Ibex Medical Analytics Ltd.
Yael Liebes Peer, Ph.D.
Official Correspondent
101 Rokach Blvd
Tel Aviv, 6153101
Israel

January 24, 2025

Re: K241232
Trade/Device Name: Galen™ Second Read™
Regulation Number: 21 CFR 864.3750
Regulation Name: Software algorithm device to assist users in digital pathology
Regulatory Class: Class II
Product Code: QPN
Dated: May 2, 2024
Received: May 2, 2024

Dear Dr. Yael Liebes Peer:

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 System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 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 systems (QS) regulation (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

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K241232

Device Name
Galen™ Second Read™

Indications for Use *(Describe)*
Galen™ Second Read™ is a software only device intended to analyze scanned histopathology whole slide images (WSIs) from prostate core needle biopsies (PCNB) prepared from hematoxylin & eosin (H&E) stained formalin-fixed paraffin embedded (FFPE) tissue. The device is intended to identify cases initially diagnosed as benign for further review by a pathologist. If Galen™ Second Read™ detects tissue morphology suspicious for prostate adenocarcinoma (AdC), it provides case- and slide-level alerts (flags) which includes a heatmap of tissue areas in the WSI that is likely to contain cancer.

Galen™ Second Read™ is intended to be used with slide images digitized with Philips Ultra Fast Scanner and visualized using the Galen™ Second Read™ user interface.

Galen™ Second Read™ outputs are not intended to be used on a standalone basis for diagnosis, to rule out prostatic AdC or to preclude pathological assessment of WSIs according to the standard of care.

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

Preparation date:

1/24/2025

Submitter:

Ibex Medical Analytics LTD

Contact person:

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Device Information:

Device Trade Name: **Galen™ Second Read™**
Version: 3.1-US
Device Class: II
Product Code: QPN
Classification Regulation: 21 CFR.864.3750
Classification Name: Software algorithm device to assist users in digital pathology
Classification Panel: Pathology
510(k) Submission Number: K241232

Predicate device:

Device Trade Name: Paige Prostate
DeNovo Number: DEN200080

I Intended Use/Indications for Use:

Galen™ Second Read™ is a software only device intended to analyze scanned histopathology whole slide images (WSIs) from prostate core needle biopsies (PCNB) prepared from hematoxylin & eosin (H&E) stained formalin-fixed paraffin embedded (FFPE) tissue. The device is intended to identify cases initially diagnosed as benign for further review by a pathologist. If Galen™ Second Read™ detects tissue morphology suspicious for prostate adenocarcinoma (AdC), it provides case- and slide-level alerts (flags) which includes a heatmap of tissue areas in the WSI that is likely to contain cancer.

Galen™ Second Read™ is intended to be used with slide images digitized with Philips Ultra Fast Scanner and visualized using the Galen™ Second Read™ user interface.

Galen™ Second Read™ outputs are not intended to be used on a standalone basis for diagnosis, to rule out prostatic AdC or to preclude pathological assessment of WSIs according to the standard of care.

Special Conditions for Use Statement(s):

Rx - For prescription use only

For *in vitro* diagnostic (IVD) use only

II Summary of Technological Characteristics:

The Galen Second Read is an *in vitro* diagnostic medical device software, derived from a deterministic deep convolutional neural network that has been developed with digitized WSIs of H&E-stained prostate core needle biopsy (PCNB) slides originating from formalin-fixed paraffin-embedded (FFPE) tissue sections, that were initially diagnosed as benign by the pathologist.

The Galen Second Read is cloud-hosted and utilizes external accessories [e.g., scanner and image management systems (IMS)] for automatic ingestion of the input. The device identifies WSIs that are more likely to contain prostatic adenocarcinoma (AdC). For each input WSI, the Galen Second Read automatically analyzes the WSI and outputs the following:

- Binary classification of the likelihood (high/low) to contain AdC based on a predetermined threshold of the neural network output.
- For slides classified with high likelihood to contain AdC, slide-level findings are flagged and visualized (AdC score and heatmap) for additional review by a pathologist alongside the WSI.
- For slides classified as low likelihood to contain AdC, no additional output is available.

Galen Second Read key functionalities include image upload and analysis, flag slides of high likelihood to contain AdC and display of all the WSIs uploaded to the system alongside their analysis results. Flagged findings constitute a recommendation for additional review by a pathologist.

Galen Second Read is operated as follows:

1. Scanned digital images of PCNB are acquired using the designated digital pathology scanner (Philips IntelliSite Pathology Solution (PIPS) Ultra Fast Scanner (UFS)). Image and other related quality control steps are performed per the scanner instructions for use and any additional user site specifications. Upon availability of the WSI

file, the scanned digital images are automatically processed (unless contraindicated) by the Galen Second Read in the background.

2. For every slide, the Galen Second Read's algorithm calculates and outputs a tissue ratio (a measure of the amount of tissue in the image), an out-of-focus ratio (a measure of the amount of blurry tissue in the image), and in case both are within predetermined ranges, it also outputs slide-level AdC score (likelihood to contain AdC), and an associated AdC heatmap.

3. Galen Second Read is used for all slides from cases with pathologist's initial benign diagnosis. In case the slide was found by the Galen Second Read to be with high likelihood to contain AdC, the device flags for additional review by the pathologist.

4. All flagged findings are available in the Galen Second Read and the pathologist can select a patient case and open each flagged WSI for an additional review. The available information for review includes AdC score (the likelihood to contain AdC) and AdC heatmap marking the region suggestive to include cancer. The heatmap opacity can be controlled and toggled on/off to allow unobstructed reexamination. The AdC likelihood and the associated heatmap are indicative for AdC. The diagnosis may be documented in another system, e.g., a Laboratory Information System (LIS).

5. A resolution by the reviewing pathologist can be either of the following options: confirm the Galen Second Read result (alter the initial diagnosis from benign to malignant), reject the Galen Second Read result (no additional action is required) or decide that more information is needed to support diagnosis, based on pathology laboratory best practices, outside of the Galen Second Read device.

The final determination of diagnosis is made by the pathologist based on the histologic findings and/or additional tests and should not be solely based on the Galen Second Read output. The flagged findings constitute a recommendation for a second pathologist review. Pathologists should follow the SoC to obtain additional information, if needed, to render a final diagnosis.

Interoperable components intended for use with Galen Second Read and minimum system requirements are provided in **Table 1** and **Table 2**, respectively.

Table 1: WSI Scanner and Display

Manufacturer	**Model**
Philips Medical Systems Nederland B.V.	Ultra-Fast Scanner (UFS) Image Management System - Philips IMS
Display	Philips PS27QHDCR, Barco N.V. NV MDPC-8127

Table 2: Computer Environment/System Requirements

Workstation component	Specifications
Computer System	RAM: 8.0 GB or higher CPU: 1 GHz or higher
Web Browser	Google Chrome v120 or later
Operating system	Windows v10 or Mac OS v11 or higher
Network	Internet access At least 20 Mbps download speed

III Comparison with Predicate(s):

The following table summarizes the similarities and differences between the Galen Second Read and the predicate device, Paige Prostate.

Device & Predicate Device(s):	K241232	DEN200080
Device Trade Name	Galen™ Second Read™	Paige Prostate
General Device Characteristic Similarities		
Intended Use/ Indications For Use	Galen™ Second Read™ is a software only device intended to analyze scanned histopathology whole slide images (WSIs) from prostate core needle biopsies (PCNB) prepared from hematoxylin & eosin (H&E) stained formalin-fixed paraffin embedded (FFPE) tissue. The device is intended to identify cases initially diagnosed as benign for further review by a pathologist. If Galen™ Second Read™ detects tissue morphology suspicious for prostate adenocarcinoma (AdC), it provides case- and slide-level alerts (flags) which includes a heatmap of tissue areas in the WSI that is likely to contain cancer. Galen™ Second Read™ is intended to be used with slide images digitized with Philips Ultra Fast Scanner and visualized using the Galen™ Second Read™ user interface. Galen™ Second Read™ outputs are not intended to be used on a standalone basis for diagnosis, to rule out prostatic AdC or to preclude	Paige Prostate is a software only device intended to assist pathologists in the detection of foci that are suspicious for cancer during the review of scanned whole slide images (WSI) from prostate needle biopsies prepared from hematoxylin & eosin (H&E) stained formalin fixed paraffin embedded (FFPE) tissue. After initial diagnostic review of the WSI by the pathologist, if Paige Prostate detects tissue morphology suspicious for cancer, it provides coordinates (X,Y) on a single location on the image with the highest likelihood of having cancer for further review by the pathologist.Paige Prostate is intended to be used with slide images digitized with Philips UFS and visualized with Paige FullFocus WSI viewing software.Paige Prostate is an adjunctive computer-assisted methodology and its output should not be used as the primary diagnosis. Pathologists should only use Paige Prostate in conjunction with their complete standard of care evaluation of the slide image.

	pathological assessment of WSIs according to the standard of care.	
Specimen Type	PCNBs prepared from H&E stained FFPE tissue	Same
Type of Test Performed	Software device intended to identify cases initially diagnosed as benign for further review by a pathologist. The Galen™ Second Read™ provides case- and slide-level alerts (flags) supported by a slide-level heatmap, as additional information for cancerous areas of concern within the WSI, if prostate adenocarcinoma (AdC) is suspected by the device.	Software device to identify digital histopathology images of PCNBs that are suspicious for cancer and to localize a focus with the highest probability for cancer
Image file format	Philips UFS iSyntax File	Same
Type of Software Application	Internet browser-based application	Same
General Device Characteristic: Differences		
Patient Population	Male Patients with hematoxylin and eosin (H&E) stained prostate core needle biopsy (PCNB) who are initially diagnosed as Benign	Male Patients with hematoxylin & eosin (H&E) stained prostate needle biopsies
End User's Interface	Galen Second Read	FullFocus (K201005)
Image Manipulation Functions	Panning, zooming and measurements (distance)	Panning, zooming, color manipulation function, annotations, and measurements (distance & area)
Principle of Operation	After WSI images are successfully acquired using PIPS UFS and related quality control steps are performed, the scanned digital images of WSIs from cases initially diagnosed as benign are sent to the Galen Second Read and immediately processed and analyzed. In case the slide analysis results indicate a high likelihood to contain AdC, per a predefined threshold by the neural network, the Galen Second Read flags for additional review by the pathologist. All flagged findings are available in the Galen Second Read and the pathologist can select a patient case and open each flagged WSI for an additional review. The available information for review includes AdC score (the likelihood to contain AdC) and the AdC heatmap marking the	After WSI images are successfully acquired using PIPS UFS and related quality control steps are performed, the scanned digital images are immediately processed by Paige Prostate. The pathologist selects a patient case and opens the WSI for review in the designated digital pathology viewing software, and after review and diagnosis done, Paige Prostate is activated and outputs binary classification (suspicious/not) for cancer based on predefined threshold by the neural network and if suspected, a single coordinate (X,Y) of the location with the highest probability of cancer on an image determined to be suspicious for cancer. Based on the device output, the pathologist can reexamine the slide and modify the original

	region suggestive to include cancer. Based on the device output, the pathologist can reexamine the slide and modify the initial diagnosis to reflect the additional findings, if required.	diagnosis to reflect the additional findings.

Galen Second Read, has similar indications for use and intended use as the predicate device. The technological characteristics differences do not raise new questions of safety and effectiveness. Thus, the Galen Second Read is substantially equivalent.

IV Summary of Performance Validation:

A. Analytical Performance:

Precision and localization studies were performed to assess the Galen Second Read precision (repeatability and reproducibility) in identifying WSI of PCNBs suspicious of cancer, its localization accuracy and its localization precision of detecting the pixels that belong to cancer foci in WSIs from PCNBs of adult male subjects. The slides were retrospectively collected, de-identified and scanned by different PIPS UFS scanners and operators. Slides were processed by Galen Second Read, and results for the slides were either positive or negative. The study has demonstrated that the Galen Second Read identification of WSI of PCNBs suspicious of cancer, is precise (repeatable and reproducible, as demonstrated for within-scanner/operator (**Table 3**) and between-scanner/operator (**Table 4**). Localization accuracy and precision was demonstrated by comparing region of interest (ROI) and an AdC heatmap generated by the device to Ground Truth (GT) determined as "positive", or "benign" by the GT pathologists. Results showed the area marked by AdC heatmap is consistent with the GT, thus the Galen Second Read localization is accurate and precise in detecting tissue area that belong to cancer foci in a population of adult male subjects who have undergone PCNB.

Table 3: Repeatability (Within-Scanner Precision): Percent of Correct Calls

Operator / Scanner / Run	Agreement with Ground Truth by Slide Type			
	Positive Slides		Negative Slides	
	Percent Correct Calls, % (n/N)	95% CI	Percent of Correct Calls % (n/N)	95% CI
Run 1	97.4% (38/39)	(86.8%, 99.5%)	86.8% (33/38)	(72.7%, 94.2%)
Run 2	97.4% (38/39)	(86.8%, 99.5%)	92.1% (35/38)	(79.2%, 97.3%)
Run 3	97.4% (38/39)	(86.8%, 99.5%)	86.8% (33/38)	(72.7%; 94.2%)
Overall Average	**97.4%**	**(92.7%, 99.1%)**	**88.6%**	**(81.5%, 93.2%)**

Table 4: Reproducibility (Between-Scanner/Operator) Precision: Percent of Correct Calls

Operator / Scanner	Agreement with Ground Truth by Slide Type			
	Positive Slides		Negative Slides	
	Percent of Correct Calls, % (n/N)	95% CI	Percent of Correct Calls, % (n/N)	95% CI
Scanner 1/Operator 1	97.4% (38/39)	(86.8%; 99.9%)	86.8% (33/38)	(72.7%; 94.2%)
Scanner 2/Operator 2	94.9% (37/39)	(83.1%;98.6%)	86.8% (33/38)	(72.7%; 94.2%)
Scanner 3/Operator 3	97.4% (38/39)	(86.8%; 99.5%)	84.2% (32/38)	(69.6%; 92.6%)
Overall Average	**96.6%**	**(91.5%, 98.7%)**	**86.0%**	**(78.4%; 91.2%)**

B. Clinical Performance:

Clinical validation studies using the Galen Second Read demonstrated the device's ability to improve clinical performance. The Galen Second Read demonstrated an increase in detection of prostatic AdC in PCNBs, enabling the identification of positive cases (cancer, including AdC, ASAP (atypical small acinar proliferation) and other rare cancer subtypes) that may have been missed at the initial read by the pathologist.

Two clinical studies were conducted to assess the performance of the Galen Second Read.

In the first study, the performance of the Galen Second Read in identifying prostatic adenocarcinoma cases (subjects) missed by Standard of Care (SoC) in a population of subjects who have undergone PCNB was assessed. This study was performed with retrospectively collected samples, and it was conducted at three sites [2 US sites and 1 Outside the US (OUS)]. The device analyzed scanned histopathology whole slide images (WSIs) of hematoxylin and eosin (H&E) from 347 cases who were initially diagnosed as benign based on the prostate core needle biopsies. The WSIs were scanned with a Philips scanner at 40x magnification. Slides from 347 cases were then processed by Galen Second Read and each slide was either "Flag" (Positive) or "No Flag" (Negative).

In the study, Ground Truth (GT) determination with regard to GT for a slide and GT for a case (subject) was performed in a following way: the GT determination for a slide was performed by two independent expert pathologists; slides where the pathologists disagreed, a third independent expert pathologist was asked to review the slide and the majority rule determined the GT for the slide. Slides with prostatic AdC or other cancer ASAP were considered GT positive slides.

For slide-level analysis, the definitions of True Positive (TP), False Positive (FP), True Negative (TN), and False Negative (FN) are as follows:

	Definition
TP slide	Slide is GT positive and Flagged by device
FP slide	Slide is GT negative and Flagged by device

FN slide	Slide is GT positive and Not Flagged by device
TN slide	Slide is GT negative and Not Flagged by device

For case-level analysis, the definitions of TP, FP, TN, and FN are as follows:

	Definition
TP case	Case has only one GT positive slide and this slide is Flagged by the device
	Case has more than one GT positive slide and at least one of these GT positive slides is Flagged by device
FP case	Case has all slides GT Negative and at least one slide is Flagged by the device
FN case	Case has one or multiple GT positive slides and all these GT positive slides are Not Flagged (missed) by the device
TN case	Case has all slides GT negative and all slides are not Flagged by the device

The Galen Second Read performance (sensitivity and specificity) is provided at the level of a slide (**Table 5**) and at the level of a case (subject) (**Table 6).**

Table 5: Slide-Level Device Performance

Parameter	**Estimate**	**95% CI**
Sensitivity	81.0%	(69.2%; 92.9%)
Specificity	91.6%	(90.9%; 92.3%)

Table 6: Case-Level Device Performance

Parameter	**Estimate**	**95% CI**
Sensitivity	80.8%	(74.1%; 87.6%)
Specificity	46.9%	(39.5%; 54.3%)

The study demonstrated that the Galen™ Second Read™ effectively identifies prostate cancer cases, including ASAP, missed by the SoC in a population of subjects who have undergone a PCNB. The study demonstrated that sensitivity of the Galen Second Read is higher than the sensitivity of the SoC read (sensitivity of SoC was 0% because all the slides were diagnosed initially as benign by SoC), both at the slide-level and case-level. In the study there was a decrease in specificity of the Galen Second Read compared to the specificity of SoC (specificity of SoC was 100% because all the slides were diagnosed initially as benign by SoC) and it can be managed by mitigation measures such as use of additional stains to confirm if the slide/case is positive.

In the second study, difference in performances of a pathologist supported by the Galen Second Read vs GT result and a pathologist with SoC vs GT result in a set of retrospectively collected slides (772 cases/slides: 376 negative cases and 396 positive

cases). The study was conducted at 4 sites (3 US and 1 OUS) with 3 pathologists at each site, for a total of 12 pathologists. The study consisted of two arms:

• **Arm A:** a SoC arm, in which slides were read digitally using the routine lab practice.

• **Arm B:** a Galen Second Read workflow arm, in which after reading slides digitally, the pathologist reviewed images flagged by the Galen Second Read and decided on a final read determination.

All cases and associated slides were read in both Arms of the study (Arm A and Arm B), each case was read 3 times, once per pathologist, with a washout period of two weeks between Arms to minimize recall bias.

Sensitivity and specificity for each pathologist were estimated and results are presented in **Table 7** and **Figure 1**.

Table 7. Sensitivity and Specificity Presented by Pathologist

	Sensitivity			Specificity		
Pathologist	**With Galen**	**SoC**	**Difference**	**With Galen**	**SoC**	**Difference**
1	96.9%	94.9%	2.0%	88.8%	91.8%	-3.1%
2	96.9%	92.9%	4.1%	72.4%	76.5%	-4.1%
3	89.8%	87.8%	2.0%	89.8%	91.8%	-2.0%
4	94.4%	94.4%	0.0%	89.2%	89.2%	0.0%
5	95.3%	95.3%	0.0%	90.3%	91.4%	-1.1%
6	89.7%	84.1%	5.6%	100%	100%	0.0%
7	96.5%	84.9%	11.6%	89.0%	97.8%	-8.8%
8	90.7%	84.9%	5.8%	85.9%	89.1%	-3.3%
9	85.9%	84.7%	1.2%	95.7%	96.7%	-1.1%
10	98.1%	96.2%	1.9%	82.8%	86.0%	-3.2%
11	92.4%	91.4%	1.0%	91.4%	91.4%	0.0%
12	99.0%	91.4%	7.6%	80.6%	92.5%	-11.8%
Combined	93.9%	90.5%	3.5%	87.9%	91.1%	-3.2%

Sensitivity and specificity for the combined data were calculated and presented in **Table 8**.

Table 8. Sensitivity and Specificity of Pathologists with Galen Device vs SoC

	Sensitivity		
	Estimate	**(n/N)**	**95%CI**
With Galen	93.9%	(1115/1187)	(92.2%; 95.8%)
SoC	90.5%	(1074/1187)	(88.5%; 92.6%)
Difference	3.5%	(41/1187)	(2.3%; 4.5%)
	Specificity		
With Galen	87.9%	(991/1127)	(85.8%; 90.4%)
SoC	91.1%	(1027/1127)	(89.3%; 93.2%)
Difference	-3.2%	(-36/1127)	(-4.3%; -1.9%)

This clinical study demonstrated a statistically significant improvement in sensitivity of 3.5% with 95%CI: (2.3%; 4.5%) and statistically significant decrease in specificity of –3.2% with 95%CI: (-4.3%; -1.9%).

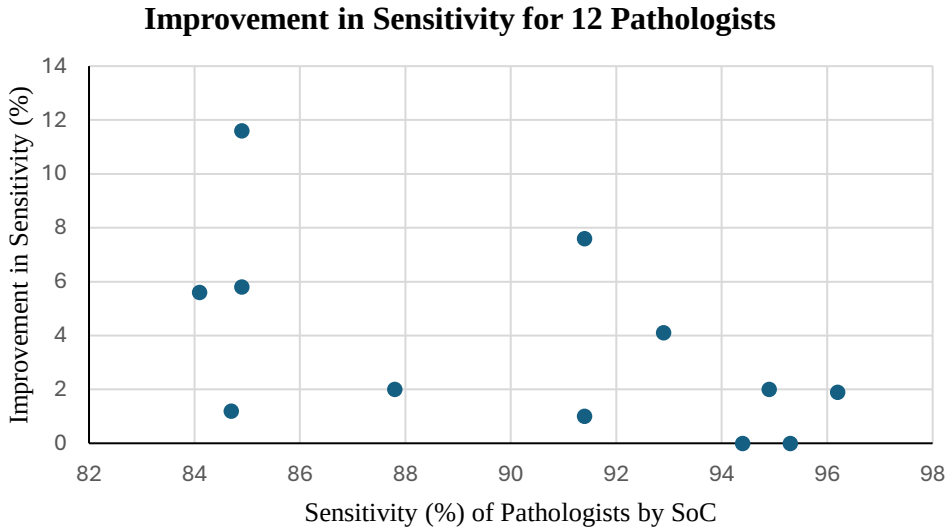

Figure 1. Improved Sensitivity for the pathologists assisted by the Galen™ Second Read™ as compared with pathologists reviewing in SoC.

Sensitivity and specificity for the slides initially assessed by a pathologist as benign (the intended use population of the device) are also calculated and presented in **Table 9**.

Table 9. Sensitivity and Specificity for the Slides Initially Assessed as Benign vs GT

	Sensitivity		Specificity	
Pathologist	**With Galen**	**(n/N)**	**With Galen**	**(n/N)**
1	40.0%	(2/5)	96.7%	(87/90)
2	57.1%	(4/7)	94.7%	(71/75)
3	16.7%	(2/12)	97.8%	(88/90)
4	0.0%	(0/6)	100%	(83/83)
5	0.0%	(0/5)	98.8%	(84/85)
6	35.3%	(6/17)	100%	(93/93)
7	76.9%	(10/13)	91.0%	(81/89)
8	38.5%	(5/13)	96.3%	(79/82)
9	7.7%	(1/13)	98.9%	(88/89)
10	50.0%	(2/4)	96.3%	(77/80)
11	11.1%	(1/9)	100%	(85/85)
12	88.9%	(8/9)	87.2%	(75/86)
Combined	36.3% 95%CI: (28.0%; 45.5%)	(41/113)	96.5% 95%CI: (95.2%; 97.5%)	(991/1027)

This study demonstrated that the sensitivity of the pathologists using the Galen Second Read for the cases/slides which were initially diagnosed as benign was 36.3% with 95%CI: (28.0%; 45.5%) (sensitivity without the device was 0% because all the slides were diagnosed initially as benign by SoC), yielding increase in sensitivity of 36.3%.

Specificity of the pathologist using the Galen Second Read for the cases/slides which were initially diagnosed as benign was 96.5% with 95%CI: (95.2%; 97.5%) (specificity without the device was 100%), yielding decrease in specificity of 3.5%. The decrease in specificity can be managed by mitigation measures such as use of additional stains to confirm if the slide/case is positive.

V Substantial Equivalence Determination:

The Galen™ Second Read™ device is substantially equivalent to the predicate device.