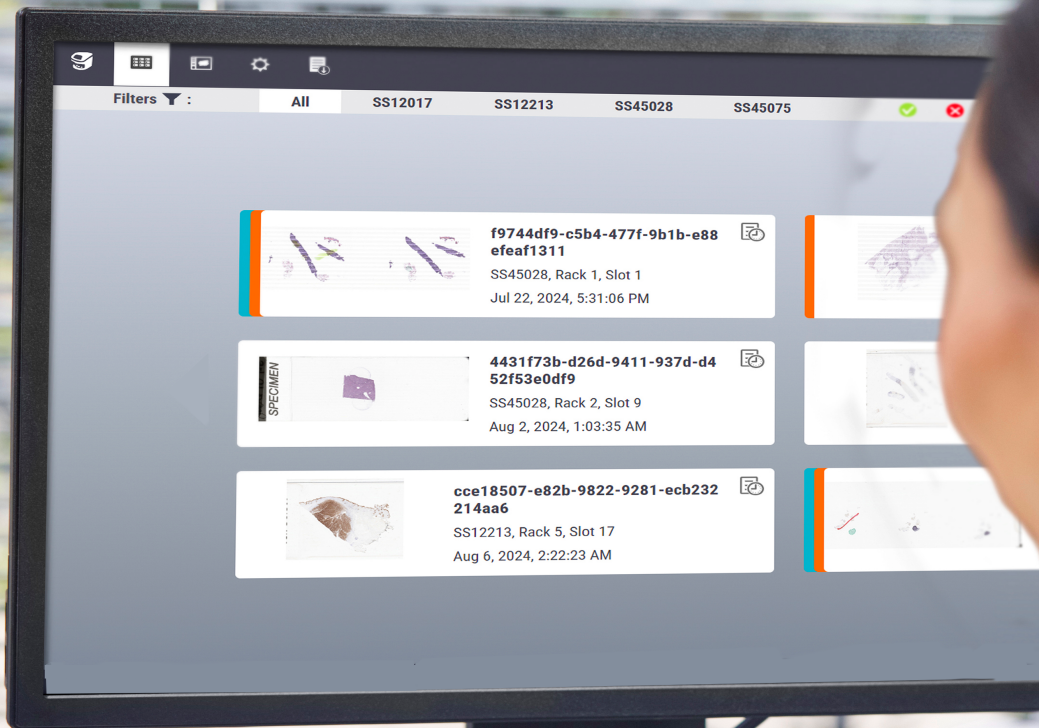


APERIO iQC™ DX

SOFTWARE

USER'S GUIDE



CE

Advancing Cancer Diagnostics
Improving Lives

Leica
BIO SYSTEMS

Aperio iQC DX Software User's Guide

MAN-0565, Revision A | November 2025

This manual applies to the Aperio iQC DX Software version 1.0 and later.

Original instructions.


Copyright notice

- Copyright © 2025 Leica Biosystems Imaging, Inc. All Rights Reserved. LEICA and the Leica logo are registered trademarks of Leica Microsystems IR GmbH. Aperio, Aperio iQC, GT, GT 180, and GT 450 are trademarks of Leica Biosystems Imaging, Inc. in the USA and optionally in other countries. Other logos, products, and/or company names might be trademarks of their respective owners.
- This product is protected by registered patents. For a list of patents, contact Leica Biosystems.




Customer resources

- For the latest information on Leica Biosystems Aperio products and services, please visit www.leicabiosystems.com.

Contact information – Leica Biosystems Imaging, Inc.

Manufacturer	Customer Support
 Leica Biosystems Imaging, Inc. 1360 Park Center Drive Vista, CA 92081 USA Tel: +1 844 534 2262	Contact your local support representative with any query or service request. https://www.leicabiosystems.com/contact-us/

For In Vitro Diagnostic Use

European Union Authorized Representative	United Kingdom Responsible Person
 CEpartner4U Esdoornlaan 13 3951 DB Maarn The Netherlands	Leica Microsystems (UK) Limited Larch House, Woodlands Business Park Milton Keynes, England, United Kingdom, MK14 6FG
Switzerland Representative	
 Leica Microsystems (Schweiz) AG Max Schmidheiny-Strasse 201 9435 Heerbrugg, Switzerland	
Importers	
 Leica Biosystems Deutschland GmbH Heidelberger Straße 17-19 69226 Nussloch, Germany	Leica Microsystems (UK) Limited Larch House, Woodlands Business Park Milton Keynes, England, United Kingdom, MK14 6FG



UDI

00815477020709

REF

23iQCDXROW

Table of contents

1	Notices	6
1.1	Revision record	6
1.2	About this manual	6
1.3	General notes	6
1.4	Intended purpose	7
1.5	Serious incident reporting	7
1.6	Quality control	8
1.7	Cybersecurity	8
1.8	Installation	8
1.9	Training	8
1.10	Standards	8
1.11	Leica Biosystems warranty	8
1.12	Related documents	9
1.13	Glossary of symbols	9
2	Introduction	11
3	Principles of operation	12
3.1	Overview	12
3.2	System architecture	12
3.3	Operational overview	14
3.4	About the artifact detection algorithms	16
3.4.1	Training of algorithms	16
3.4.2	iQC algorithm details	17
3.4.3	Artifact threshold settings	18
3.4.4	Limitations of artifact detection	19
4	Using the Aperio iQC DX Software	20
4.1	Before you start	20
4.1.1	Installing the Aperio iQC DX Software	20
4.1.2	Preparing to use the Aperio iQC DX Software	20
4.2	Icons and toolbar	21
4.2.1	Icons	21
4.2.2	Toolbar	23
4.3	Starting the Aperio iQC DX Software	24

4.4	Navigating to a slide	26
4.4.1	Paging through slides	26
4.4.2	Applying filters	27
4.4.3	Searching for a slide	27
4.5	Performing quality checks	28
4.5.1	Viewing the slide details	28
4.5.2	Assessing the image	33
4.5.3	Resolving artifact issues	34
4.6	Settings	35
4.6.1	Viewing the About window	35
4.6.2	Adjusting artifact threshold settings	37
4.7	Exporting list of rejected iQC slides	39
4.8	Logging out	40
4.9	Viewing iQC results on the scanner console	40
5	Troubleshooting	41
5.1	Symptom-based troubleshooting	41
5.1.1	End-user quality control issues	42
5.1.2	System/network issues	43
5.2	Error flags	44
6	Datasets	45
6.1	Verification and validation datasets	45
7	Aperio iQC DX Software Precision Study	48
7.1	Precision Study	48
7.2	Precision Study results	49
8	Aperio iQC DX Analytical Study	50
8.1	Analytical Study	50
	Glossary	52

1

Notices

1.1 Revision record

Rev.	Issued	Sections Affected	Detail
A	November 2025	All	Initial release.

1.2 About this manual

This manual provides information about the Aperio iQC DX, a software-only device intended for in vitro diagnostic use. This manual is intended for use by laboratory technicians. For information about Aperio iQC DX that is geared to the IT administrator, see the *Aperio iQC DX IT Administrator's Guide*. For product specifications, see the *Aperio iQC DX Specifications*.



The Aperio iQC DX Software is used with Aperio GT scanners. In this document the term "Aperio GT scanners" is used to refer to devices in the Aperio GT 450 and Aperio GT 180 scanner families.

1.3 General notes

General Aperio iQC DX Software cautions and notes appear below. Other notes appear in relevant sections in the manual.



Do not rely solely on Aperio iQC DX Software for quality assurance of WSIs. Continue existing quality assurance sampling practices. Aperio iQC DX Software may not always flag slides with certain artifacts, and it might incorrectly flag slides that contain no artifacts or multiple artifacts. Users should exercise discretion and verify results accordingly. See the *Aperio iQC DX Software Specifications* for artifact detection accuracies.



Aperio iQC DX Software is designed to assist and enhance, but not replace, human evaluation for slide quality. It is not intended to replace professional evaluation and judgment. Users should always rely on their expertise and consider the outputs of Aperio iQC DX as supplementary information and as an additional tool in the quality control process, not as the sole determinant for decision-making. The user should review all Aperio iQC software output. The final decisions and actions should be made by qualified individuals.

If there is uncertainty about the ability to accurately interpret results using Aperio iQC software alone, it is recommended to exercise professional judgment in each clinical situation and examine the glass slides using conventional microscopy.



The Aperio iQC DX Software was developed and validated for use with WSIs derived from tissue specimens processed using standard histopathology workflows and scanned with GT Platform scanners. These workflows include widely accepted tissue types, staining methods, and slide preparation protocols. The accuracy and reliability of artifact detection may be impacted if WSIs deviate from these validated conditions. Such deviations may include, but are not limited to, the use of non-GT Platform scanners, non-standard tissue types, unconventional stains, or institution-specific slide preparation or scanning methods. Under these conditions, performance drift is to be expected.



Aperio iQC DX Software is not intended to be used in the diagnosis of disease.



Aperio iQC DX Software does not have any control over any connected devices (the scanner or any other component of the WSI system). If changes are needed to the WSI system to communicate with the Aperio iQC DX Software, those changes are the responsibility of the WSI system.

1.4 Intended purpose

Aperio iQC DX Software is an artificial intelligence-based software intended to be used by laboratory professionals as an aid in the identification of digital (out of focus, image striping, and missing and clipped tissue) and/or histological (air bubbles and pen marks) artifacts in hematoxylin and eosin (H&E) and immunohistochemistry (IHC) stained, formalin-fixed paraffin embedded (FFPE) tissue, whole slide images (WSIs) from Aperio GT 450 DX and Aperio GT 180 DX scanners that should undergo further evaluation for quality prior to diagnostic review.

Laboratory professionals should only use Aperio iQC DX Software in conjunction with their complete in-house laboratory image quality control workflow. Aperio iQC DX Software is not intended to be used for the diagnosis, prognosis, or prediction of disease.

1.5 Serious incident reporting

Any serious incident that has occurred in relation to the Aperio iQC DX Software shall be reported to the manufacturer and the competent authority of the member state in which the user and/or the patient is established.

1.6 Quality control

For information on image quality checks, see the user's guides for the Aperio iQC DX Software and for the Aperio GT scanner.

1.7 Cybersecurity

The Aperio iQC DX resides on the customer's hosting server. It is deployed within a network that includes the Aperio GT scanner, the Aperio SAM DX software, a virtual machine (VM), an image repository, and other software components. User authentication and access controls occur through the authentication server (Auth Server) hosted on the Aperio SAM DX server.

End-to-end data encryption protects data both in transit and at rest, maintaining confidentiality and integrity. The scanner and Aperio iQC DX connection is secured through an encrypted, secure SSL/TLS connection.

For further details about how LBS safeguards protected electronic healthcare information and for cybersecurity recommendations to help protect cybersecurity, see the *Aperio iQC DX Software IT Manager and Lab Administrator Guide*.

1.8 Installation

Aperio iQC DX Software must be installed only by a trained Leica Biosystems Technical Services representative. It is installed on a customer-provided network server. Contact Leica Biosystems for installation assistance.

For system requirements, see the *Aperio iQC DX Software Specifications*.

1.9 Training

Contact Leica Biosystems for training on Aperio iQC DX Software.

1.10 Standards

The Aperio iQC DX Software is designed and developed in strict accordance with industry standards. For a complete list of standards, contact Leica Biosystems.

1.11 Leica Biosystems warranty

View the Leica Biosystems Leica Biosystems warranty here:

<https://www.leicabiosystems.com/us/about/terms-and-conditions/>

1.12 Related documents

The Aperio iQC DX Software resides on a hosted server. It is deployed within a network that includes Aperio GT scanners and the Aperio SAM (Scanner Administration Manager) DX server.

For complete information about the use and deployment of the Aperio iQC DX Software into the laboratory environment, see the following documents. For specific details about the scanner, see the user documentation for the scanner. For specific details about Aperio SAM DX, see the *Aperio SAM DX IT Manager and Lab Administrator Guide*.






Document No.	Description
MAN-0565	Aperio iQC DX Software User's Guide
MAN-0570	Aperio iQC DX Software Specifications
MAN-0566	Aperio iQC DX Software IT Administrator's Guide



1.13 Glossary of symbols

The following is a list of symbols used on the product labeling and their meanings.




ISO 15223-1

Medical devices – symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements.

Symbol	Standard/ Regulation	Reference	Description
	ISO 15223-1	5.1.1	Manufacturer Indicates the medical device manufacturer.
	ISO 15223-1	5.1.2	Authorized representative in the European community Indicates the Authorized representative in the European Community.
	ISO 15223-1	5.1.6	Catalog number / Reference number Indicates the manufacturer's catalog number so that the medical device can be identified.
	ISO 15223-1	5.1.8	Importer Indicates the entity importing the medical device into the European Union.
	ISO 15223-1	5.4.4	Caution Indicates the need for the user to consult the instructions for use for important cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device itself.

Symbol	Standard/ Regulation	Reference	Description
	ISO 15223-1	5.5.1	In Vitro Diagnostic medical device Indicates a medical device that is intended to be used as an in vitro diagnostic medical device.
	ISO 15223-1	5.7.10	Unique Device Identifier The unique device identification (UDI) is a unique numeric or alphanumeric code related to a medical device. It allows for a clear and unambiguous identification of specific devices on the market and facilitates their traceability.

Other symbols and markings

Symbol	Standard/ Regulation	Description
	The instrument Declaration of Conformity lists the Directives with which the system complies	European Conformity The instrument Declaration of Conformity lists the Directives with which the system complies.
	N/A	UK Conformity Assessment Device is in compliance with UK Conformity Assessment requirements.
	Ordinance on In Vitro Diagnostic Medical Devices (IvDO) of 4 May 2022.	Swiss Authorised Representative Indicates the Swiss Authorised representative.

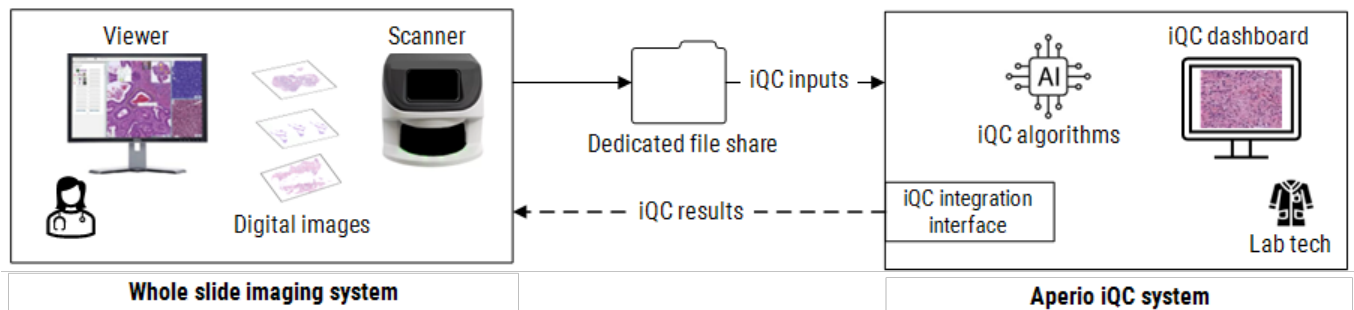
2 Introduction

The Aperio iQC DX Software is a standalone software application intended to assist in identifying artifacts in whole slide images (WSIs) produced by Aperio GT scanners. The Aperio iQC DX Software analyzes copies of WSIs of hematoxylin and eosin (H&E) and immunohistochemistry (IHC) stained slides in SVS format.

When Aperio iQC DX Software is running, copies of WSIs from connected Aperio GT scanners are automatically analyzed. The WSIs, along with the artifact detection results, are displayed on the iQC dashboard for laboratory staff review and disposition. The user can accept or reject the WSI and add comments for each scan.

To analyze images, Aperio iQC DX algorithms use locked AI. The Aperio iQC DX Software is executed on copies of the original images. The Aperio iQC DX Software does not modify those images.

Figure 2-1: System diagram showing Aperio iQC DX



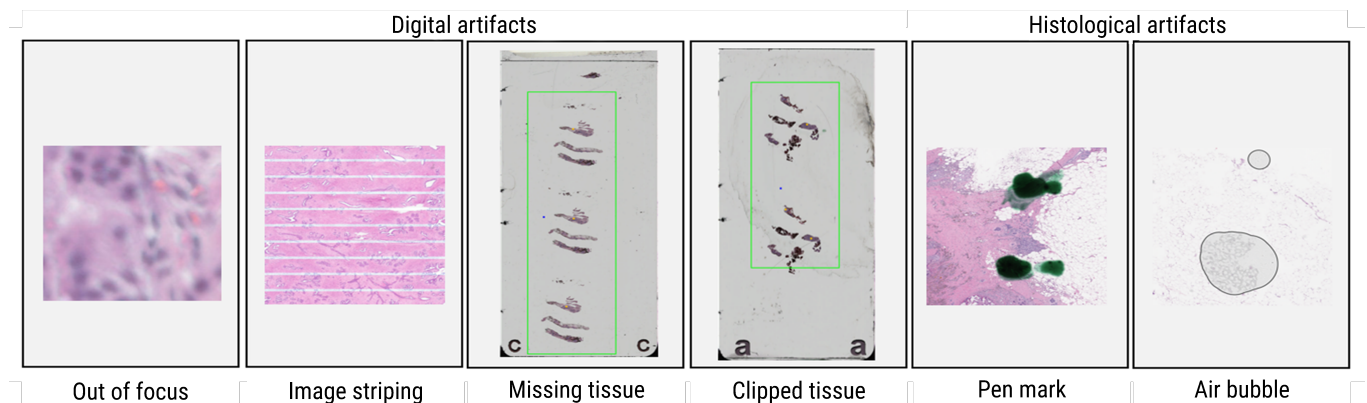
The Aperio iQC DX Software is deployed within a network that includes Aperio GT scanners. Each copy of Aperio iQC DX Software can support up to four scanners, including a combination of scanners from both the Aperio GT 180 and Aperio GT 450 scanner families.

3

Principles of operation

3.1 Overview

The Aperio iQC DX Software detects and identifies the artifacts shown below.

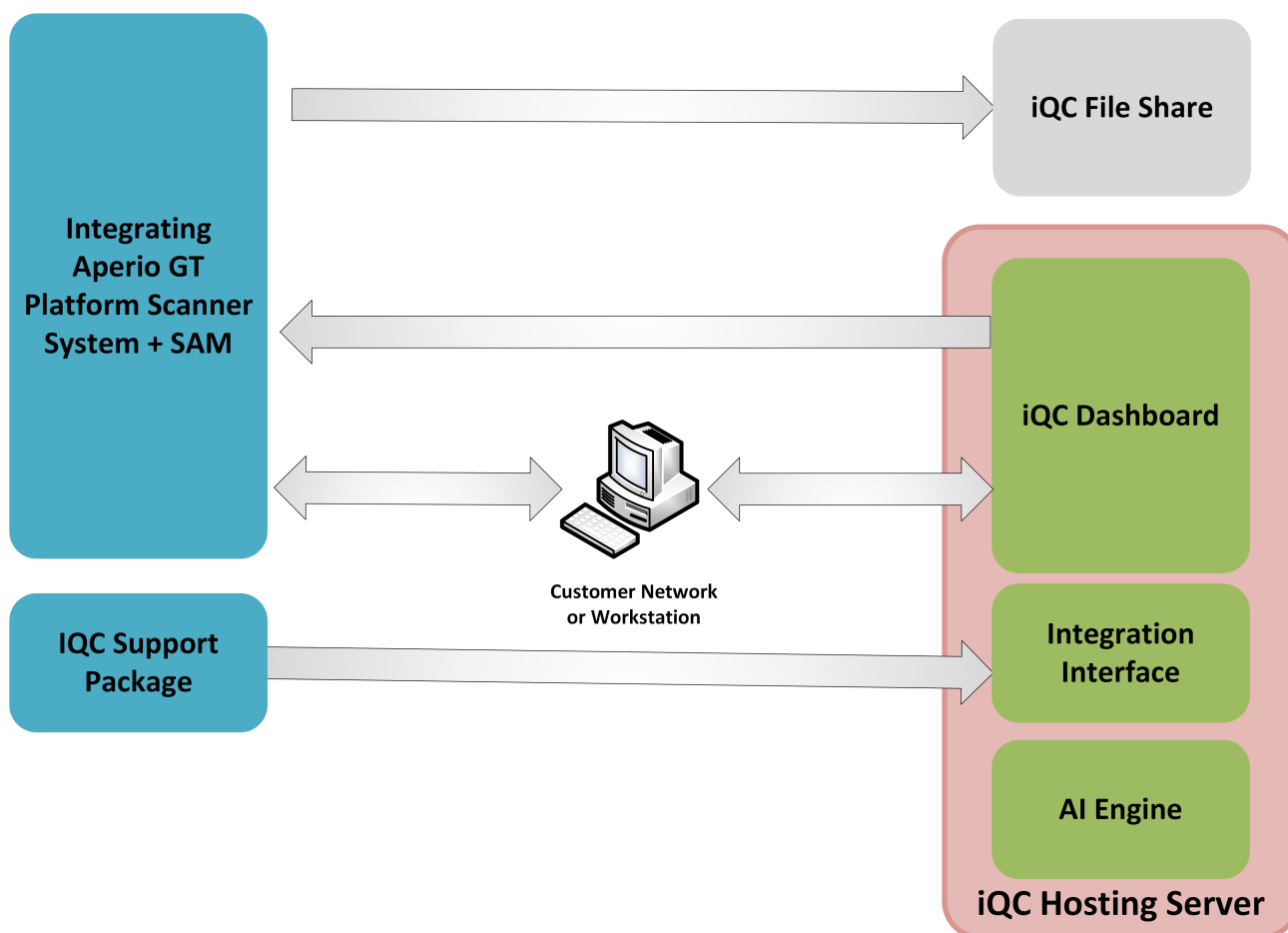


A dashboard displays the results once they become available. On the dashboard, the user can interact with each image to perform image quality review. The dashboard is the central hub for managing scanned slides and artifact detection within the system.

3.2 System architecture

The Aperio iQC DX Software is deployed on the customer's server. It doesn't interact directly with the scanner, but rather it retrieves image files produced by the scanner. [Figure 3-1 Aperio iQC DX Software system architecture](#) shows how the Aperio iQC DX fits into the overall Aperio GT scanner system. Together, these components work to ensure monitoring, processing, and analysis of whole slide images (WSIs).

Figure 3-1: Aperio iQC DX Software system architecture



The data that is exchanged between the scanner and Aperio iQC DX Software has these attributes:

Data attribute	Source	Destination	Notes
Image data (WSI)	Scanner	DICOM-SVS converter (on Aperio SAM DX server)	DICOM file
Image data (SVS file)	DICOM-SVS converter (on Aperio SAM DX server)	iQC file system	Duplicate of file sent to the image repository. SVS file includes image data, metadata, and hash file.
Web page	iQC dashboard	Web browser	The iQC dashboard is displayed on the user's workstation by the web browser
Authentication data	iQC dashboard	Auth Server (hosted on Aperio SAM DX server)	Authentication is performed using Aperio SAM DX credentials

Data attribute	Source	Destination	Notes
Request data	Aperio iQC DX Software	iQC support package (on Aperio SAM DX server)	–
Request data	iQC support package (on Aperio SAM DX server)	Scanner	–

3.3 Operational overview



The Aperio iQC DX Software is designed to detect possible artifacts in images from microscope slides. It does not exhibit any automation features. Aperio iQC DX Software processes are manually controlled and require user intervention for operation.



Aperio SAM DX manages time synchronization for the Aperio iQC DX Software system. For details, see the *IT Manager and Lab Administrator Guide* for Aperio SAM DX.

The following section details the operation of the Aperio iQC DX Software, with an overview shown in [Figure 3-2 iQC operational overview](#).

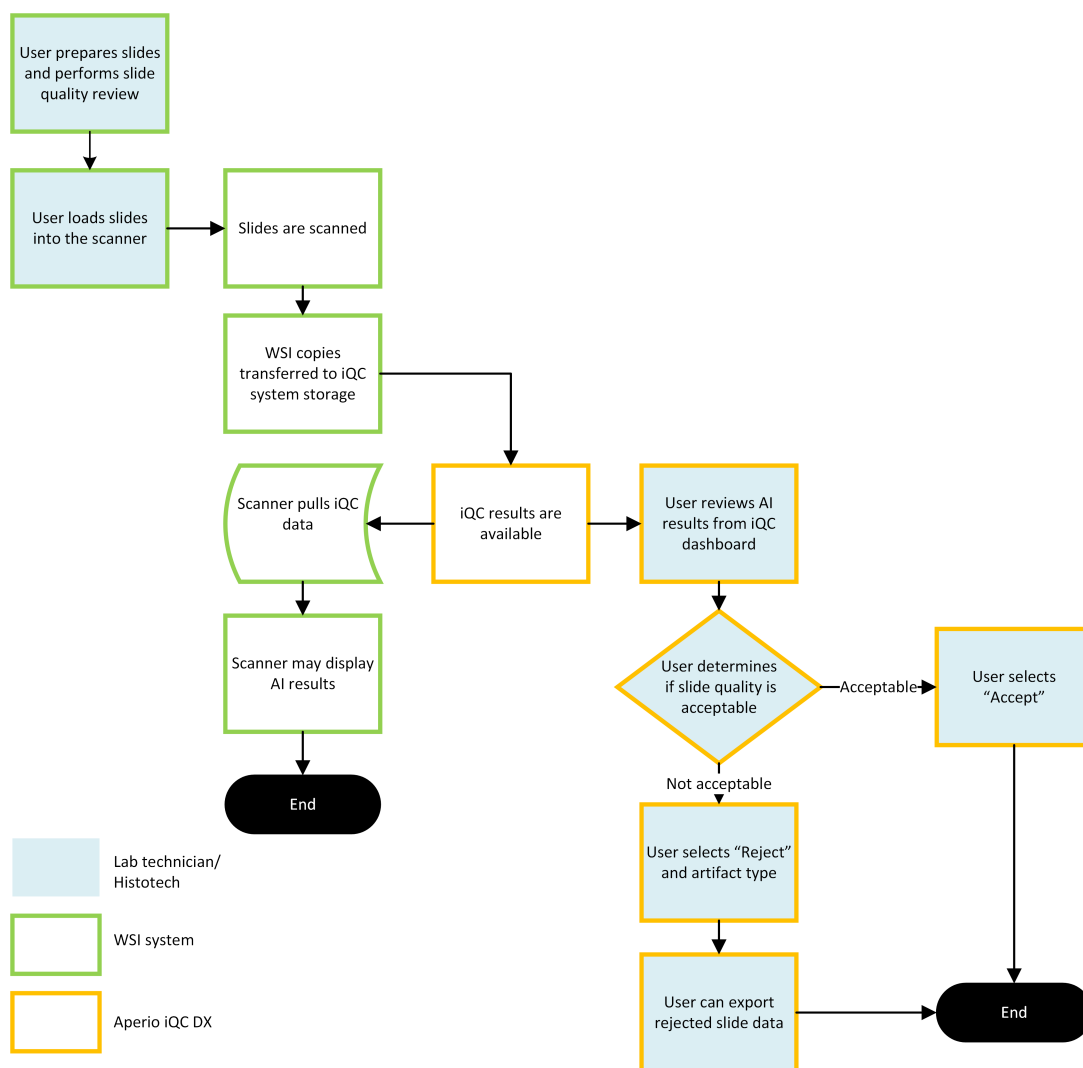
- 1 The Aperio iQC DX Software continuously checks for new packages on a dedicated iQC file share. Each package is associated with a scanner, and only packages for licensed scanners are processed by the Aperio iQC DX Software. This process does not require a user to be logged in.
- 2 Data incoming to the Aperio iQC DX Software is validated to ensure that it meets the required format and licensing conditions. The validated data is then queued for processing.
- 3 AI algorithms detect artifacts in the WSIs. See [3.4 About the artifact detection algorithms](#) for details about how Aperio iQC DX Software detects each type of artifact. The results are collected and stored in a location that can be accessed by the iQC dashboard and scanner software.

Any errors encountered during artifact detection, including issues with AI model loading, data corruption, or resource constraints, are logged. All significant events, including data processing and artifact detection, are logged.

- 4 Licensed scanners simultaneously poll iQC for results, using interfacing software installed on a designated Aperio SAM DX hosting server. Notifications of detected artifacts are passed by Aperio SAM DX to the scanner for display on the console.

- 5 The user logs into iQC through the iQC login page on their workstation, using their Aperio SAM DX login credentials.
 - a The user credentials are validated by the Auth Server on the Aperio SAM DX hosting server. Once the user is authenticated, a session token is used to grant them access to iQC. The iQC dashboard is now displayed on the user's browser.
 - b Following successful authentication, the iQC module's back-end API manages user authorization. Based on their role (Operator or Lab Admin), users are granted appropriate levels of access for their role. For details on creating and managing user accounts, see the *IT Manager and Lab Administrator Guide* for Aperio SAM DX.
- 6 The dashboard retrieves and displays all the images and the iQC results for the user-selected scanner. Images and iQC results are retained for up to seven days. If desired, this retention setting can be modified by Leica Biosystems.
- 7 The user reviews the information on the dashboard and enters their assessment, which is then stored in the iQC database.

Figure 3-2: iQC operational overview



3.4 About the artifact detection algorithms

AI is incorporated into the Aperio iQC DX Software to detect digital and histological artifacts in WSIs. It recognizes patterns learned by analyzing large datasets of images containing similar artifacts.

Aperio iQC DX Software algorithms process the scanned data exported from the scanner and perform a series of AI techniques to identify the presence of artifacts on each slide. These algorithms use AI to capture and quantify known features related to specific artifacts. The inference results generated from the algorithms are further processed by a rules engine (based on predefined or user-defined artifact threshold settings) to determine the presence of each artifact.

Each artifact uses a separate detection algorithm, which is built on its own unique model with its own learning paradigm and distinct architecture. [3.4.2 iQC algorithm details](#) describes the algorithms used to detect each artifact, along with notes on how that algorithm was trained.

3.4.1 Training of algorithms

The iQC algorithms are static, non-continuous-learning AI software algorithms. The presence of artifacts is determined using convolutional neural network (CNN) machine learning, a type of deep learning network specifically designed for image classification and object recognition. The algorithms learned features from images containing artifacts using supervised learning. The trained algorithms are used to detect, classify, and label artifacts. With locked AI, the algorithm is trained and tested in a controlled environment and then locked before deployment. In other words, it doesn't learn or adapt on its own once deployed.

3.4.1.1 Training and test data

The data used to train, validate, and test Aperio iQC DX Software was from histology slide samples that exhibit variability in their input features. These variable input features include stain type, tissue type, and tissue size. The training dataset contained a balanced representation of tissue samples both with and without artifacts.

3.4.2 iQC algorithm details

Algorithm/artifact	Artifact definition	How the algorithm is trained and works
Out-of-focus region	An out-of-focus artifact in whole slide images (WSIs) is characterized by blurriness or a lack of sharpness in certain areas of the image, resulting from improper focus during scanning. These artifacts can obscure important details, making accurate tissue analysis difficult.	The out-of-focus algorithm generates a range of out-of-focus scores for the tissue region on WSIs. This output, combined with user-defined artifact threshold settings—out-of-focus coverage area and severity—determines the presence of the artifact.
Missing and clipped tissue	Missing tissue is a section of tissue that is outside of the WSI and is only visible in the macro image of the slide. Clipped tissue is a section of tissue partially captured in the WSI, with some portion being outside the WSI boundary. In both situations, the tissue is unavailable for assessment.	The missing and clipped tissue algorithm compares the detected tissue region to the scanned region used to produce the WSI. If tissue is detected outside of the scanned region, the slide is flagged for missing or clipped tissue.
Image striping	A scanner may occasionally generate faint, striped patterns on the WSIs. These stripes traverse the entire slide image exhibiting varying degrees of intensity. They can hinder visual image review and assessment.	The image striping algorithm can distinguish between striping and non-striping features. The ratio of striping regions to all regions, along with user-defined artifact threshold setting for image striping, determines the presence of this artifact.
Air bubble	Air bubbles are histological artifacts that could obscure regions of interest on a glass slide or tissue. These artifacts appear as air pockets trapped between the coverslip and the slide.	The air bubble algorithm identifies features that pinpoint air bubbles within tissue at the pixel level. This output, along with a user-defined artifact threshold setting for air bubble coverage area, determines the presence of this artifact.
Pen marks	Pen marks are histological artifacts that can appear either as printed or hand-drawn markings (for example, by markers of distinct colors on the tissue), and they can obscure tissue features and regions of interest on the tissue.	The pen mark algorithm identifies features that pinpoint pen marks. This output, along with a user-defined artifact threshold setting for pen mark coverage area, determines the presence of this artifact.

3.4.3 Artifact threshold settings

A user with the Lab Admin role can configure the artifact thresholds using the Settings function.

3.4.3.1 Out-of-focus threshold

Out of Focus Coverage Area: This threshold, set as a percentage, defines the minimum percentage of out-of-focus tissue regions for a slide to be flagged as out of focus. If the out-of-focus tissue percentage is larger than this threshold, the slide is flagged for the out-of-focus artifact. Increasing the threshold (moving the pointer to the right) requires a higher percentage of out-of-focus tissue to flag the artifact. This makes the algorithm less sensitive to out-of-focus artifacts and may cause fewer slides to be flagged.

Out of Focus Severity: This threshold, set as a percentage, defines the minimum blurry level of a tissue region required to be identified as out-of-focus. If the detected blurry level of the tissue region is larger than this threshold, the region is identified as out-of-focus. Increasing the threshold (moving the pointer to the right) requires a higher blurry level to identify a region as out-of-focus. This makes the algorithm less sensitive to out-of-focus artifacts and may cause fewer slides to be flagged.

3.4.3.2 Image striping threshold

The **Image Striping % Detected** threshold, set as a percentage, defines the minimum striped percentage for a slide to be flagged for the striping artifact.

If the striping percentage in a slide is greater than or equal to this threshold, the slide is flagged for the image striping artifact. Increasing the threshold (moving the pointer to the right) requires a higher percentage of striped region to flag the slide for image striping. This requires the algorithm to see more image striping artifacts to flag a slide and thus cause fewer slides to be flagged.

3.4.3.3 Air bubbles threshold

The **Air Bubbles Coverage Area** threshold, set as a percentage, is converted to the minimum number of pixels required to flag a slide for air bubbles.

If the detected air bubble pixels in a slide exceed this threshold, the slide is flagged for the air bubble artifact. Increasing the threshold (moving the pointer to right) requires more air bubble coverage to flag the artifact. This makes the algorithm less sensitive to air bubble artifacts and may cause fewer slides to be flagged.

3.4.3.4 Pen marks threshold

The **Pen Marks Coverage Area** threshold, set as a percentage, defines the minimum number of pixels required to flag a slide for pen marks.

If the detected pen mark pixels in a slide exceed this threshold, the slide is flagged for the pen mark artifact. Increasing the threshold (moving the pointer to the right) requires more pen mark coverage to flag the artifact. This makes the algorithm less sensitive to the pen mark artifacts and may cause fewer slides to be flagged.

3.4.4 Limitations of artifact detection

The Aperio iQC DX Software may not detect artifacts in certain cases, as described below.



When multiple artifacts are present on a WSI, one artifact may obscure another. For example, a severely out-of-focus region could conceal the presence of other artifacts, such as air bubbles. If both artifacts are visible in the WSI, both are expected to be detected. However, if one artifact fully occludes another, only the visible artifact is expected to be detected. In such cases, a histological artifact that exists on the physical glass slide but is completely hidden in the WSI is not expected to be detected. Detection algorithms are expected to identify only the artifacts that are visible within the WSI, regardless of whether additional artifacts are physically present on the glass slide.

3.4.4.1 Missing and clipped tissue

- Tissue samples outside of the coverslip are not flagged as missing.
- Very small tissue fragments may not be detected.
- Faintly stained slides may prevent tissue from being detected.
- Air under the coverslip may cause tissue to be confused for debris, as the tissue appears black within the image.
- Excessive mounting media or similar artifacts that may occlude the tissue may prevent the tissue from being detected.

3.4.4.2 Image striping

- A slide having an image striping outside the tissue is not flagged.
- Faint image striping (usually disappears at higher magnifications) that does not significantly affect the tissue may not be detected.
- Faintly stained slides (with very faint image striping) may prevent image striping from being detected.

3.4.4.3 Out of focus

- Out-of-focus visualization may appear on non-tissue areas, particularly if those areas are not clean.
- Out-of-focus areas caused by tissue folds may not always be detected and visualized.
- If the tissue is extremely faint or understained, out-of-focus areas may not be detected.

3.4.4.4 Air bubbles

- Air bubble visualization may appear blocky in the presence of large air bubbles.
- A severely out-of-focus slide may cause inaccurate predictions for air bubbles.

4

Using the Aperio iQC DX Software



Slides are available for review for only seven days after scanning. Make sure to review slides promptly.

Follow these instructions to use the Aperio iQC DX Software.

4.1 Before you start

4.1.1 Installing the Aperio iQC DX Software

The Aperio iQC DX Software is installed by Leica Biosystems. Contact Leica Biosystems for installation assistance.

When the Aperio iQC DX Software is properly installed, the log-in screen appears when you enter the hostname or address into your browser.

4.1.2 Preparing to use the Aperio iQC DX Software

The Aperio iQC DX Software is compatible with Aperio GT SVS or DICOM image workflow. The inputs will always be SVS. These images are created from WSIs that are prepared from FFPE surgical pathology slides. The images are automatically sent to the Aperio iQC DX Software for processing. There is no action required by the user.



Aperio iQC DX Software can process images that are up to 32 GB in size.

For details about preparing and scanning the slides, see the user's guide for your scanner.













CAUTION: Before running the Aperio iQC DX Software, make sure that user access restrictions are in place. Unauthorized actions taken during the session could lead to data corruption or integrity issues. For details, see the *IT Manager and Lab Administrator Guide* for Aperio SAM DX.




4.2 Icons and toolbar

This section describes the the icons and toolbar used in Aperio iQC DX.

4.2.1 Icons

See the table below for definitions of the icons on the Aperio iQC DX screens.

Symbol	Meaning
	Histological artifact A teal icon indicates that histological artifacts are present in the marked slide, or in one or more slides in the marked scanner.
	Digital artifact An orange icon indicates that digital artifacts are present in the marked slide, or in one or more slides in the marked scanner.
 	These two icons denote the visibility of an overlay mask for the algorithm. Click on an icon to toggle the overlay mask on or off. The eye icon with a slash indicates that the overlay mask is hidden. Overlay masks are available only for out-of-focus, missed tissue, or air bubble artifacts.
	Images that are not yet reviewed
	Settings Accesses the About window, log-out function, and for Lab Admin users only, artifact threshold settings for some artifacts.
	Accepted slides
	Rejected slides
	No artifacts found
	Search














Symbol	Meaning
	Filter bar
	Aperio iQC DX Software is processing this slide. Results are pending.
	Error There was an error running the algorithm for that artifact, and there are no results displayed for that artifact.

4.2.2 Toolbar

To access iQC functions, click the appropriate icon on the toolbar at the top of the screen.



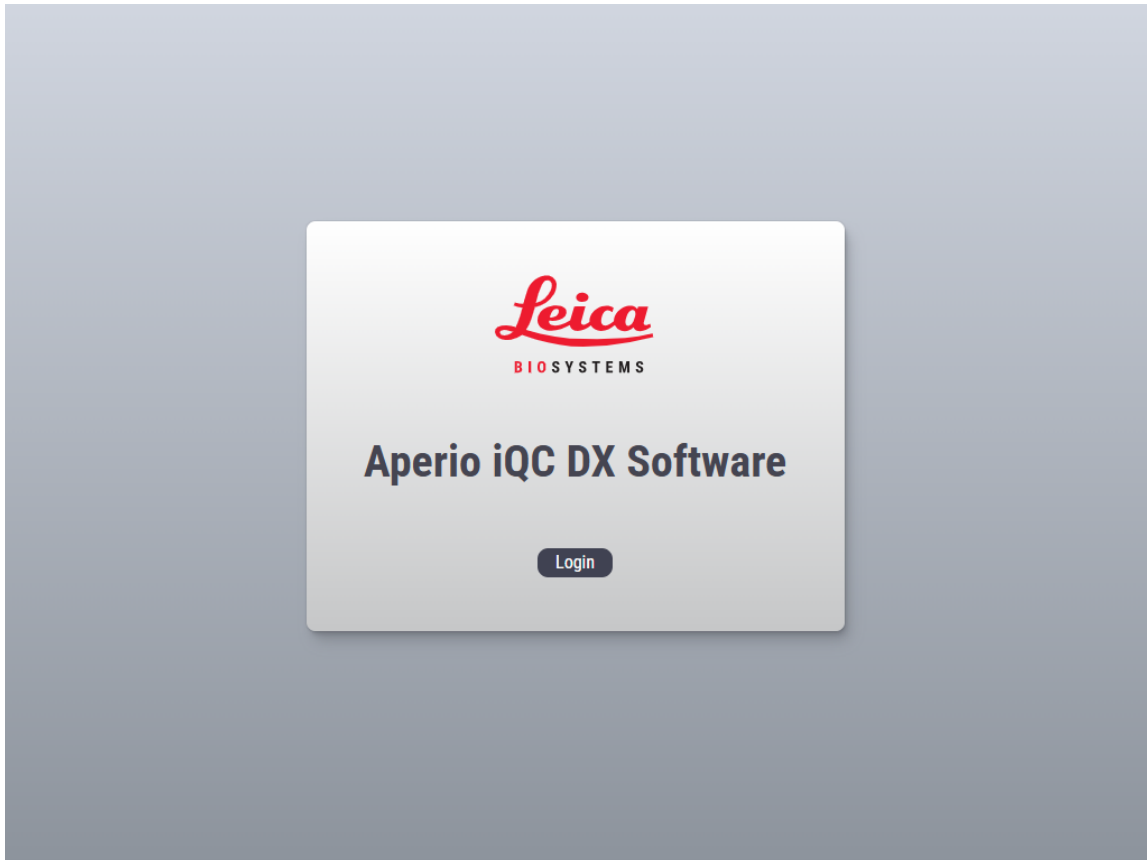
Legend

- | | | | | | |
|---|---|---|----|---|---|
| 1 |  | Opens the scanners screen | 8 |  | Shows accepted slides |
| 2 |  | Opens the slides screen | 9 |  | Shows rejected slides |
| 3 |  | Opens the slide visualization screen | 10 |  | Shows slides that are not yet reviewed |
| 4 |  | Opens Settings | 11 |  | Shows slides with no artifacts |
| 5 |  | Exports a CSV (comma-separated value) file of rejected slide | 12 |  | Show slides with digital artifacts |
| 6 |  | Filter bar
To view a subset of the available slides, select one of more of the filters below. If no filters are selected, all available slides are shown, with the oldest scanned slide in the upper-left corner. | 13 |  | Show slides with histological artifacts |
| 7 | Example: | Shows slides from the indicated scanner | 14 |  | Type a complete or partial slide name to show slides that match the search term |

4.3 Starting the Aperio iQC DX Software

- 1 Type the hostname or address of the iQC server into the browser.

The login window opens.

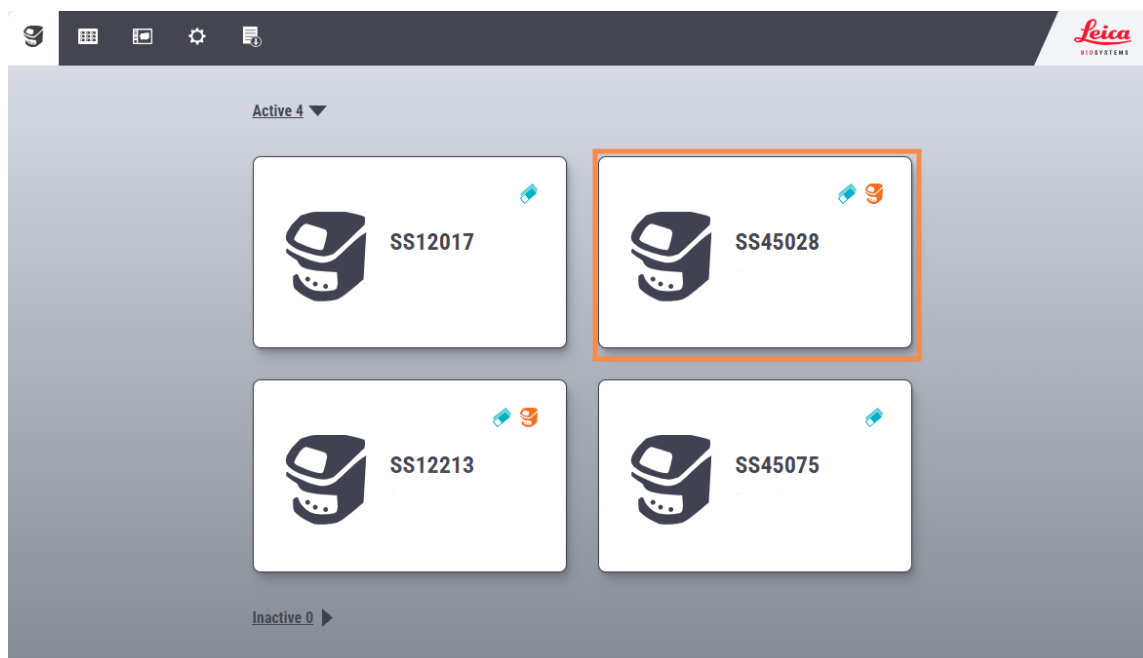


- 2 Click **Log In**, and enter your credentials.



If you cannot log in (for example, due to forgotten password), contact your laboratory administrator for assistance.

- 3 The scanner selection screen opens. It displays the connected scanners. Click a scanner to open the slide selection screen for that scanner.



Scanners that have slides with detected artifacts are marked with one of these icons.



A teal icon in the scanner box indicates that one or more slides in that scanner have histological artifacts.



An orange icon in the scanner box indicates that one or more slides in that scanner have digital artifacts.



This symbol in the scanner box indicates that no artifacts were found in the slides in that scanner.

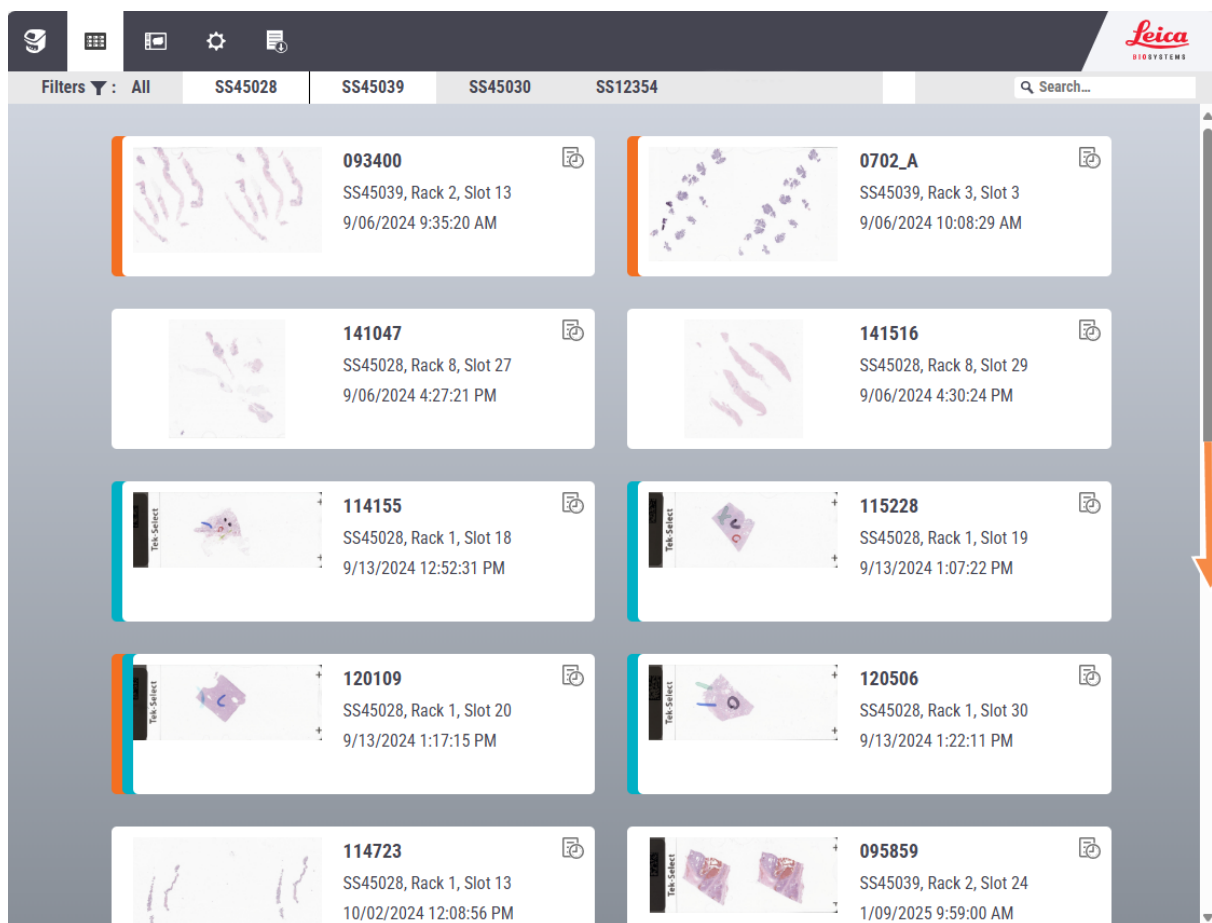
The **Active** section of the screen shows all connected scanners with active licenses. Scanners with expired licenses are initially hidden, but can be shown by clicking the arrow next to **Inactive**.

4.4 Navigating to a slide

On the slide selection screen, slides are displayed in a grid pattern, arranged from left to right, top to bottom, and oldest to newest. The earliest scanned slide is in the upper-left corner, and the most recently scanned slide is last.

4.4.1 Paging through slides

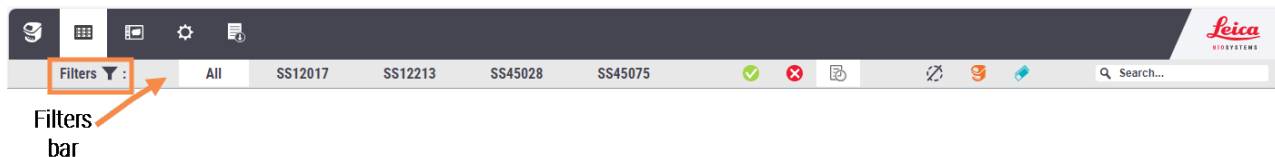
To page through the slides, use the scroll bar to scroll up or down the page to view additional slides.



4.4.2 Applying filters

To filter iQC results to view just a subset of slides, do the following:

- 1 Locate the Filters bar below the top toolbar.



- 2 To view only the slides from one or more scanners, click one or more scanner names, or click **All** to view slides from all scanners.
- 3 Select one or more additional filters:

Example: Show only the accepted slides, only the rejected slides, or only the slides that have not been reviewed.

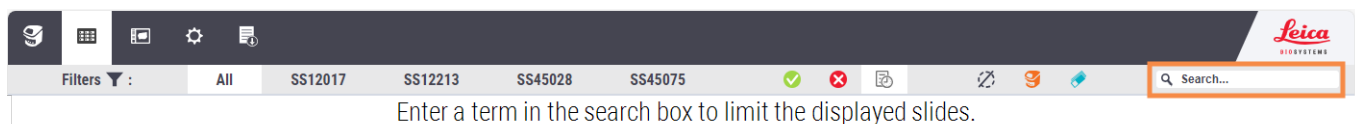


Example: Show only slides without artifacts, only slides with histological artifacts, or only slides with digital artifacts.



4.4.3 Searching for a slide

To search for a slide by complete or partial slide name, type a term in the search box, and press Enter.



4.5 Performing quality checks



If several users are simultaneously reviewing the same slide, the final assessment will reflect that of the first user to save their changes.

4.5.1 Viewing the slide details

- 1 Click the selected slide.



A teal stripe to the left of a slide indicates that a histological artifact has been detected. An orange stripe to the left of a slide indicates that a digital artifact has been detected.

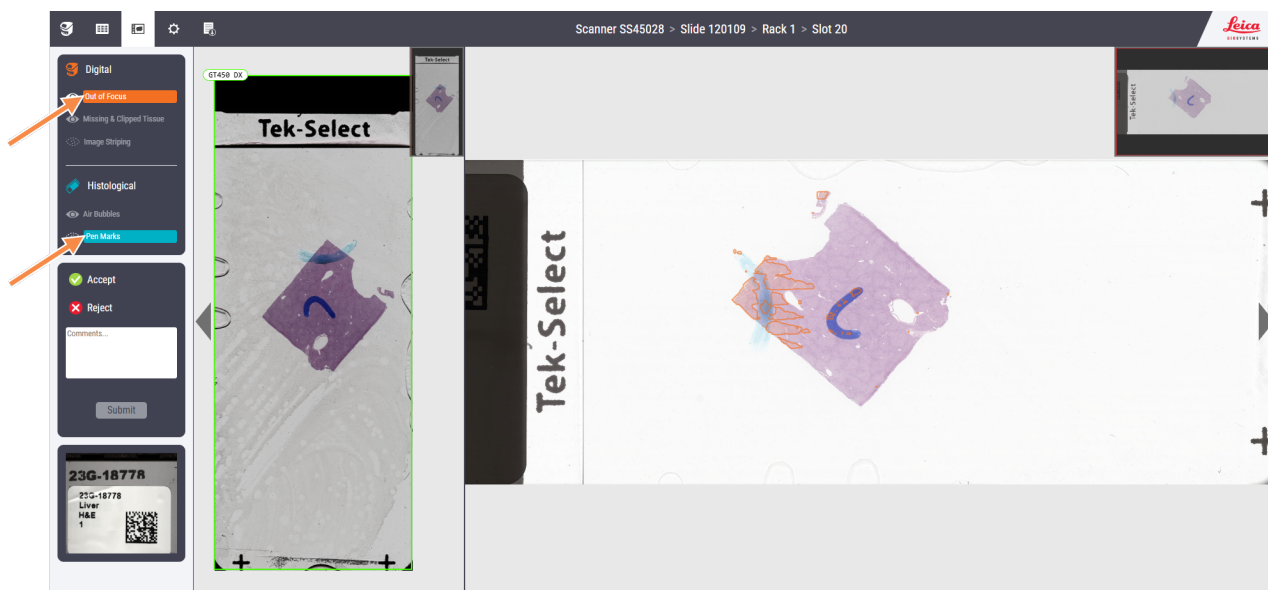
The screenshot displays the Leica Biosystems iQC DX software interface. At the top, there is a navigation bar with icons for home, grid, view, settings, and help. Below this is a filter bar showing 'Filters: All' and several slide IDs: SS45028, SS45039, SS45030, and SS12354. A search bar is located on the right side of the filter bar. The main area contains a grid of slide cards. Each card shows a thumbnail of a slide, a slide ID, the rack and slot information, and the timestamp. The slide with ID 120109 is highlighted with an orange stripe on the left, and an orange arrow points to it. Other slides in the grid include 093400, 0702_A, 141047, 141516, 114155, 115228, 120506, and 095859.

- 2 The slide detail screen opens. For guidance when viewing the screen, see [Figure 4-1 Interpreting the slide detail screen](#).

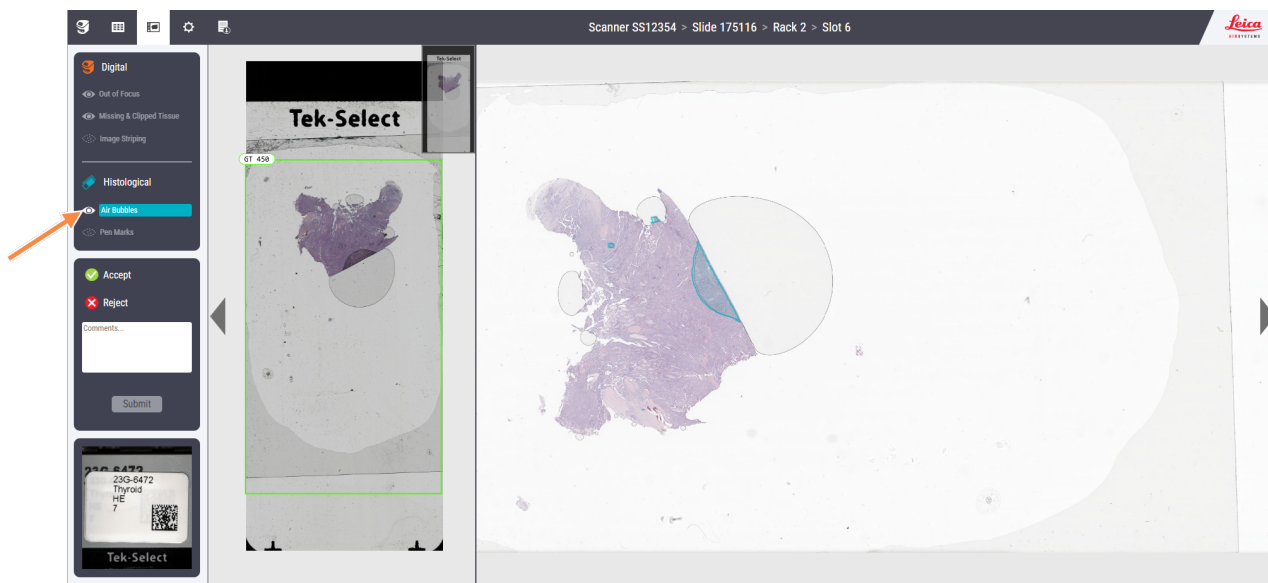
- Note any detected artifacts (digital artifacts are highlighted in orange; histological artifacts are highlighted in teal).



Digital artifacts can obscure histological artifacts. For example, an out-of-focus artifact may conceal an air bubble, so the air bubble artifact would not be detected, and the slide would not be reprocessed correctly.



- 4 If a detected artifact has an eye icon to the left, the artifact can be highlighted by a visualization overlay that is placed on top of the artifact. The overlay is placed by default. When the overlay is placed, the diagonal slash through the eye icon disappears. Unclick the eye icon to remove the overlay.

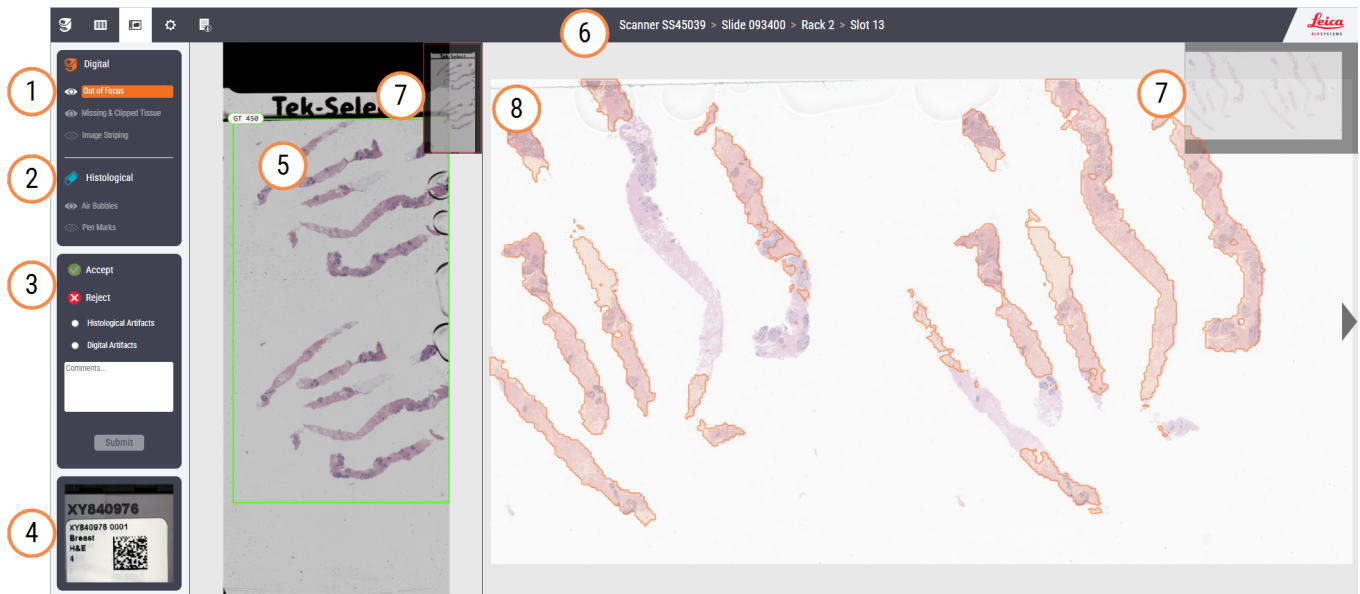


Below to the left is a slide with an air bubble artifact, which is not highlighted. To the right is the same slide with the overlay. Note the teal color used to highlight the artifact.



- 5 Inspect the scanned image.
- To pan an image**, click on the image and drag the full image, or click on the image and use the keyboard arrows to move around the image. You can also click on an area of the thumbnail image in the upper-right corner to navigate to that area of the slide image.
- To zoom in or out**, scroll using your mouse wheel.
- 6 To move to the previous or next slide, click the arrows to the left and right of the detail image.
- Alternatively, you can use the keyboard right and left arrows to move between slides. Click on the sidebar area to use these keyboard shortcuts.

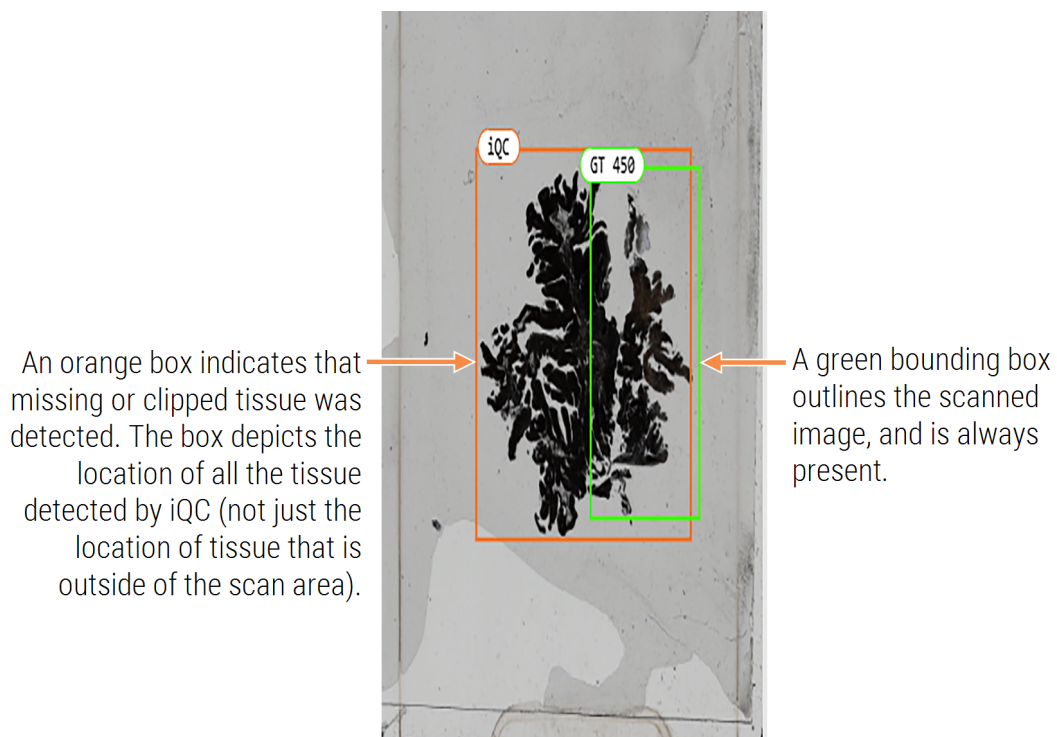
Figure 4-1: Interpreting the slide detail screen



Legend

- | | |
|---|---|
| <p>1 Digital artifacts
Artifacts that are detected are highlighted in orange. Click on the eye icon to toggle the visualization overlay on or off.</p> <p>2 Histological artifacts
Artifacts that are detected are highlighted in teal. Click on the eye icon to toggle the visualization overlay on or off.</p> <p>3 Slide assessment
Accept or reject the slide. Add comments.</p> <p>4 Slide label image</p> | <p>5 Macro image of entire slide
A green bounding box outlines the scanned image, and is always present. If missing or clipped tissue is detected, an orange box is also shown. This orange box outlines all the tissue detected by iQC (not just the tissue that is outside of the scan area). See Figure 4-2 Missing & Clipped Tissue bounding boxes.</p> <p>6 Slide details</p> <p>7 Thumbnail of macro slide or detail slide for navigation purposes</p> <p>8 Slide detail view</p> |
|---|---|

Figure 4-2: Missing & Clipped Tissue bounding boxes



4.5.2 Assessing the image

- 1 Assess the image. The iQC algorithms and the artifacts that can be detected are summarized in [Table 4-1 Summary of Aperio iQC DX Software algorithms/artifacts detected](#).
 - a If the image quality is acceptable, click **Accept** or press the **A** key on your keyboard.
 - b If the image quality is unacceptable, select the **Reject** option or press the R key on your keyboard and then select the option that matches the artifact that appears on the slide.
 - c Enter any comments.
 - d Click **Submit**.



- Make sure that you accurately assess each slide. Unintentionally accepting a slide may cause legitimate artifacts to be missed. Unintentionally rejecting slides with clinically insignificant artifacts may result in needless extra work.
- Once you accept or reject a slide, you cannot change your assessment.

- 2 To navigate to the previous or next slide, click the arrows to the left and right of the slide images, or use the arrow keys on your keyboard.

If your cursor is in the image, first click off the image, in the sidebar, and then use the arrow keys to navigate between slides.

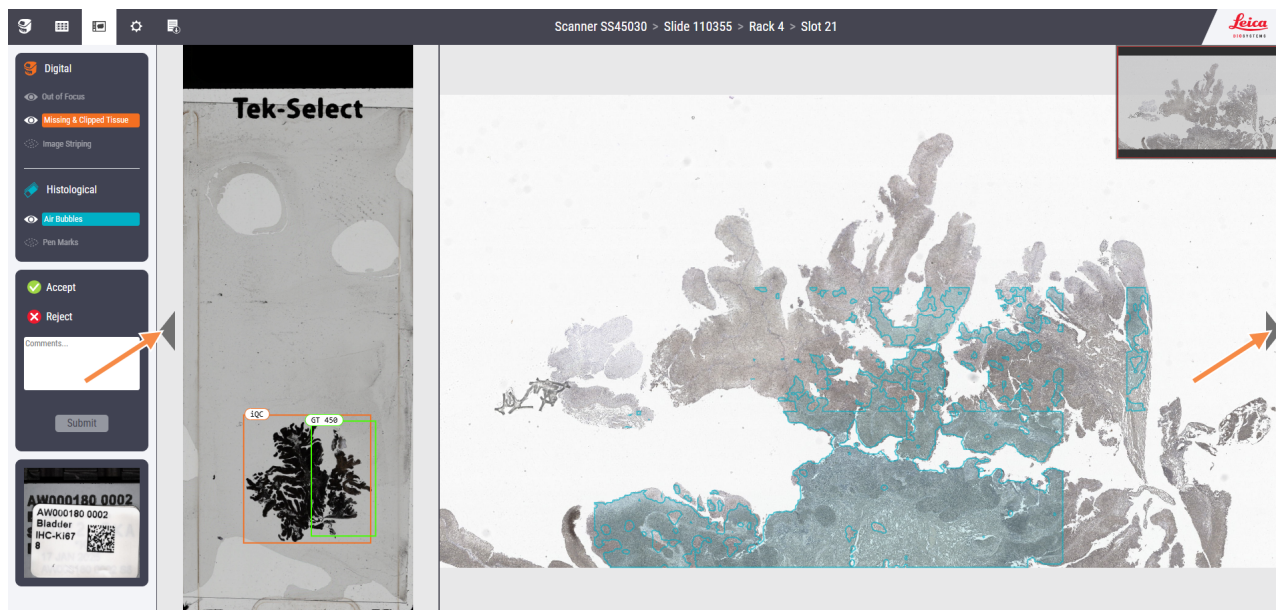


Table 4-1: Summary of Aperio iQC DX Software algorithms/artifacts detected

Artifact detected	Visual location indicator	User-configurable threshold?
Out of focus	Yes	Yes
Missing and clipped tissue	Yes	No
Image striping	No	Yes

Table 4-1: Summary of Aperio iQC DX Software algorithms/artifacts detected (continued...)

Artifact detected	Visual location indicator	User-configurable threshold?
Air bubbles	Yes	Yes
Pen marks	No	Yes

4.5.3 Resolving artifact issues

See the table below to resolve issues related to detected artifacts.



You may need to rescan a slide to resolve some issues with artifacts. **However, rescanned slides are not re-evaluated by Aperio iQC DX Software and require manual quality verification.**

Artifact detected	Resolution
Out of focus	Use the visual location indicator to find the out-of-focus regions. Rescan the slide.
Missing and clipped tissue	Rescan the slide.
Image striping	Rescan the slide.
Air bubbles	Use the visual location indicator to find the air bubbles. Replace the coverslip, and rescan the slide.
Pen marks	Clean the coverslip, and rescan the slide.

4.6 Settings

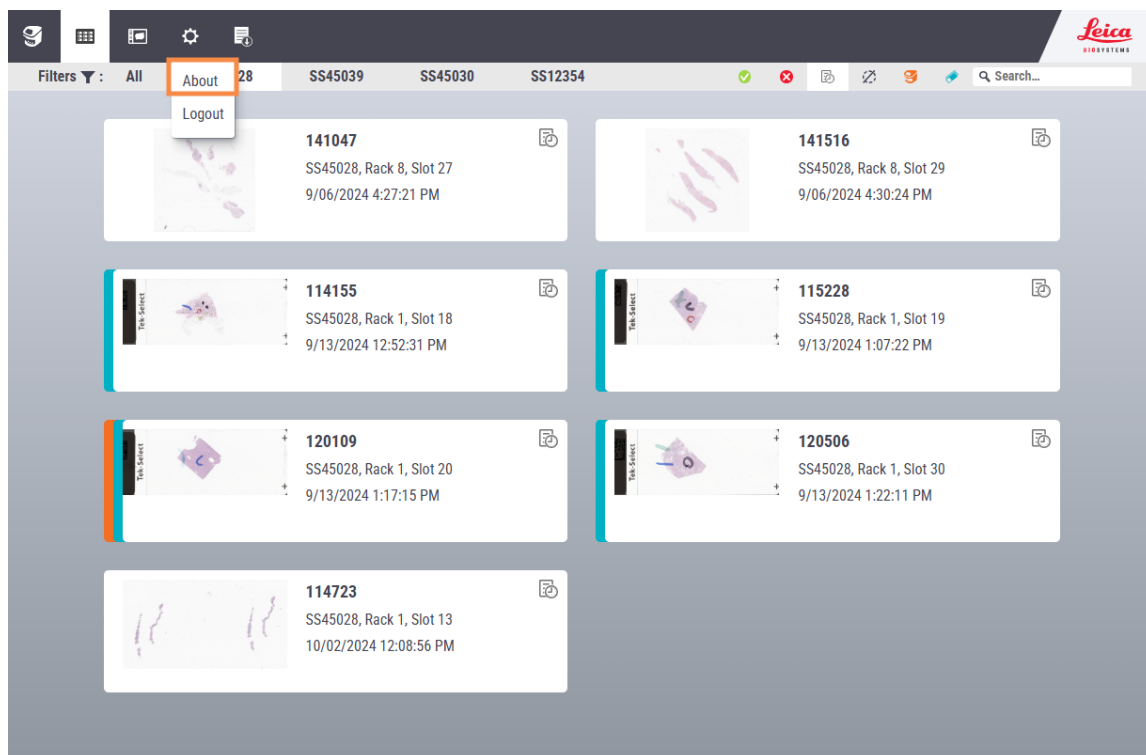
With the Settings function, you can view product details, log out, and adjust artifact thresholds (Lab Admin role only).

For details about logging out, see [4.8 Logging out](#).

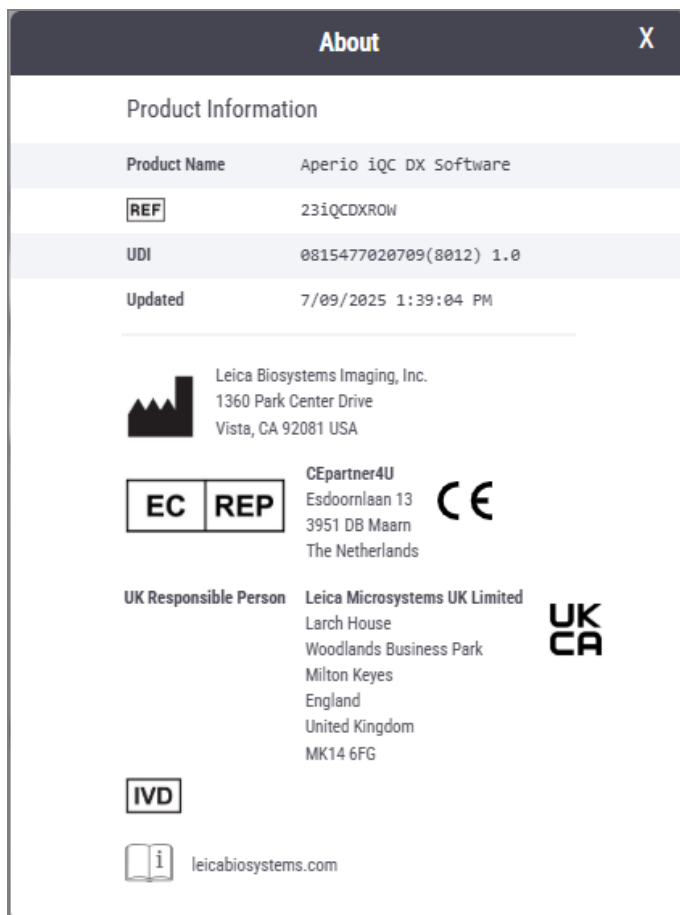
4.6.1 Viewing the **About** window

View details about Aperio iQC DX Software as follows:

- 1 Click the Settings (gear) icon in the upper-left corner of the screen.
- 2 Click **About**.



The **About** window opens. It shows details such as the Aperio iQC DX version, and revision.



4.6.2 Adjusting artifact threshold settings



CAUTION: Ensure that you set thresholds to obtain the results you expect to see. Be aware that if a threshold is set too high, the Aperio iQC DX Software may fail to identify legitimate artifacts.

Periodically confirm the threshold settings.



The artifact threshold adjustment is restricted to Lab Admin users only.

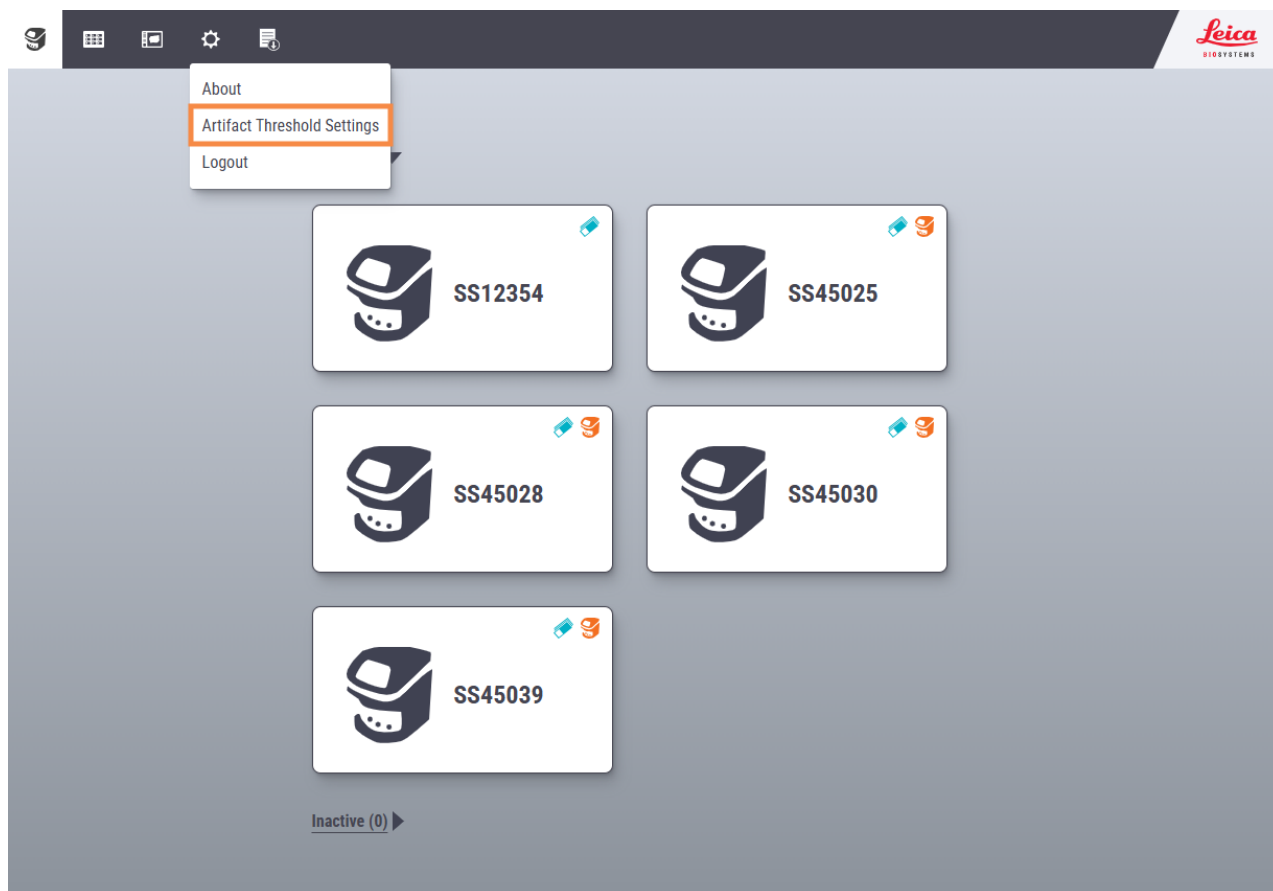


If several users are simultaneously adjusting an artifact threshold setting, the final setting will reflect that of the first user to save their change.

To adjust the threshold settings that Aperio iQC DX uses to detect artifacts, follow these steps. The threshold setting is applied to new scanned slides only, not already scanned slides.

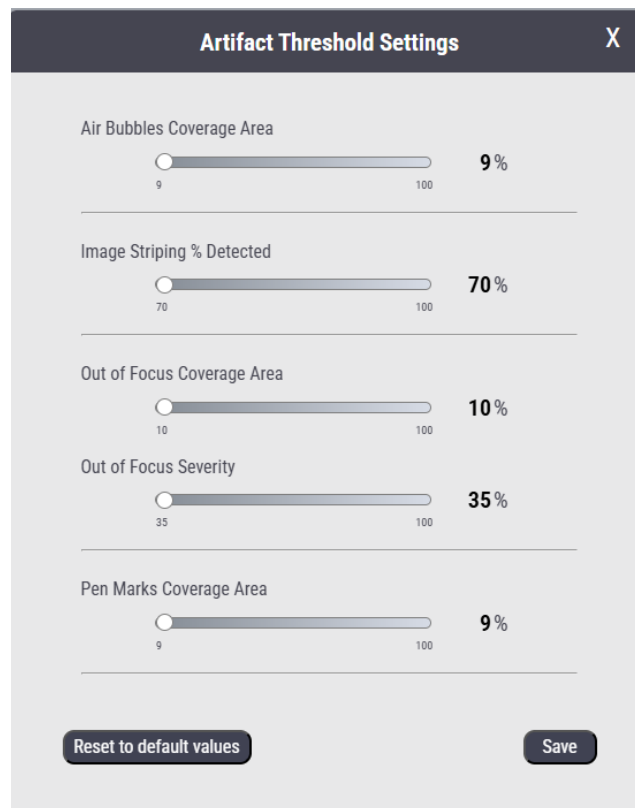
For details about the artifact threshold settings, see [3.4.3 Artifact threshold settings](#).

- 1 Click the Settings (gear) icon in the upper-left corner of the screen.
- 2 Click **Artifact Threshold Settings**.



- 3 The **Artifact Threshold Settings** window opens, showing the algorithms with artifact threshold adjustments and their current settings.

Adjust any desired settings by clicking and dragging the pointer on the adjustment bar. The lower the artifact threshold, the more sensitive the algorithm is. For details about how threshold settings work, see [3 Principles of operation](#).



- 4 Click **Save**.

4.7 Exporting list of rejected iQC slides



If you are unable to export the list of rejected slides, make sure that you have selected the correct target directory and that the directory contains adequate space. Also, ensure that you have the necessary permissions to save to the directory.

You can export a list of rejected slides, in CSV (comma-separated values) format, for import into spreadsheets. The CSV file includes the slide identifier; scanner identifier, rack and slot number; reason for rejection (digital versus histological artifact); as well as any comments you have entered.

To export the list, click the Export icon in the upper-left corner of the screen: The file is automatically downloaded.



Only slides that were scanned within the last 7 days are available for review and export.

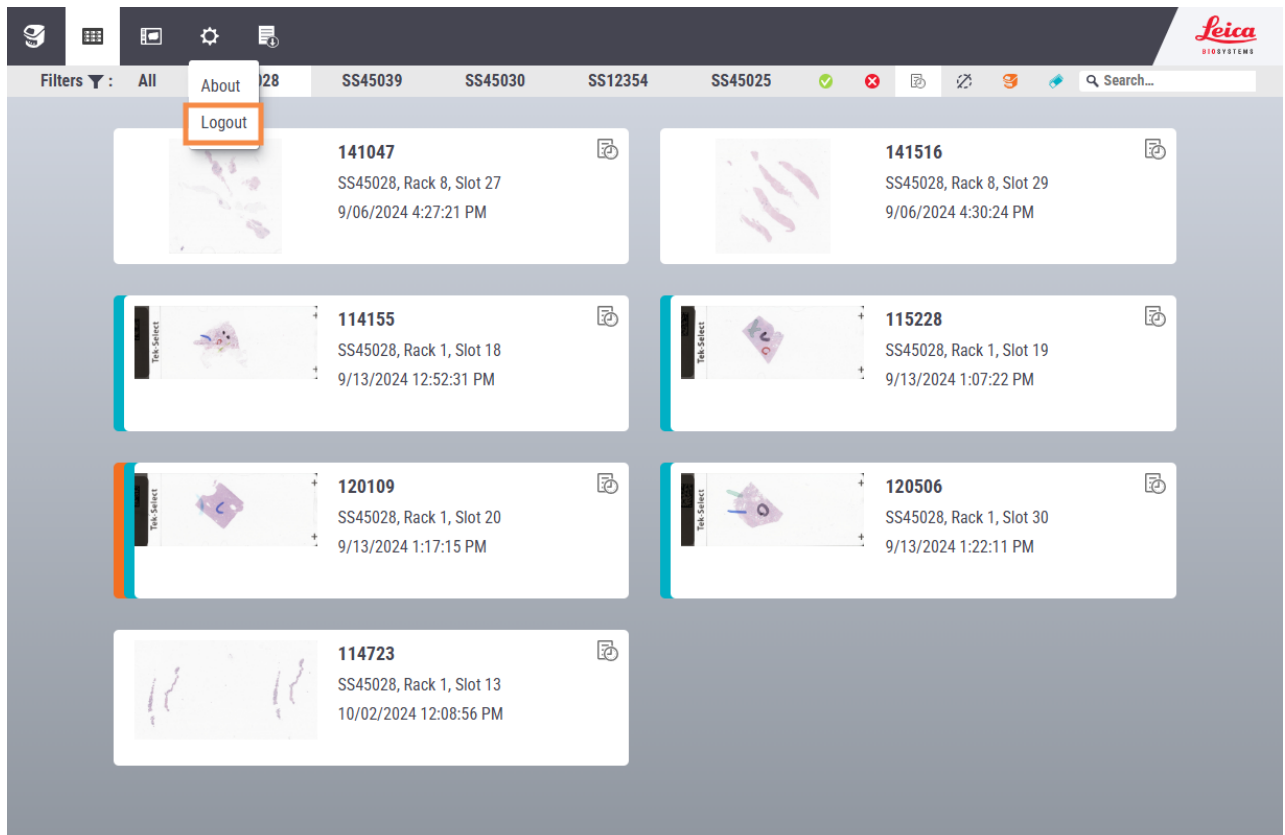
4.8 Logging out



After 30 minutes of inactivity, a user is automatically logged out.

To log out of the Apero iQC DX, follow these steps:

- 1 Click the Settings (gear) icon in the upper-left corner of the screen
- 2 Click **Logout**.



4.9 Viewing iQC results on the scanner console

The Apero GT scanner console indicates slides that are flagged for artifacts. For details, see the scanner user's guide

5

Troubleshooting

Troubleshoot Aperio iQC DX issues from symptoms or error messages. Some issues may require assistance from your lab IT administrator.

If these troubleshooting steps don't resolve the issue, contact Leica Biosystems for assistance.

5.1 Symptom-based troubleshooting



Results should be visible on the Aperio iQC DX dashboard within 30 minutes after scanning is completed. If results aren't visible within that time, troubleshoot the issue from the tables below. If you can't resolve the issue, contact Leica Biosystems for assistance.

The tables below list possible reasons why results don't appear and suggest some more detailed corrective actions to take or troubleshooting steps to help pinpoint the root cause.

5.1.1 End-user quality control issues

Symptom	Potential cause	Suggested action
Software detected the artifact when not present (false positive)	Slides are of insufficient quality for digitization	Manually review the WSI.
	Faint or insufficiently stained tissue	Manually review the WSI.
	Insufficient tissue size	Manually review the WSI.
	Algorithm threshold settings are inappropriate	Manually review the WSI. Working with your lab administrator, review and adjust the artifact threshold settings.
Software failed to detect the artifact when expected (false negative)	Slides are of insufficient quality for digitization (that is, they contain dust, debris)	Manually review the WSI.
	Tissue is occluded by artifacts	Manually review the WSI.
	Faint or insufficiently stained tissue	Manually review the WSI.
	Insufficient tissue size	Manually review the WSI.
	Algorithm threshold settings are inappropriate	Manually review the WSI. Working with your lab administrator, review and adjust the artifact threshold settings.
	Missing/Clipped tissue algorithm incorrectly detected the tissue region.	Manually review the WSI.
	Faint image striping	Manually review the WSI.
	Tissue finder failed to detect the tissue region because of dust, dirt, debris, faint staining, etc., on the slide	Manually review the WSI.
Software displayed incorrect localization	The software misidentified insufficient regions within the slide	Manually review the WSI.
	The software misidentified extraneous regions within the slide	Manually review the WSI.

5.1.2 System/network issues

Symptom	Potential cause	Suggested action
iQC results do not display on scanner console OR scanned WSI is not available in iQC	Network error (Communication between iQC and connected scanner interrupted or misconfigured)	Ensure that SAM is correctly configured for iQC. (See the <i>Aperio SAM DX IT Manager and Lab Administrator Guide</i> .) Work with your IT administrator as needed. Contact Leica Biosystems for support.
Unacceptable processing time. Results aren't visible/available within the target time range	Large backlog of unprocessed images	Ensure that the system meets the system requirements listed in <i>Aperio iQC DX Software Specifications</i> . Work with your IT administrator as needed. Contact Leica Biosystems for support.
	Network storage out of disk space	Ensure that the system meets the system requirements listed in <i>Aperio iQC DX Software Specifications</i> . Work with your IT administrator as needed. Contact Leica Biosystems for support.
iQC is unable to process	Hardware malfunction or misconfigured installation with insufficient/inappropriate system or GPU resources	Ensure that the system meets the system requirements listed in <i>Aperio iQC DX Software Specifications</i> . Work with your IT administrator as needed. Contact Leica Biosystems for support.

5.2 Error flags

Use this table to identify and resolve errors indicated by an error flag on the dashboard.



Meaning	Cause	Suggested action
Unacceptable processing time	Process hung—deadlock for resource acquisition	Ensure that the system meets the system requirements listed in <i>Aperio iQC DX Software Specifications</i> . Work with your IT administrator as needed. Contact Leica Biosystems for support.
	Processing timeout due to large files	Ensure that the system meets the system requirements listed in <i>Aperio iQC DX Software Specifications</i> . Work with your IT administrator as needed. Remove glass slide from rack, reload, and rescan. Contact Leica Biosystems for support.
	Hardware malfunction or misconfigured installation with insufficient/inappropriate system or GPU resources	Ensure that the system meets the system requirements listed in <i>Aperio iQC DX Software Specifications</i> . Work with your IT administrator as needed. Contact Leica Biosystems for support.
	Server malfunction or deviation from install configuration (temporarily insufficient system or GPU resources)	Ensure that the system meets the system requirements listed in <i>Aperio iQC DX Software Specifications</i> . Work with your IT administrator as needed. Contact Leica Biosystems for support.

6

Datasets

For the development and validation of the Aperio iQC DX Software, datasets comprising whole slide images (WSIs) and their corresponding ground truth annotations were collected. The WSIs were generated by Aperio GT series scanners. The ground truth was manually identified on WSIs by eligible experts following specified annotation protocols. Only annotated ground truth data was used to train and test the algorithms.

6.1 Verification and validation datasets

Comprehensive datasets representative of the device's intended use were used for verification and validation (V&V) studies. The datasets included 2 stain types (Hematoxylin & Eosin and Immunohistochemistry), 12 distinct tissue types, biopsies and resections, variability in tissue placement, and both benign and malignant tissue samples. The 12 tissue types are breast, colon, kidney, liver, lung, prostate, brain, lymph node, thyroid, pancreas, skin, and bladder.

For further details about V&V studies and the study results, see Sections 6 and 7.

WSIs from the histology glass slides were generated by Aperio GT scanners. WSI counts for the studies are shown in [Table 6-1](#) and [Table 6-2](#).

Table 6-1: Verification and validation data scanned by Aperio GT 450 DX Scanner

Artifact	Total WSIs Count	Positive WSIs Count	Negative WSIs Count	H&E WSIs Count	IHC WSIs Count
Missing and Clipped Tissue	2568	1284	1284	858	1710
Image Striping	2222	1167	1055	660	1562
Out of Focus	924	221	703	414	510
Air Bubble	2134	883	1251	688	1446
Pen Mark	2478	1376	1102	935	1543

Table 6-2: Verification and validation data scanned by Aperio GT 180 DX Scanner

Artifact	Total WSIs Count	Positive WSIs Count	Negative WSIs Count	H&E WSIs Count	IHC WSIs Count
Missing and Clipped Tissue	576	288	288	192	384
Image Striping	439	158	281	142	297
Out of Focus	486	243	243	231	255
Air Bubble	645	190	455	201	444
Pen Mark	424	142	282	144	280

Performance when multiple artifacts are present on the WSI was also evaluated to demonstrate the robustness of Aperio iQC DX Software. The multiple artifacts introduce greater complexity than the single artifacts and provide a more realistic representation of real-world performance. To achieve this, WSIs containing double, triple, quadruple and quintuple artifacts were used. The multiple artifact dataset breakdown is included in Table 6-3 - Table 6-4. The dataset listed in Table 6-3 was used to evaluate the performance of missing and clipped tissue while Table 6-4 was used to evaluate the performance of air bubbles, image striping, out-of-focus, and pen marks. Table 6-5 shows the positive and negative WSI counts of each artifact used in multiple artifacts in the Analytical Study.

Table 6-3: Verification and validation dataset – WSI counts in multiple artifacts analytical study (Performance of Missing and Clipped Tissue Algorithm)

Total WSIs	Double artifacts WSIs	Triple artifacts WSIs	Quadruple artifacts WSIs	Quintuple artifacts WSIs
505	172	132	138	63

Table 6-4: Verification and validation dataset – WSI counts in multiple artifacts analytical study (Performance of Air Bubbles, Image Striping, Out of Focus, and Pen Marks Algorithms)

Total WSIs	Double artifacts WSIs	Triple artifacts WSIs	Quadruple artifacts WSIs
522	241	106	175

Table 6-5: Verification and validation dataset – Positive and negative WSI counts in multiple artifacts Analytical Study

Artifact	Total WSIs	Positive WSIs	Negative WSIs
Missing and Clipped Tissue	505	305	200
Image Striping	522	440	82
Out of Focus	522	368	154
Air Bubbles	522	308	214
Pen Marks	522	384	138

Aperio iQC DX Software generates the visualization of detected artifact regions for Missing and Clipped Tissue, Out of Focus, and Air Bubbles. A localization performance study was conducted to quantitatively evaluate Aperio iQC DX Software’s visualization performance in indicating the location of the artifacts on the WSI. The WSI counts for the localization performance study are shown in [Table 6-6](#).

Table 6-6: Distribution of WSIs per artifact for the Localization validation dataset

Artifact	WSIs count
Missing and Clipped Tissue	1988
Out of Focus	67
Air Bubbles	60

The Precision Study evaluated the repeatability and reproducibility of Aperio iQC DX Software in its ability to detect artifacts. In this study, each artifact detection model was tested separately, thereby ensuring test results are attributable solely to that model. In the precision study, the dataset was comprised of 350 WSIs: 50 WSIs containing an artifact for each artifact (positive cases), 50 WSIs containing multiple artifacts (positive cases), and 50 WSIs containing no artifacts (negative cases). The slide counts for precision study are shown in [Table 6-7](#). For further details about the Precision Study and the study results, see Section 6.

Table 6-7: Distribution of WSIs per artifact for precision study

Artifact	WSIs count
Out of Focus	50
Air Bubbles	50
Pen Marks	50
Missing Tissue	50
Image Striping	50
Multiple artifacts	50
No artifact	50

7

Aperio iQC DX Software Precision Study

This section presents the precision study design and results. The precision study evaluated the repeatability and reproducibility of Aperio iQC DX Software in its ability to detect artifacts. In this study, each artifact detection model was tested separately thereby ensuring test results are attributable solely to that algorithm.

Precision of Aperio iQC DX Software was evaluated for both single artifacts and multiple artifacts.

7.1 Precision Study

Two studies were conducted to assess precision: Intra-System Study (within systems) and Inter-System (between systems).

Intra-System precision: to evaluate repeatability. WSIs created using Aperio GT 450 DX Scanners were processed three separate times, using a single Aperio iQC DX system, creating three separate Aperio iQC DX Software inference results for each artifact. The agreement rate between inference results for each processing run has been calculated (see [Table 7-2](#)) and met or exceeded the primary endpoints in [Table 7-1](#).

Inter-System precision: to evaluate reproducibility, WSIs created using Aperio GT 450 DX scanners were processed by three different Aperio iQC DX Software systems and Aperio iQC DX Software inference results were generated by each system for each artifact to assess the inter-system precision. The agreement rate between the inference results from each system was calculated (see [Table 7-2](#)) and met or exceeded the primary endpoints in [Table 7-1](#).

Table 7-1: Precision primary endpoints

Primary endpoints (precision study)	Acceptance criteria	Sample size
Overall percent agreement (OPA), Positive Percent Agreement (PPA), Negative Percent Agreement (NPA) (intra-system, intersystem)	Lower bound of the 95% CI must be \geq 85%	\geq 300 WSIs (50 WSIs per artifact x 5 artifacts + 50 normal WSIs)

For the precision study, each Aperio iQC DX system was deployed across multiple web environments representative of typical clinical deployment. This configuration allowed assessment of intra-system precision (repeatability within a single system) and intersystem precision (variability across different systems).

Dataset: All test runs conducted during the precision study used the same WSI distribution dataset. The precision study was completed using a subset of the verification and validation dataset described above in section 6. Three hundred fifty (350): 50 WSIs containing the specific artifact for each of 5 artifacts in scope (positive cases); 50 WSIs containing multiple artifacts (positive cases); 50 WSIs containing no artifacts (negative cases) shown in [Table 6-7](#).

Analysis and statistics: The pairwise method was used to obtain overall percentage agreement (OPA), positive percent agreement (PPA), negative percent agreement (NPA) for each precision sub-test.

7.2 Precision Study results

Aperio iQC DX Software demonstrated 100% agreement across repeated runs (Intra-System precision) and across different systems (Inter-System precision).

Table 7-2: Intra-system precision performance of Aperio iQC DX Software

	WSIs	OPA (%)	95% CI (%)	PPA (%)	95% CI (%)	NPA (%)	95% CI (%)
Run 1 vs Run 2	350	100	(98.91, 100)	100	(98.74, 100)	100	(92.86, 100)
Run 1 vs Run 3	350	100	(98.91, 100)	100	(98.74, 100)	100	(92.86, 100)
Run 2 vs Run 3	350	100	(98.91, 100)	100	(98.74, 100)	100	(92.86, 100)

Table 7-3: Inter-system precision performance of Aperio iQC DX Software

	WSIs	OPA (%)	95% CI (%)	PPA (%)	95% CI (%)	NPA (%)	95% CI (%)
System 1 vs System 2	350	100	(98.91, 100)	100	(98.74, 100)	100	(92.86, 100)
System 1 vs System 3	350	100	(98.91, 100)	100	(98.74, 100)	100	(92.86, 100)
System 2 vs System 3	350	100	(98.91, 100)	100	(98.74, 100)	100	(92.86, 100)

8

Aperio iQC DX Analytical Study

This section presents the performance study design and results for analytical accuracy, analytical sensitivity, analytical specificity, and localization accuracy.

The primary method for analytical performance testing is through the execution of formal verification and validation protocols. To ensure the algorithms perform consistently across different tissue types, scanners, and scan settings, a diverse verification and validation dataset was assembled, as described in section 6.

8.1 Analytical Study

Analytical studies were performed to demonstrate the performance characteristics of Aperio iQC DX Software in detecting image artifacts, including air bubbles, image striping, pen marks, and missing or clipped tissue. These studies evaluated analytical accuracy, sensitivity, and specificity for each artifact type individually and under conditions where multiple artifacts were present.

In addition, the software provides visualization of detected regions for missing or clipped tissue, out-of-focus areas, and air bubbles. Accordingly, an analytical localization study was conducted to verify the software's capability to accurately identify and localize these artifacts within WSIs.

Table 8-1: Analytical performance

Analytical performance metric	Objective	Acceptance criteria	Results from V&V testing
Analytical accuracy in the single artifact scenario	Measure the algorithms' ability to detect single artifacts (i.e., Out of Focus, Missing and Clipped Tissue, Image Striping, Air Bubbles, and Pen Marks) on WSIs.	Analytical accuracy of algorithms is $\geq 90\%$.	Missing and Clipped Tissue: 93.73% Image Striping: 99.82% Out of Focus: 97.29% Air Bubbles: 95.60% Pen Marks: 99.19%
Analytical accuracy in the multiple artifact scenario	Measure the AI algorithms' ability to detect artifacts (i.e., Out of Focus, Missing and Clipped Tissue, Image Striping, Air Bubbles, and Pen Marks) on WSIs.	Analytical accuracy of AI algorithms is $\geq 90\%$.	Missing and Clipped Tissue: 93.27% Image Striping: 99.43% Out of Focus: 95.79% Air Bubbles: 95.40% Pen Marks: 97.70%

Table 8-1: Analytical performance (continued...)

Analytical performance metric	Objective	Acceptance criteria	Results from V&V testing
Analytical sensitivity in the single artifact scenario	Measures the algorithms' ability to correctly identify positive WSIs.	Analytical sensitivity is \geq 90%.	Missing and Clipped Tissue: 94.10% Image Striping: 99.74% Out of Focus: 91.94% Air Bubbles: 93.20% Pen Marks: 99.13%
Analytical sensitivity in the multiple artifact scenario	Measures the algorithms' ability to correctly identify positive WSIs.	Analytical sensitivity is \geq 90%.	Missing and Clipped Tissue: 93.11% Image Striping: 99.32% Out of Focus: 96.47% Air Bubbles: 92.53% Pen Marks: 99.48%
Analytical. specificity in the single artifact scenario	Measures the algorithms' ability to correctly identify negative WSIs.	Analytical specificity is \geq 90%.	Missing and Clipped Tissue: 92.68% Image Striping: 99.91% Out of Focus: 98.44 Air Bubbles: 97.28% Pen Marks: 99.27%
Analytical specificity in the multiple artifact scenario	Measures the algorithms' ability to correctly identify negative WSIs.	Analytical specificity is \geq 90%.	Missing and Clipped Tissue: 93.50% Image Striping: 100% Out of Focus: 94.16% Air Bubbles: 99.53% Pen Marks: 92.75%
Intersection over union (IoU)	Measures the ability of the Missing and Clipped Tissue algorithm to correctly localize the positive (artifact) areas.	90% of WSIs achieve IoU \geq 70%.	Missing and Clipped Tissue localization test has 90.74% cases achieved IoU \geq 70%.
Localization sensitivity and specificity	Measures the ability of the Out of Focus and Air Bubbles algorithms to correctly localize the positive and negative (non-artifact) areas.	Localization sensitivity and specificity is \geq 90%.	Out of Focus: Sensitivity: 96.99% Specificity: 99.72% Air Bubbles: Sensitivity: 91.29% Specificity: 96.01%

Glossary

Abbreviation	Meaning
AI	Artificial intelligence
AoS	Authentication and authorization server
API	Application programming interface
CSV	Comma-separated values
DICOM	Digital Imaging and Communications in Medicine, a standard protocol for the management and transmission of medical images and related data
FFPE	Formalin-fixed and paraffin-embedded, a type of surgical pathology slides.
H&E	Hematoxylin and eosin, which are stains used to highlight tissue structures in microscopic images.
IHC	Immunohistochemistry
intended purpose	Used in Europe. The use for which a device is intended, under the In Vitro Diagnostic Medical Devices Regulation (IVDR), (Regulation (EU) 2017/746).
IVD	In vitro diagnostics
JSON	JavaScript Object Notation, a data interchange format. This format is used for metadata files.
mTLS	Mutual Transport Layer Security, an extension of the standard TLS (Transport Layer Security) protocol that provides mutual authentication between the client and the server.
PHI	Protected Health Information
PII	Personally Identifiable Information
SAM	Scanner Administration Manager
SSL	Secure Sockets Layer
SVS	ScanScope Virtual Slide
TLS	Transport Layer Security
VM	Virtual machine
WSI	Whole slide image