iQC DX Software was evaluated using a diverse dataset WSIs across multiple tissue types, staining methods (H&E and IHC), and the intended use scanners (Aperio GT 450 DX and GT 180 DX). Software performance for artifact detection was tested using a verification and validation dataset that was independent of the training dataset.

The study assessed the software's ability to detect and localize digital, slide preparation, and other artifacts, including missing/clipped tissue, image striping, out of focus, air bubbles, and pen marks when single and multiple artifacts were present.

The evaluation was conducted by comparing Aperio iQC DX Software's results against the ground truth annotations determined by qualified experts.

Algorithm Accuracy Results:

Device accuracy was tested for single and multiple artifacts. For single artifacts, WSIs were created using the Aperio GT 450 DX scanner and the Aperio GT 180 DX scanner. The distribution of positive and negative H&E and IHC WSIs are represented in **Table 4** and **Table 5**.

Table 4: Dataset Distribution for Aperio GT 450 DX for singe artifact testing

	Total WSIs	H&E WSIs	IHC WSIs
Missing and Clipped Tissue	2568 (1284 positive, 1284 negative)	858 (429 positive, 429 negative)	1710 (855 positive, 855 negative)
Image Striping	2222 (1167 positive, 1055 negative)	660 (408 positive, 252 negative)	1562 (759 positive, 803 negative)
Out of Focus	924 (221 positive, 703 negative)	414 (100 positive, 314 negative)	510 (121 positive, 389 negative)
Air Bubble	2134 (883 positive, 1251 negative)	688 (255 positive, 433 negative)	1446 (628 positive, 818 negative)
Pen Mark	2478 (1376 positive, 1102 negative)	935 (530 positive, 405 negative)	1543 (846 positive, 697 negative)

Table 5: Dataset Distribution for Aperio GT 180 DX for single artifact

	Total WSIs	H&E WSIs	IHC WSIs
Missing and Clipped Tissue	576 WSIs (288 positive, 288 negative)	192 (96 positive, 96 negative)	384 (192 positive, 192 negative)
Image Striping	439 WSIs (158 positive, 281 negative)	142 (46 positive, 96 negative)	297 (112 positive, 185 negative)
Out of Focus	486 WSIs (243 positive, 243 negative)	231 (142 positive, 89 negative)	255 (101 positive, 154 negative)
Air Bubble	645 (190 positive, 455 negative)	201 (69 positive, 132 negative)	444 (121 positive, 323 negative)
Pen Mark	424 WSIs (142 positive, 282 negative)	144 (48 positive, 96 negative)	280 (94 positive, 186 negative)

Each artifact was assessed independently to demonstrate overall performance of Aperio iQC DX Software achieved sensitivity and specificity of ≥90% and ≥85% for the lower bound of corresponding 95% CI, for the analysis of the combined H&E and IHC dataset. Overall performance of Aperio iQC DX Software using WSIs scanned on Aperio GT 450 DX is provided in **Table 6**. H&E performance and IHC performance are included in **Table 7** and **Table 8** respectively. Performance of Aperio iQC DX Software using WSIs scanned on Aperio GT 180 DX is provided in **Tables 9, 10, and 11**.

Table 6: Overall performance of Aperio iQC DX Software using Aperio GT 450 DX scanner by evaluating each artifact independently

	Accuracy (%)	95% CI Accuracy (%)	Sensitivity (%)	95% CI Sensitivity (%)	Specificity (%)	95% CI Specificity (%)
Missing and Clipped Tissue	93.73	(92.73, 94.60)	94.78	(93.42, 95.87)	92.68	(91.12, 93.98)
Image Striping	99.82	(99.54, 99.93)	99.74	(99.24, 99.91)	99.91	(99.47, 99.98)
Out of Focus	97.29	(96.04, 98.16)	93.67	(89.65, 96.19)	98.44	(97.22, 99.12)
Air Bubble	95.60	(94.64, 96.39)	93.20	(91.35, 94.68)	97.28	(96.22, 98.05)
Pen Mark	99.19	(98.75, 99.47)	99.13	(98.48, 99.50)	99.27	(98.57, 99.63)

Table 7: Performance of Aperio iQC DX Software using Aperio GT 450 DX scanner and H&E-stained slides by evaluating each artifact independently

	Accuracy (%)	95% CI Accuracy (%)	Sensitivity (%)	95% CI Sensitivity (%)	Specificity (%)	95% CI Specificity (%)
Missing and Clipped Tissue	94.76	(93.05, 96.06)	95.80	(93.47, 97.33)	93.71	(91.00, 95.64)
Image Striping	100	(99.42,100.00)	100	(99.07,100.00)	100	(98.50,100.00)
Out of Focus	96.62	(94.41,97.98)	93	(86.25,96.57)	97.77	(95.47,98.92)
Air Bubble	98.40	(97.16,99.10)	99.61	(97.82,99.93)	97.69	(95.80,98.74)
Pen Mark	99.14	(98.31,99.56)	99.06	(97.82,99.60)	99.26	(97.85,99.75)

Table 8: Performance of Aperio iQC DX Software using Aperio GT 450 DX scanner and IHC-stained slides by evaluating each artifact independently

	Accuracy (%)	95% CI Accuracy (%)	Sensitivity (%)	95% CI Sensitivity (%)	Specificity (%)	95% CI Specificity (%)
Missing and Clipped Tissue	93.22	(91.93, 94.31)	94.27	(92.50, 95.64)	92.16	(90.17, 93.78)
Image Striping	99.74	(99.34,99.90)	99.60	(98.84,99.86)	99.88	(99.31,99.98)
Out of Focus	97.84	(96.18,98.79)	94.21	(88.53,97.17)	98.97	(97.38,99.60)
Air Bubble	94.26	(92.94,95.35)	90.61	(88.08,92.65)	97.07	(95.68,98.02)
Pen Mark	99.22	(98.64,99.55)	99.17	(98.30,99.60)	99.28	(98.33,99.69)

Table 9: Overall performance of Aperio iQC DX Software in Aperio GT 180 DX scanner by evaluating each artifact independently

	Accuracy (%)	95% CI Accuracy (%)	Sensitivity (%)	95% CI Sensitivity (%)	Specificity (%)	95% CI Specificity (%)
Missing and Clipped Tissue	93.40	(91.07, 95.15)	94.10	(90.75, 96.28)	92.71	(89.11, 95.18)
Image Striping	99.77	(98.72, 99.96)	99.37	(96.51, 99.89)	100	(98.65, 100)
Out of Focus	93.62	(91.09, 95.47)	92.18	(88.11, 94.94)	95.06	(91.57, 97.15)
Air Bubble	96.43	(94.70, 97.61)	93.16	(88.65, 95.96)	97.80	(97.51, 99.55)
Pen Mark	99.06	(97.60, 99.63)	99.30	(96.13, 99.88)	98.94	(96.93, 99.64)

Table 10: Performance of Aperio iQC DX Software using Aperio GT 180 DX scanner and H&E-stained slides by evaluating each artifact independently

	Accuracy (%)	95% CI Accuracy (%)	Sensitivity (%)	95% CI Sensitivity (%)	Specificity (%)	95% CI Specificity (%)
Missing and Clipped Tissue	94.27	(90.03,96.77)	95.83	(89.77,98.37)	92.71	(85.71,96.42)
Image Striping	100	(97.37,100.00)	100	(92.29,100.00)	100	(96.15,100.00)
Out of Focus	96.10	(92.76,97.93)	97.89	(93.98,99.28)	93.26	(86.07,96.87)
Air Bubble	97.51	(94.31,98.93)	95.65	(87.98,98.51)	98.48	(94.64,99.58)
Pen Mark	99.31	(96.18,99.88)	100	(92.59,100.00)	98.96	(94.34,99.82)

Table 11: Performance of Aperio iQC DX Software using Aperio GT 180 DX scanner and IHC-stained slides by evaluating each artifact independently

	Accuracy (%)	95% CI Accuracy (%)	Sensitivity (%)	95% CI Sensitivity (%)	Specificity (%)	95% CI Specificity (%)
Missing and Clipped Tissue	92.97	(89.96,95.12)	93.23	(88.76,96.00)	92.71	(88.14,95.61)
Image Striping	99.66	(98.11,99.94)	99.11	(95.12,99.84)	100	(97.97,100.00)
Out of Focus	91.37	(87.28,94.23)	84.16	(75.81,90.01)	96.10	(91.76,98.20)
Air Bubble	95.95	(93.69,97.42)	91.74	(85.46,95.45)	97.52	(95.19,98.74)
Pen Mark	98.93	(96.90,99.64)	98.94	(94.22,99.81)	98.92	(96.16,99.70)

For multiple artifacts, WSIs were created using the Aperio GT 450 DX scanner to demonstrate performance for the detection of each artifact when multiple artifacts are present. The multiple artifacts data set was positive for multiple artifacts ranging from two (2) to (5) five artifacts per WSI. To evaluate the performance of air bubbles, image striping, out of focus, and pen marks 522 WSIs positive for multiple artifacts (241 doubles, 106 triples, 175 quadruple) were used. To evaluate the performance of missing and clipped tissue: 505 WSIs positive for multiple artifacts (172 doubles, 132 triples, 138 quadruple, 63 quintuple). The data set distribution is included in **Table 12**. Overall performance of Aperio iQC DX Software in multiple artifact performance is summarized in **Table 13**. H&E Performance and IHC performance are captured in **Tables 14** and **15**.

Table 12: Dataset Distribution for Aperio GT 450 DX multiple artifact testing

	Total WSIs	H&E WSIs	IHC WSIs
Missing and Clipped Tissue	505 (305 positive, 200 negative)	225 (140 positive, 85 negative)	280 (165 positive, 115 negative)
Image Striping	522 (440 positive, 82 negative)	255 (213 positive, 42 negative)	267 (227 positive, 40 negative)
Out of Focus	522 (368 positive, 154 negative)	255 (182 positive, 73 negative)	267 (186 positive, 81 negative)
Air Bubble	522 (308 positive, 214 negative)	255 (162 positive, 93 negative)	267 (146 positive, 121 negative)
Pen Mark	522 (384 positive, 138 negative)	255 (169 positive, 86 negative)	255 (215 positive, 52 negative)

Table 13: Overall performance of Aperio iQC DX Software using Aperio GT 450 DX scanner for multiple artifacts

	Accuracy (%)	95% CI Accuracy (%)	Sensitivity (%)	95% CI Sensitivity (%)	Specificity (%)	95% CI Specificity (%)
Missing and Clipped Tissue	93.27	(90.74, 95.14)	93.11	(89.70, 95.45)	93.50	(89.20, 96.16)
Image Striping	99.43	(98.33, 99.81)	99.32	(98.02, 99.77)	100	(95.52, 100)
Out of Focus	95.79	(93.71, 97.20)	96.47	(94.05, 97.93)	94.16	(89.27, 96.90)
Air Bubble	95.40	(93.25, 96.90)	92.53	(89.04, 94.97)	99.53	(97.40, 99.92)
Pen Mark	97.70	(96.02, 98.68)	99.48	(98.12, 99.86)	92.75	(87.17, 96.01)

Table 14: Performance of Aperio iQC DX Software using Aperio GT 450 DX scanner and H&E-stained slides for evaluating multiple artifacts

	Accuracy (%)	95% CI Accuracy (%)	Sensitivity (%)	95% CI Sensitivity (%)	Specificity (%)	95% CI Specificity (%)
Missing and Clipped Tissue	94.67	(90.91, 96.92)	97.14	(92.88, 98.88)	90.59	(82.51, 95.15)
Image Striping	99.22	(97.19, 99.78)	99.06	(96.64, 99.74)	100	(91.62, 100.00)
Out of Focus	95.69	(92.44, 97.57)	95.60	(91.57, 97.76)	95.89	(88.60, 98.59)
Air Bubble	96.86	(93.93, 98.40)	95.68	(91.35, 97.89)	98.92	(94.16, 99.81)
Pen Mark	96.08	(92.93, 97.86)	100	(97.78, 100.00)	88.37	(79.90, 93.56)

Table 15: Performance of Aperio iQC DX Software using Aperio GT 450 DX scanner and IHC-stained slides for evaluating multiple artifact

	Accuracy (%)	95% CI Accuracy (%)	Sensitivity (%)	95% CI Sensitivity (%)	Specificity (%)	95% CI Specificity (%)
Missing and Clipped Tissue	92.14	(88.39, 94.75)	89.70	(84.12, 93.47)	95.65	(90.22, 98.13)
Image Striping	99.63	(97.91, 99.93)	99.56	(97.55, 99.92)	100	(91.24, 100.00)
Out of Focus	95.88	(92.77, 97.68)	97.31	(93.86, 98.85)	92.59	(84.77, 96.56)
Air Bubble	94.01	(90.49, 96.28)	89.04	(82.94, 93.14)	100	(96.92, 100.00)
Pen Mark	99.25	(97.31, 99.79)	99.07	(96.67, 99.74)	100	(93.12, 100.00)

The results of the accuracy study demonstrate that overall performance of Aperio iQC DX Software achieved sensitivity and specificity of ≥90% and ≥85% for the lower bound of corresponding 95% CI for single and multiple artifact detection, for the analysis of the combined H&E and IHC dataset.

B. Localization Accuracy

Aperio iQC DX Software generates the visualization of detected artifact regions for Missing and Clipped Tissue, Out of Focus, and Air Bubble. There are two types of visualizations: 1) overlays for out of focus and air bubbles and 2) a bounding box for missing and clipped tissue.

Evaluation Method: Localization testing was conducted to quantitatively evaluate Aperio iQC DX Software's ability to indicate the location of the artifacts on the WSI. To evaluate the performance of Missing and Clipped Tissue localization, the overlap of Aperio iQC DX Software's predicted bounding box and the ground truth bounding box was calculated using Intersection over Union (IoU) ratio to measure how accurately a model's predicted region aligns with the ground truth. IoU is calculated as follows:

$$\text{IoU} = \frac{\text{Overlapping Area of Prediction and Ground Truth}}{\text{Union Area of Prediction and Ground Truth}}$$

IoU was calculated for each WSI, then averaged across the dataset and reported.

To evaluate the performance of Out of Focus and Air Bubble localization, qualified experts annotated regions on the WSI indicating the presence or absence of specified artifacts. True positive or true negative for each specified artifact were assigned at the pixel level based on annotated regions. Localization sensitivity and specificity for each WSI were computed by comparing the algorithms predictions against the annotated ground truth. Sensitivity and specificity were calculated for each WSI, then averaged across the dataset and reported.

Localization Accuracy Results: The dataset for localization performance was comprised of: missing and clipped tissue WSIs (1988), out of focus WSIs (67), and air bubble WSIs (60).

The results of the localization accuracy study for missing and clipped tissue artifact detection demonstrate that Aperio iQC DX Software met the predetermined acceptance criteria of ≥90% of WSIs achieve IoU ≥70% **(Table 16).**

The results of the localization study for out of focus and air bubble artifact detection demonstrate that Aperio iQC DX Software met the predetermined acceptance criteria of ≥90% sensitivity and specificity **(Table 17)**.

Table 16: Localization performance of Missing and Clipped Tissue detection

	Average IoU	Number of WSIs achieve IoU ≥ 70%	Ratio of the WSIs achieve IoU ≥ 70%
Missing and Clipped Tissue	88.41%	1804	90.74%

Table 17: Localization performance of Out of Focus and Air Bubble detection

	Localization Sensitivity (%)	95% CI Sensitivity (%)	Localization Specificity (%)	95% CI Specificity (%)
Out of Focus	96.99	(95.44%, 98.02%)	99.72	(99.02%, 99.92%)
Air Bubble	91.29	(88.75%, 93.30%)	96.01	(94.12%, 97.31%)

C. Precision

The precision (repeatability and reproducibility) testing was conducted to evaluate the Aperio iQC DX Software using H&E and IHC WSIs generated from the Aperio GT 450 DX and Aperio GT 180 DX scanners.

The dataset for H&E was comprised of 63 whole slide images (WSIs) per scanner:

- 3 WSIs per artifact across five artifacts (positive cases)
- 3 WSIs containing multiple artifacts (positive cases)
- 3 WSIs that contain no artifacts (negative cases)

Each WSI was rotated in two different orientations generating three replicates per WSI.

The dataset for IHC was comprised of 63 whole slide images (WSIs) per scanner:

- 3 WSIs per artifact across five artifacts (positive cases)
- 3 WSIs containing multiple artifacts (positive cases)
- 3 WSIs that contain no artifacts (negative cases)

Each WSI was rotated in two different orientations generating three replicates per WSI.

Ground truth was established through annotations performed by a group of qualified annotators.

Evaluation Method: To assess precision under variable conditions, each WSI was subjected to two deterministic image orientations, generating three replicates per WSI, for a total of nine replicate evaluations per artifact category.

A controlled study was conducted on a single instance of Aperio iQC DX Software to assess repeatability and reproducibility of artifact detection across replicates of the whole slide image (WSI) for each scanner (Aperio GT 450 DX and Aperio GT 180 DX) and each stain type (H&E and IHC). For each replicate, the output was compared to the established ground truth, and percent agreement (% correct call) and their corresponding 95% CI were calculated for each artifact category and reported for each scanner and each stain type (**Tables 18 - 21**).

The validation data demonstrates that Aperio iQC DX Software achieves 100% for correct call for all types of cases.

Table 18: Precision performance under variable conditions for H&E WSIs using GT 450 DX

Type of Cases	Type of Artifacts	#WSIs	#Replicates /WSI	#Total Replicates	%Correct Call	95%CI (%) *
Positive Cases-Single Artifact	Missing and Clipped Tissue	3	3	9	100%	(70.1%, 100%)
	Image Striping	3	3	9	100%	(70.1%, 100%)
	Out of Focus	3	3	9	100%	(70.1%, 100%)
	Air Bubble	3	3	9	100%	(70.1%, 100%)
	Pen Mark	3	3	9	100%	(70.1%, 100%)
Positive Cases-Multiple Artifacts	Multiple Artifacts	3	3	9	100%	(70.1%, 100%)
Negative Cases	No Artifact	3	3	9	100%	(70.1%, 100%)
Overall				63	100%	(94.3%, 100%)

*95%CI was calculated by Wilson score method

Table 19: Precision performance under variable conditions for H&E WSIs using GT 180 DX

	Type of Artifacts	#WSIs	#Replicates /WSI	#Total Replicates	%Correct Call	95%CI (%) *
Positive Cases-Single Artifact	Missing and Clipped Tissue	3	3	9	100%	(70.1%, 100%)
	Image Striping	3	3	9	100%	(70.1%, 100%)
	Out of Focus	3	3	9	100%	(70.1%, 100%)
	Air Bubble	3	3	9	100%	(70.1%, 100%)
	Pen Mark	3	3	9	100%	(70.1%, 100%)
Positive Cases-Multiple Artifacts	Multiple Artifacts	3	3	9	100%	(70.1%, 100%)
Negative Cases	No Artifact	3	3	9	100%	(70.1%, 100%)
Overall				63	100%	(94.3%, 100%)

*95%CI was calculated by Wilson score method

Table 20: Precision performance under variable conditions for IHC WSIs using GT 450 DX

	Type of Artifacts	#WSIs	#Replicates /WSI	#Total Replicates	%Correct Call	95%CI (%) *
Positive Cases-Single Artifact	Missing and Clipped Tissue	3	3	9	100%	(70.1%, 100%)
	Image Striping	3	3	9	100%	(70.1%, 100%)
	Out of Focus	3	3	9	100%	(70.1%, 100%)
	Air Bubble	3	3	9	100%	(70.1%, 100%)
	Pen Mark	3	3	9	100%	(70.1%, 100%)
Positive Cases-Multiple Artifacts	Multiple Artifacts	3	3	9	100%	(70.1%, 100%)
Negative Cases	No Artifact	3	3	9	100%	(70.1%, 100%)
Overall				63	100%	(94.3%, 100%)

*95%CI was calculated by Wilson score method

Table 21: Precision performance under variable conditions for IHC WSIs using GT 180 DX

	Type of Artifacts	#WSIs	#Replicates /WSI	#Total Replicates	%Correct Call	95%CI (%) *
Positive Cases-Single Artifact	Missing and Clipped Tissue	3	3	9	100%	(70.1%, 100%)
	Image Striping	3	3	9	100%	(70.1%, 100%)
	Out of Focus	3	3	9	100%	(70.1%, 100%)
	Air Bubble	3	3	9	100%	(70.1%, 100%)
	Pen Mark	3	3	9	100%	(70.1%, 100%)
Positive Cases-Multiple Artifacts	Multiple Artifacts	3	3	9	100%	(70.1%, 100%)
Negative Cases	No Artifact	3	3	9	100%	(70.1%, 100%)
Overall				63	100%	(94.3%, 100%)

*95%CI was calculated by Wilson score method

V. Additional Non-Clinical Testing

Human Factors and Usability testing was completed, and documentation was provided in the submission as recommended in Guidance for Industry and Food and Drug Administration Staff: Applying Human Factors and Usability Engineering to Medical Devices (February 2016).

Cybersecurity testing was completed, and documentation was provided as recommended in Guidance for Industry and Food and Drug Administration Staff: Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions (June 2025).

Software verification and validation testing was completed, and documentation was provided as recommended in Guidance for Food and Drug Administration Staff: Content of Premarket Submissions for Device Software Functions (June 2023).

VI. Substantial Equivalence Determination

Aperio iQC DX Software is substantially equivalent to the predicate device.