AI-Powered Slide Quality Control Workflows for Life Science and Clinical Applications

A reliable and sound pathology workflow requires high-quality, artifact-free slides. However, many steps in the slide generation and whole slide image (WSI) creation process can introduce artifacts, from microtomy and staining to coverslipping and scanning. These imperfections, created by dust, out-of-focus areas, tissue folds, pen marks, and coverslip issues, can not only affect the appearance of a slide, they can also interfere with clinical reporting and degrade the performance of image analysis algorithms. In some cases, they may render WSIs diagnostically useless and lead to the depletion of valuable tissue samples.

The current method of manual slide quality control is inefficient and ineffective. Manual review requires a significant amount of staff time and resources. Most laboratories limit their review to a small subset of all slides created. Slides with artifacts that are not reviewed pass downstream to the pathologist or researcher, where they can cause delays and diagnostic errors.

Fortunately, the slide digitization process creates an opportunity to introduce automated slide quality control tools like SlideQC BF, the artificial intelligence (AI) powered quality control algorithm from Indica Labs. AI in this context refers to advanced computational algorithms capable of processing and interpreting large amounts of visual data with accuracy and speed. SlideQC BF uses AI to scan and analyze all WSIs within a clinical workflow or large research project for artifacts. It can automatically triage slides that breach a laboratory-defined artifact threshold for rescan or recut and exclude artifacts from downstream image analysis for all analyzed slides. SlideQC BF fundamentally alters the quality control process in a way that enhances efficiency, improves the quality of diagnostic, research, and archival material, and future-proofs labs.

In this application note, we showcase the life science and clinical quality control applications of SlideQC BF. This automated, AI-powered quality control algorithm for brightfield H&E and IHC WSIs is available for life science use cases in HALO AI and can be seamlessly deployed in the HALO AP® enterprise digital pathology platform for clinical applications. **Figure 1** illustrates common artifacts found in WSIs and the associated markups generated by SlideQC BF, highlighting its ability to accurately identify and annotate artifacts.

Importance of Slide Quality Control in Digital Pathology

Slide artifacts create a myriad of problems for downstream research and clinical applications. In one study analyzing a database of digitized WSIs, nearly 10% of all scanned slides were found to have artifacts that affected interpretation.[1] To ensure the quality of diagnostic and research evaluations, slides must be as free from artifacts as possible, or the conclusions drawn from these assessments may be called into question. For AI and image analysis algorithms, the presence of artifacts can lead to incorrect results. Therefore, quality control is of the utmost importance and has widespread effects on laboratory workflows.

Traditionally, slide quality control is performed by histotechs or other laboratory personnel on a small selection of all slides generated, usually using low power magnification. With only a small portion of slides being assessed, many artifacts escape detection and are passed to downstream applications and analysis. Consequently, most slides are not reviewed for quality until they

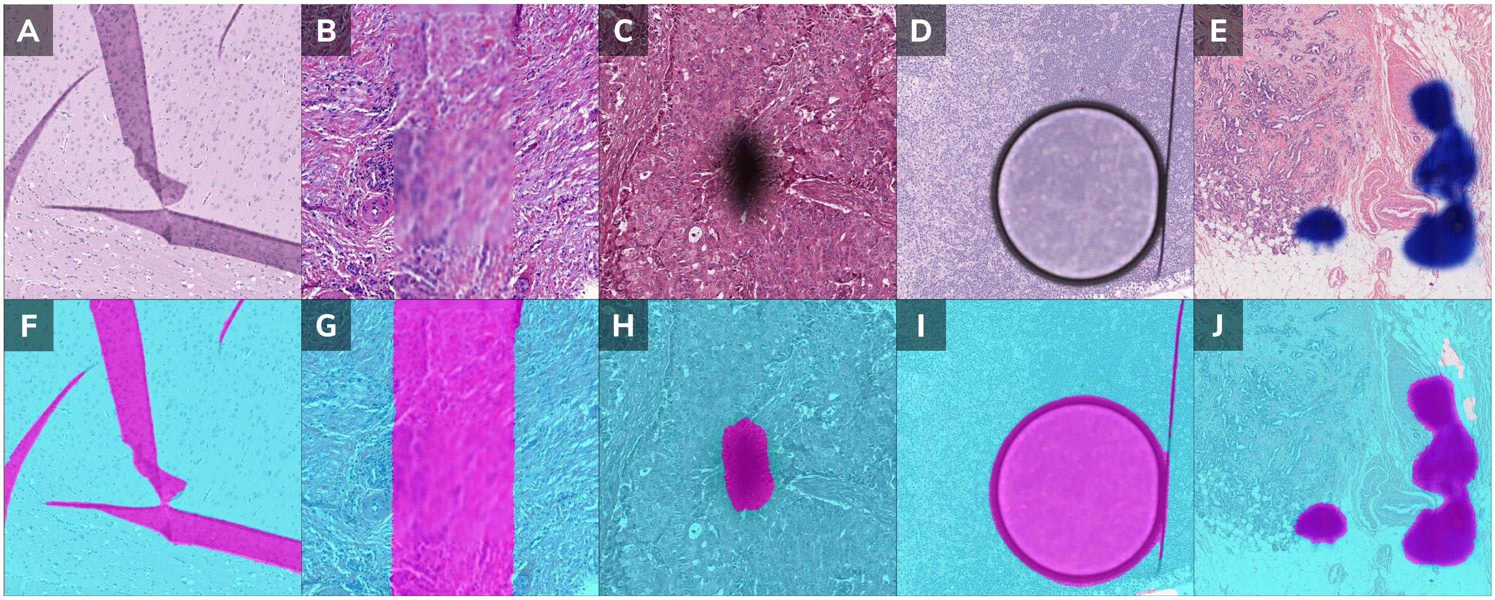

Figure 1. Common slide artifacts before and after analysis by SlideQC BF. **A-E**: Tissue folds, out-of-focus areas, dust, air bubbles, and pen marks. **F-J**: Analysis markup by SlideQC BF, with cyan indicating acceptable, artifact-free tissue and magenta indicating annotated artifacts.

are seen by the pathologist at sign-out, where they may cause diagnostic delays and affect interpretation.

Flagging slides for further review and potential rescan or recut earlier in the process would save time and resources. For small specimens where blocks are easily exhausted, it would be ideal to be able to exclude artifacts from analysis without the need to cut a new slide. An optimal solution would also allow the threshold for whether a recut is performed to be adjustable on a per-lab or per-study basis.

SlideQC BF can identify artifacts in both H&E and IHC images, annotate them, and pass these annotations to downstream analysis for exclusion. Slides with a laboratory-determined percentage of area affected by artifacts can be flagged to be reprocessed or recut before the case is ever released to the pathologist. As only the slides identified and flagged by SlideQC BF require intervention from laboratory staff, this leads to a significant time savings while ensuring cases are ready for sign-out the moment they are viewed by the pathologist.

Research Applications of SlideQC BF

For life science applications, SlideQC BF is integrated with HALO AI, a suite of trainable deep learning networks for the HALO® image analysis platform. SlideQC BF utilizes a chained classifier workflow, illustrated in **Figure 2**, where a tissue detection algorithm is followed by an artifact detection algorithm. Initially, the tissue detection algorithm classifies areas into tissue and background, directing artifact analysis only to the tissue present on the slide. The artifact detection algorithm then analyzes the tissue class.

In HALO AI, SlideQC BF outputs data including Total Classified Area, Acceptable Tissue Area, Artifact Area, and the percentage of tissue classified as Acceptable or Artifact. It also provides Object Data, highlighting the perimeter, area, and coordinates of each artifact. SlideQC BF can be trained for highly specific use cases and workflows with a variety of unique artifact types using HALO AI, making it adaptable to the unique needs and challenges of each lab. This workflow allows researchers to conduct downstream image analysis on artifact-free slide material, ensuring that artifacts do not compromise the quality of their data and results.

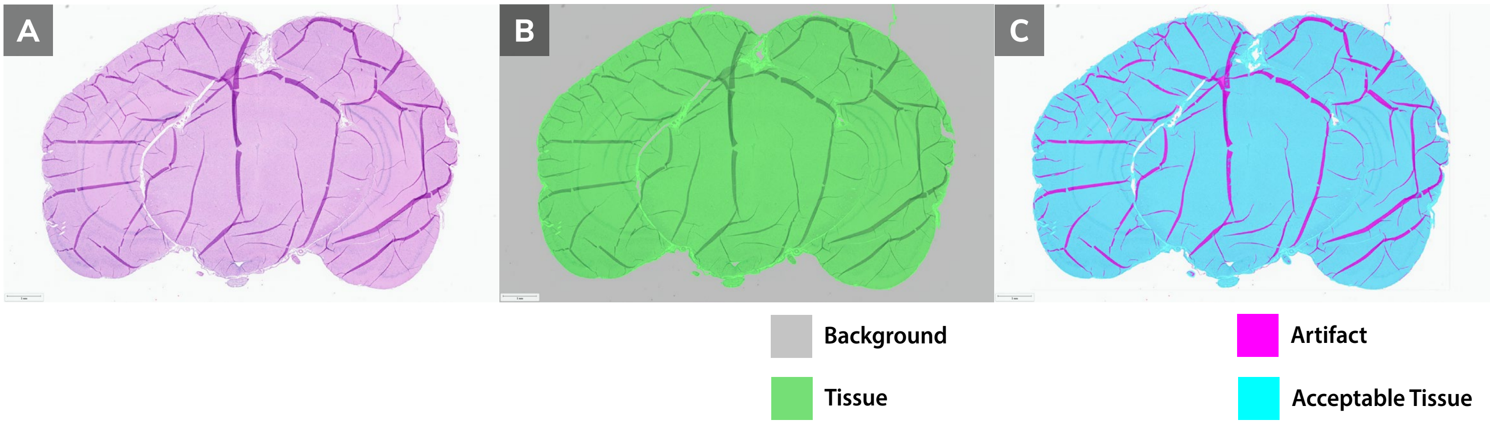

Figure 2. SlideQC BF workflow in HALO AI. **A**. WSIs are scanned. **B**. Tissue detection separates background class (gray) from tissue class (green). **C**. Artifact detection on the tissue class separates artifacts (magenta) from acceptable, artifact-free tissue (cyan).

Within HALO modules, SlideQC BF can be added as a classifier before workflows such as Multiplex IHC, resulting in the entire analysis running as a single step. The resulting analysis is performed exclusively on areas classified as artifact-free, acceptable tissue, as demonstrated in **Figure 3**. In this figure, large tissue folds at the top and bottom of the image are automatically excluded from a Multiplex IHC analysis.

A classifier pipeline feature in HALO AI 4.0 enables users to chain classifiers together themselves. For example, SlideQC BF can analyze a slide, and another classifier can then be automatically run on only the acceptable, artifact-free tissue output of SlideQC BF with no manual annotation input required. An example of a chained SlideQC BF and DenseNet tissue classifier is shown in **Figure 4**.

The chained classifier feature empowers users to create customized workflows and run multiple analyses in a single automated step, significantly enhancing efficiency and precision. This capability not only streamlines the analytical process but also ensures that only high-quality, artifact free data is used for critical research evaluations. By harnessing the power of SlideQC BF within a seamless, automated workflow, laboratories can achieve unprecedented quality levels while simultaneously saving time and resources.

Within HALO Link, the collaborative image management platform from Indica Labs, users can connect to HALO and HALO AI to utilize SlideQC BF, allowing artifact thresholds to be set on a per-lab or per-study basis. HALO Link provides tools for evaluating the particular artifact patterns

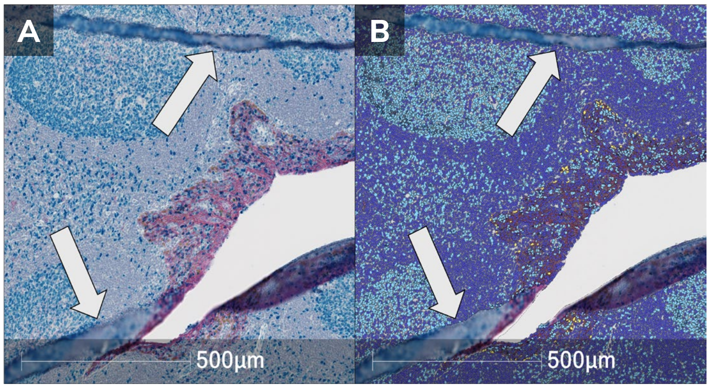

Figure 3. Example of multiplex IHC image analysis with the SlideQC BF tissue classifier. **A**. WSI with tissue folds present (white arrows). **B**. Multiplex IHC image analysis with embedded SlideQC BF tissue classifier, where analysis is performed only on the artifact-free tissue class.

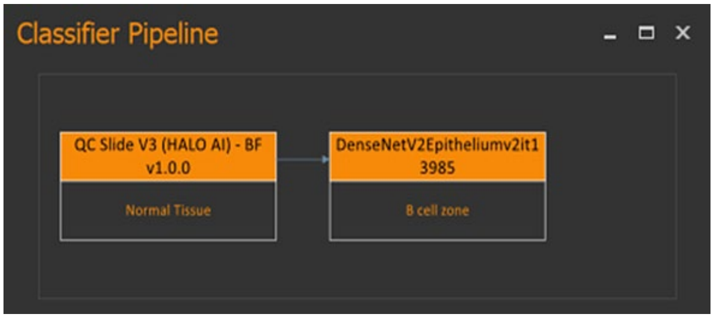

Figure 4. Constructing a HALO AI classifier pipeline with SlideQC BF. SlideQC BF can be chained with other classifiers, using the algorithm output to guide downstream analysis. In this example, the "Normal Tissue" output from SlideQC BF is fed into a DenseNet trained to identify the B cell zone, creating an overall output that results in the identification of only the B cell zones in the tissue not affected by artifact.

of individual laboratories, including information on what stains produce the most artifacts, which tissues are the most problematic, and more. These tools enable users to home in on which artifacts are the most prevalent in their laboratory quickly and easily, with easy-to-read graphs and key statistics, as shown in **Figure 5.** This, in turn, allows labs to track and adapt their practices in real-time. With these tools, identifying problematic workflows within the lab becomes a simple process.

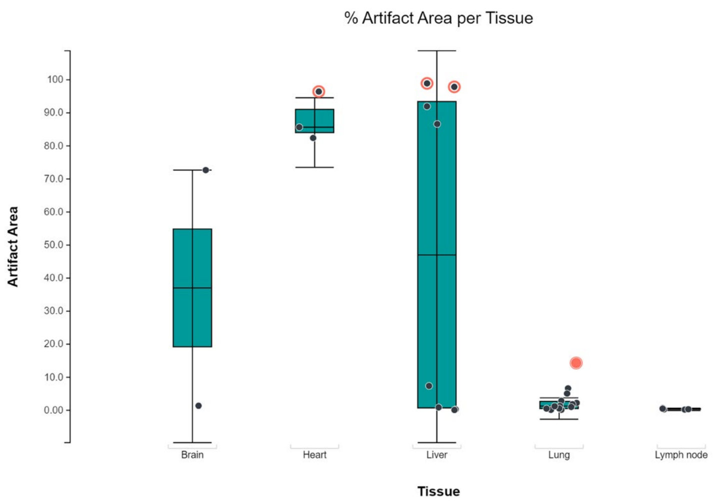

Figure 5. Analysis of artifacts based on tissue type within HALO Link. A box and whisker plot demonstrates the percentage of area affected by artifact for each brain, heart, liver, lung, and lymph node tissue.

Clinical Applications of SlideQC BF

For clinical IHC and H&E applications, SlideQC BF is indispensable. It allows all slides generated within a laboratory, not merely a selection of slides, to be scanned for artifacts and flagged for review without demanding significant investments of laboratory staff time. As shown in **Figure 6**, slides are uploaded to HALO AP® and automatically analyzed by SlideQC BF. Slides that do not exceed the laboratory-defined artifact threshold are passed along to the pathologist with their artifacts annotated. These annotations can be used by AI and image analysis tools to exclude the artifact affected areas.

Within HALO AP®, the enterprise digital pathology platform from Indica Labs, slides that exceed the laboratory-defined artifact threshold are tagged and automatically moved to a worklist for review and quality control, as shown in **Figure 7.** This

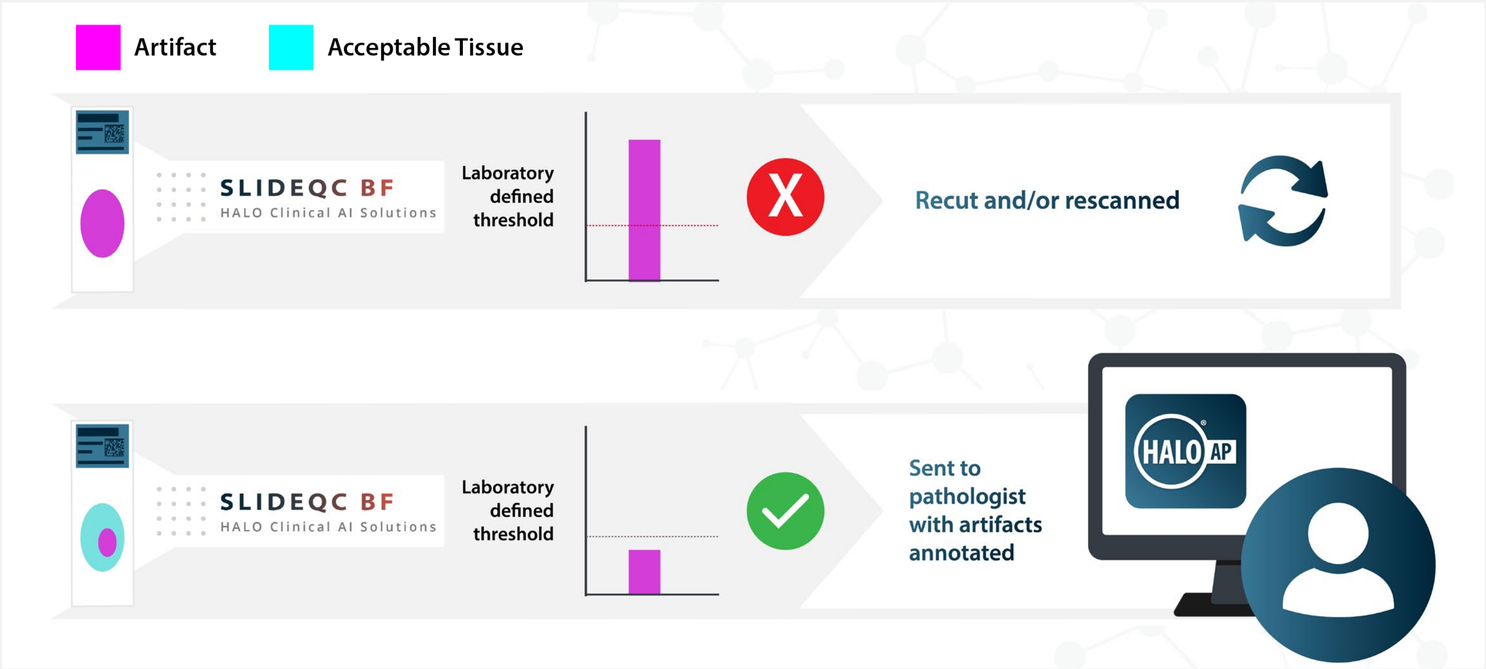

Figure 6. SlideQC BF is available for seamless deployment in HALO AP®. A high-level workflow is shown, highlighting how slides exceeding the laboratory defined artifact threshold are flagged for further processing, while slides that do not exceed the threshold are sent to the pathologist with their artifacts annotated.

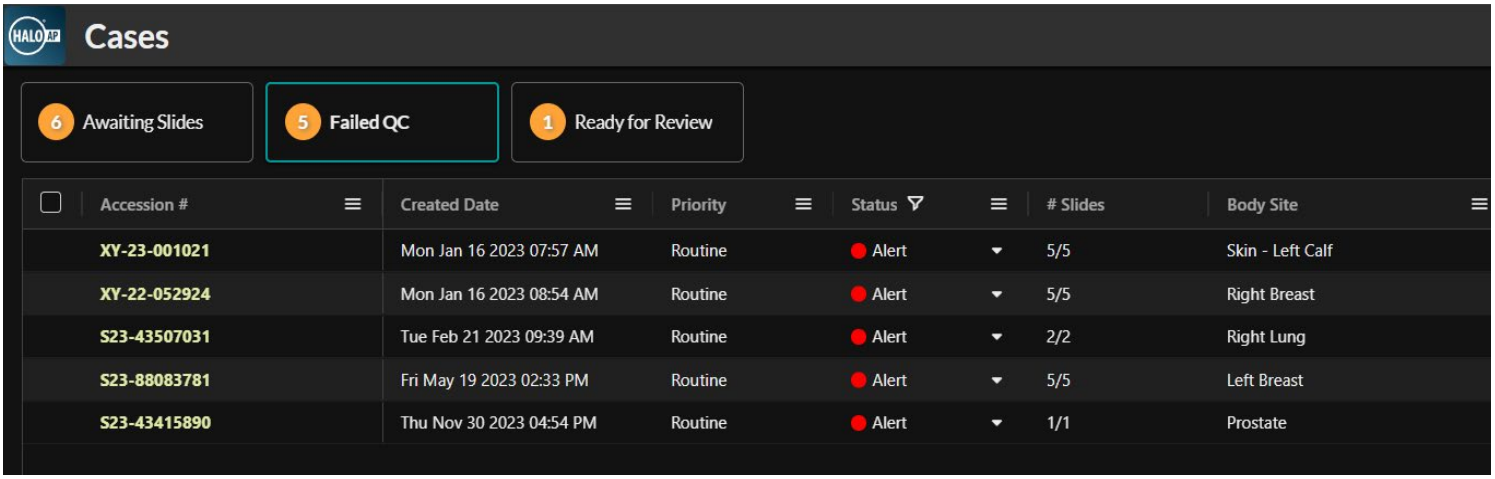

Figure 7. A worklist within HALO AP® demonstrating the auto-triage function of SlideQC BF. Slides with artifacts that breach the laboratory defined maximum are marked with "Alert" and automatically moved to the quality control worklist. Slides that have passed QC are marked as "Ready" and automatically moved to pathologist worklists for review and sign-out.

ensures staff only review slides with known artifacts, freeing them for more complex tasks.

Since SlideQC BF runs automatically once the slides are uploaded, labs can easily scale to accommodate more cases and slides. As a result, datasets as well as diagnostic and archival material will contain fewer artifacts, creating higher-quality clinical reporting and WSIs that are conducive to analysis by current and future image analysis and AI algorithms.

Validation of SlideQC BF on H&E and IHC

Analysis of SlideQC BF on an H&E and IHC external and multi-source test set, as shown in **Table 1**, demonstrates the utility of the algorithm in identifying the most common artifacts involved in slide generation. Recall represents the algorithm's ability to reliably detect all artifacts present. An algorithm that detects all artifacts has a recall of 1.0. Precision complements recall by indicating the likelihood an area identified by the algorithm as positive actually contains artifacts. An algorithm with no false positives has a precision of 1.0. F1-score represents the harmonic mean between recall and precision.

Artifact	Precision	Recall	F1-Score
Air Bubble	0.99 +/- 0.01	0.85 +/- 0.11	0.91 +/- 0.06
Debris/Dust	0.97 +/- 0.10	0.96 +/- 0.12	0.96 +/- 0.11
Folds	0.93 +/- 0.12	0.91 +/- 0.12	0.91 +/- 0.10
Pen Marks	1.00 +/- 0.00	0.99 +/- 0.04	0.99 +/- 0.02
Out-of-Focus	0.98 +/- 0.00	0.98 +/- 0.04	0.98 +/- 0.02

Table 1. SlideQC BF precision, recall, and F1-score. The results of SlideQC BF analysis on a test set of images from HistoQCRepo and the LYON19 database.2

Conclusions

An automated method of slide quality control is essential for streamlined pathology, reliable diagnostics and research, and maintaining a high-quality service to patients. SlideQC BF provides a robust solution to the challenges associated with manual slide quality control by ensuring that each slide meets a laboratory- or study-defined quality standard and by effectively removing artifacts from downstream analysis.

Automated quality control with SlideQC BF reduces the chance of error and facilitates a higher throughput of slide processing, maintaining high quality without necessitating additional investments in laboratory staff. It is the ideal solution for pathology laboratories of all types and paves the way for more consistent, reproducible, and scalable research and diagnosis.

References

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2. Swiderska-Chadaj Z, Pinckaers H, van Rijthoven M, *et al*. Learning to detect lymphocytes in immunohistochemistry with deep learning. *Medical Image Analysis*. **58**: 101547 (2019). DOI: 10.1016/j.media.2019.101547

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Regulatory Text

SlideQC BF is intended to be used as a quality control tool for whole slide images and is not regulated as a medical device in the EU/UK. SlideQC BF is for Research Use Only in the USA and is not FDA cleared for clinical diagnostic use. SlideQC BF is accessed via the HALO AP® enterprise digital pathology platform.

HALO AP® is CE-IVDR marked for in-vitro diagnostic use in Europe, the UK, and Switzerland. HALO AP® is For Research Use Only in the USA and is not FDA cleared for clinical diagnostic use. In addition, HALO AP® provides built-in compliance with FDA 21 CFR Part 11, HIPAA, and GDPR.

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