510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K260755

B Applicant

OptraSCAN, Inc.

C Proprietary and Established Names

OptraSCAN System

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
NOT	Class II	21 CFR 864.1860	Pathology

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Type of Test:

Computer-assisted image analysis software for scoring immunohistochemically stained HER2/neu breast cancer tissue slides using Dako HercepTest™. The score provided by the image analysis software is confirmed by the pathologist after reviewing the images before reporting the scores.

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The OptraSCAN System is an automated digital slide creation, management, viewing and analysis system which consists of the OS-Ultra Scanner, Color Display Monitor (Model No. Dell U2424HE) and a Workstation, preinstalled with software to operate the scanner and the ImagePath application (Image Management software and HER2 Image Analysis Software).

The OptraSCAN System is intended for in vitro diagnostic use as an aid to the pathologist in the review and semi-quantitative scoring of HER2 protein expression in scanned digital images obtained using OS-Ultra Scanner of slides prepared from formalin-fixed paraffin embedded (FFPE) breast tissue and stained with the Dako HercepTest™.

The HER2 Image Analysis Software outputs the scores for individual Regions of Interest (ROIs) as well as the slide level score based on all the ROIs. The pathologist is responsible for making the final decision of the score, based on the output provided by the system. The OptraSCAN System software makes no independent interpretations of the data.

Note: The HER2 Image Analysis Software is an adjunctive computer-assisted methodology to assist qualified pathologists in HER2 scoring in breast cancer. The accuracy of the test result depends upon the quality of the immunohistochemical staining.

It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for use for the Dako HercepTest™ to assure the validity of the HER2 Image Analysis Software assisted HER2 score. The actual correlation of the Dako HercepTest™ to Herceptin® clinical outcome has not been established.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

IV Device/System Characteristics:

A Device Description:

The OptraSCAN System is intended as an aid to the pathologist in the review and semi-quantitative scoring of HER2 protein expression in digital whole slide images (WSIs) of slides prepared from formalin-fixed paraffin embedded (FFPE) breast tissue and stained with the Dako HercepTest™. The system uses computer-assisted image analysis software to support the pathologist in the semi-quantitative assessment of Dako HercepTest™ -stained histological specimens. It does not contain any artificial intelligence/machine language (AI/ML) based algorithms.

The OptraSCAN System is an automated digital pathology system that scans glass microscope slides and produces high-resolution WSIs and provides tools for managing, viewing, and

analyzing those images on a display workstation. This system is intended to be used in a clinical laboratory environment.

The OptraSCAN System is comprised of the following main components:

- OS-Ultra Scanner
- Color Monitor Display: Dell Model No. U2424HE.
- Dell Precision 3680 Tower Workstation computer loaded with
    - Scanner App Software – Version 1.0.0
    - ImagePath Image Management Software (which includes the image viewing software) – Version 1.0.0
    - HER2 Image Analysis Software – Version 1.0.0

The OptraSCAN System is operated as below:

1. The pathologist reviews all positive and negative control slides under the microscope for each staining run per the instructions for use for the HercepTest to ensure that the staining is as expected. If the control slides do not have acceptable staining, slides should be re-stained to ensure acceptable staining.
2. The pathologist selects the appropriate slide(s) to be scanned. The selected slides are loaded into the OptraSCAN OS-Scanner basket.
3. Scanning is initiated and WSIs of pathology glass slides are produced.
4. The WSIs are viewed on the Color Dell Monitor Display, Model No. U2424HE.
5. Using the Image Management Software, the pathologist views, navigates, annotates, and reviews the WSIs. The pathologist runs the HER2 Image Analysis Software on the selected WSIs.
6. OptraSCAN System supports pathologist interpretation based on Regions of Interests (ROIs) selected by the pathologist and outputs the HER2 scores for individual ROIs. Additionally, a slide level score is generated based on all selected ROIs. Note: The Pathologist is responsible for making the final decision of the score, based on the output provided by the system. The system makes no independent interpretations of the data.
7. A report is generated.

B Instrument Description Information:

1. Instrument Name:
   OptraSCAN System

2. Specimen Identification:
   The OptraSCAN System identifies each specimen by linking the physical glass slide to its corresponding digital image during scanning. Identification information—such as accession number, or barcode (Case ID)—is captured from the slide label (via barcode reader or user entry) and stored as metadata within the system software. This unique specimen identifier (Case ID) remains associated with the image throughout storage, retrieval, viewing, and analysis, ensuring full traceability between the physical specimen and the digital file during HER2 slide review.

3. Specimen Sampling and Handling:
   Breast tissue specimens are collected, fixed in formalin, and processed into FFPE blocks using routine histopathology procedures. Glass slides are prepared from the FFPE blocks and stained according to the laboratory's established protocols. Slides, including stained assay control slides are arranged into trays (up to four slides per tray), placed into the scanner's automated slide-handling baskets, and digitized into WSIs. Laboratories use internal quality control procedures throughout specimen preparation and handling.

4. Calibration:
   The OptraSCAN System includes calibration procedures designed to ensure consistent optical and imaging performance. Calibration is performed during system installation and when directed by OptraSCAN technical support or service protocols. OptraSCAN-provided calibration targets are used to verify optical alignment, illumination uniformity, focus accuracy, and spatial resolution to ensure consistent image acquisition performance.

5. Quality Control:
   The OptraSCAN System incorporates quality control (QC) such as automated system checks during scanner startup and before scanning to confirm that imaging components and internal systems are functioning as intended. The quality of the scanned image should be verified by the pathologist before HER2 scoring.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Aperio ePathology eIHC IVD System, AT Turbo and CS2 Models

B Predicate 510(k) Number(s):
K141109

C Comparison with Predicate(s):

Device & Predicate Device(s):	K260755	K141109
Device Trade Name	OptraSCAN System	Aperio ePathology eIHC IVD System, AT Turbo and CS2 Models
General Device Characteristic Similarities		
Intended Use/Indications For Use	The OptraSCAN System is an automated digital slide creation, management, viewing and analysis system which consists of the OS-Ultra Scanner, Color Display Monitor (Model No. Dell U2424HE) and a Workstation, preinstalled with software to operate the scanner and the ImagePath application (Image	The Aperio ePathology eIHC IVD System is an automated digital slide creation, management, viewing and analysis system. It is intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting and classification of tissues and cells of clinical interest based on particular color, intensity, size, pattern and shape. The IHC HER2 Image Analysis application is

	Management software and HER2 Image Analysis Software). The OptraSCAN System is intended for in vitro diagnostic use as an aid to the pathologist in the review and semi-quantitative scoring of HER2 protein expression in scanned digital images obtained using OS-Ultra Scanner of slides prepared from formalin-fixed paraffin embedded (FFPE) breast tissue and stained with the Dako HercepTest™. The HER2 Image Analysis Software outputs the scores for individual Regions of Interest (ROIs) as well as the slide level score based on all the ROIs. The pathologist is responsible for making the final decision of the score, based on the output provided by the system. The OptraSCAN System software makes no independent interpretations of the data. Note: The HER2 Image Analysis Software is an adjunctive computer-assisted methodology to assist qualified pathologists in HER2 scoring in breast cancer. The accuracy of the test result depends upon the quality of the immunohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for use for the Dako HercepTest™ to assure the validity of the HER2 Image Analysis Software assisted HER2 score. The actual correlation of the Dako HercepTest™ to Herceptin® clinical outcome has not been established.	intended for use as an aid to the pathologist in the detection and semi-quantitative measurement of HER2/neu (c-erbB-2) in formalin-fixed, paraffin embedded neoplastic tissue. The IHC HER2 Image Analysis application is intended for use as an accessory to the Dako HercepTest™ to aid in the detection and semi-quantitative measurement of HER2/neu (c-erbB-2) in formalin-fixed, paraffin-embedded neoplastic tissue. When used with the Dako HercepTest™, it is indicated for use as an aid in the assessment of breast cancer patients for whom HERCEPTIN®(Trastuzumab) treatment is being considered. Note: The IHC HER2 Image Analysis application is an adjunctive computer-assisted methodology to assist the reproducibility of a qualified pathologist in the acquisition and measurement of images from microscope slides of breast cancer specimens stained for the presence of HER-2 receptor protein. The IHC HER2 Image Analysis application is intended to be used on images viewed on a computer monitor. The accuracy of the test result depends upon the quality of the immunohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the Dako HercepTest™ to assure the validity of the IHC HER2 Image Analysis application assisted HER-2/neu score. The actual correlation of the Dako HercepTest™ to Herceptin® clinical outcome has not been established.
Method of Operation/ Cell Detection	Use of deterministic image processing and pattern matching based image analysis rule engine to determine the HER2 score for each ROI based on completeness of membrane staining. Threshold-based segmentation techniques are used to detect	Same

	tumor cells.	
Assay Type Used	DAKO HercepTest Reagent Kit	Same
Immunohistochemistry Test Type	HER2	HER2, ER, PR
Specimen Type	Formalin-Fixed, Paraffin embedded breast tissue specimens	Same
Software Description	The software makes no independent interpretations of the data and requires competent human intervention for all steps in the analysis process.	Same
General Device Characteristic Differences		
System Components	1. OS-Ultra Scanner 2. Color Display Monitor 3. Workstation with ImagePath Software (Image Management Software with HER2 Image Analysis Software)	1. ScanScope AT Turbo Slide Scanner 2. Color Monitor 3. Workstation with eSlideManager Software and IHC HER2 Image Analysis Software

VI Standards/Guidance Documents Referenced:

1. FDA Guidance "Content of Premarket Submissions for Device Software Functions"; June 14, 2023
2. FDA Guidance, "Cybersecurity in Medical Devices: Quality Management System Considerations and Content of Premarket Submissions"; June 27, 2025
3. FDA Guidance "Off-The-Shelf Software Use in Medical Devices"; August 11, 2023
4. CLSI EP12-Ed3 "Evaluation of Qualitative, Binary Output Examination Performance"

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. **Precision**:

The Precision (repeatability and reproducibility) study was designed to generate evidence that the OptraSCAN System produces consistent HER2 scoring outputs when subjected to expected sources of operational variability.

Forty FFPE breast cancer specimens stained with Dako HercepTest for HER2 IHC were selected to cover the score distribution across HER2 scoring categories (0, 1+, 2+, 3+). The slides were scanned using the OptraSCAN with 40x objective.

The following precision components were evaluated:

- Between-scan repeatability (same scanner, repeated scans, same pathologist)]
- Between-scanner reproducibility (different scanners)
- Within-pathologist repeatability (same pathologist, same scanner, repeated reads)

- Between-pathologist precision (different pathologist, same scanner)
- Between-laboratory reproducibility (different sites)

Between-Scan Precision (Repeatability)
Each slide was scanned 1 time per day on the same OptraSCAN scanner across 10 non-consecutive days (i.e., 1 scanner * 1 scan/day * 10 non-consecutive days = 10 scans per slide). A single operator conducted all the scans. Study activities were scheduled across multiple days with at least one-day separation between repeat measurements. For each slide, multiple ROIs that were annotated by a single pathologist were used across different scans, followed by the software scoring on the slide level. The HER2 score generated from each repeated scan was compared across runs to assess whether repeated digitization of the same physical slide using the same instrument yields consistent HER2 scoring results. Below are the results.

Table 1: Between-Scan Repeatability

HER2 score	#slides	#scans	%agreement
0	7	70	100%
1	16	160	100%
2	6	60	100%
3	11	110	100%
Total	40	400	100%

Between-Scanner Reproducibility
Each slide was scanned 5 times (per scanner) using three independent OptraSCAN scanners that were located at 3 different sites (i.e., 1 scan/scanner/day * 5 non-consecutive days * 1scanner/site * 3 sites = 15 scans per slide). Note the scans were conducted based on lab availability over a period of approximately 3 weeks. For each slide, multiple regions of interest (ROIs) were annotated by the pathologist to ensure representative sampling of invasive tumor areas in accordance with HER2 scoring guideline. The ROIs were used across different scans, followed by the algorithm scoring on the slide level.

Table 2: Between-Scanner Reproducibility

HER2	#slides	#scans/category	scanner1 %agreement	scanner2 %agreement	scanner3 %agreement	Overall %agreement
0	7	105	100%	100%	100%	100%
1	16	240	100%	100%	100%	100%
2	6	90	100%	100%	100%	100%
3	11	165	100%	100%	100%	100%
Total	40	600	100%	100%	100%	100%

Between-Pathologist Precision
Two different pathologists drew their own ROIs on the same set of digital images that were scanned with the same scanner, under blinded conditions. HER2 scores used for analysis were software-generated scores based on pathologist-defined ROIs.

Table 3: Between-Pathologist Precision

	0 vs 0	0 vs 1+	1+ vs 1+	1+ vs 2+	2+ vs 2+	2+ vs 3+	3+ vs 3+
#slides	7	2	15	0	3	3	10

Overall percent agreement = (7+15+3+10)/40 = 87.5%

Within-Pathologist Repeatability
The same slides were scanned 1 time/day using the same scanner across 5 non-consecutive days (i.e., 1scan/day * 5 days). Then a single qualified pathologist annotated the ROIs for all the 5 digital images for the same physical slide, and the software generated HER2 score based on the pathologist-defined ROIs were compared. ROI annotation and scoring were performed on each respective day of scanning. The pathologist independently reviewed the corresponding digital image and annotated ROIs on that same day.

Within-pathologist repeatability was calculated using all pairwise comparisons of repeated reads for each slide. Each slide was read five times, generating ten read-pair comparisons per slide (total comparisons = 400). A "read-pair" represents a comparison between two independent reads (Run 1 vs Run 2, Run 1 vs Run 3, etc.) of the same slide by the same pathologist.

Table 4: Within-Pathologist Repeatability

Metric	Result
Agreeing pairs	347
Total pairs	400
Overall Percent Agreement	86.75% (95%CI: 0.834-0.900)

Between-Laboratory Reproducibility
Digital images generated from a single scanner were distributed to all three participating sites, where one pathologist per site independently scored the slides. The HER2 score was software generated at each site which was confirmed by the pathologist at the individual site. The between-laboratory reproducibility analysis was conducted on the final pathologist-confirmed scores.
HER2 scores produced across sites was compared to evaluate whether differences in laboratory environment, workflow conditions, or local operational factors influence scoring outcomes.

Agreement across clinical sites was evaluated using pairwise site comparisons and are summarized below using mean pairwise agreement.

Table 5a: Between-Laboratory Reproducibility

Site Pair	OPA	95% CI
Site1 vs Site2	82.5%	0.7874 - 0.9897
Site1 vs Site3	75.0%	0.74779 - 0.96138
Site2 vs Site3	77.5%	0.82365 - 0.96459

The table below presents the number of slides for each score pair type observed in pairwise site comparisons. Score pair types reflect exact agreement (e.g., 0 vs 0, 1+ vs 1+) and adjacent-category disagreement (e.g., 0 vs 1+, 1+ vs 2+, 2+ vs 3+). Each site pair evaluates the same set of 40 slides scored independently at each site using the OptraSCAN System digital workflow.

Table 5b: Between-Laboratory Reproducibility

Site Pair	0 vs 0	0 vs 1+	1+ vs 1+	1+ vs 2+	2+ vs 2+	2+ vs 3+	3+ vs 3+
Site1 vs Site2	6	1	13	2	5	3	9
Site1 vs Site3	4	3	10	5	5	1	11
Site2 vs Site3	4	2	10	5	6	2	11
Overall	14	6	33	12	16	6	31

The OptraSCAN System demonstrated acceptable precision.

2. Linearity:
   Not applicable

3. Analytical Specificity/Interference:
   Not applicable

B Other Supportive Instrument Performance Characteristics Data:

Clinical Performance Study

This study evaluated pathologist performance when using the OptraSCAN System for [Image analysis (IA)] assisted scoring of Dako HercepTest HER2 immunohistochemistry (IHC) slides from breast cancer specimens compared to the performance of pathologist manual microscope based HER2 scoring classification. Pathologist manual scoring and OptraSCAN System assisted scoring were evaluated in comparison to independently established Ground Truth (GT) scores for each study slide. The study was conducted across three U.S. sites using a total of 300 slides, with 100 slides evaluated per site. At each site:

- Two qualified pathologists participated as study readers
- Each pathologist independently evaluated 50 slides
- The same 50 slides assigned to each pathologist were evaluated using both Manual Optical Microscopy and the OptraSCAN Digital workflow, with a washout period of a minimum of two weeks in between the study arms

Performances were assessed using performance measures of sensitivity and specificity for three clinically relevant HER2 classification scoring cutoff thresholds (0 versus 1+/2+/3+, 0/1+ versus 2+/3+, and 0/1+/2+ versus 3+) derived from standard diagnostic categories.
The results are provided in Table 6 below and show differences in sensitivity and differences in specificities for different scoring cutoff thresholds.

Table 6: Summary Results–Clinical Performances (Manual and IA-assisted vs GT)

Table 6a: Sensitivity: Manual and "IA- assisted" vs Ground Truth (GT)

Scoring Category	Manual vs GT (%) 95%CI	"IA- assisted" vs GT (%) 95%CI	Point of Estimate Difference (IA–M)	95%CI Difference
0,1+,2+ vs 3+	62.774% (62.774%, 83.357%)	75.875% (75.875%, 92.647%)	13.10%	(3.66%, 19.72%)
0,1+ vs 2+,3+	79.462% (79.462%, 90.782%)	82.292% (82.292%, 92.789%)	2.83%	(-1.71%, 6.64%)
0 vs 1+,2+,3+	96.330% (96.330%, 99.737%)	96.972% (96.972%, 99.897%)	0.64%	(-1.65%, 1.65%)

Table 6b: Specificity: Manual and "IA- assisted" vs GT

Scoring Category	Manual vs GT (%) 95%CI	"IA- assisted" vs GT (%) 95%CI	Point of Estimate Difference (IA–M)	95%CI Difference
0,1+,2+ vs 3+	98.359% (98.359%, 100.000%)	96.119% (96.119%, 99.722%)	-2.24%	(-2.86%, 0.17%)
0,1+ vs 2+,3+	82.707% (82.707%, 93.787%)	90.777% (90.777%, 98.388%)	8.07%	(0.43%, 12.62%)
0 vs 1+,2+,3+	64.307% (64.307%, 86.248%)	66.030% (66.030%, 87.493%)	1.72%	(-11.97%, 15.14%)

- For the scoring cutoff (0, 1+, 2+ vs 3+), the difference in sensitivity was 13.10% with 95%CI: (3.66%; 19.72%) and difference in specificities was -2.24% with 95%CI: (-2.86%; 0.17%). An improvement in sensitivity of 13.10% was observed, which was statistically significant, as evidenced by a lower bound of 95%CI of 3.66%. Decrease in specificity was not statistically significant.
- For the scoring cutoff (0,1+ vs 2+,3+), the difference in sensitivity was 2.83% with 95%CI: (-1.71%; 6.64%) and difference in specificities was 8.07% with 95%CI: (0.43%; 12.62%). Improvements were observed in both sensitivity and specificity. The improvement in sensitivity of 2.83% was not statistically significant and an improvement in specificity of 8.07% was statistically significant, with a lower bound of the 95%CI of 0.43%.
- For the scoring cutoff (0 vs 1+/2+/3+ cutoff), the difference in sensitivity was 0.64% with 95%CI: (-1.65%; 1.65%) and difference in specificities was 1.72% with 95%CI: (-11.97%;

15.14%). Improvements were observed in both sensitivity and specificity, but these improvements were not statistically significant.

The three-way tables below stratified by Ground Truth category provide a detailed view of how both IA-assisted and Manual scoring classify slides within each true HER2 stratum.

Table 7. "IA-Assisted" and Manual Scoring Agreement for GT = 0/1+ (All Sites Pooled)

GT=0/1+					
		Manual			Total
		0/1+	2+	3+	
"IA-assisted"	0/1+	118	14	0	132
	2+	5	1	0	6
	3+	0	0	0	0
	Total	123	15	0	138

- Percent of 0/1+ by Manual= 89.1% (123/138) with 95%CI: (82.8%; 93.3%)
- Percent of 0/1+ by "IA- assisted"= 95.7% (132/138) with 95%CI: (90.8%; 93.3%)
- Across pooled Ground Truth 0/1+ cases, both methods predominantly classified slides within the negative/low-expression category; however, IA-assisted scoring demonstrated higher alignment with the Ground Truth category compared to Manual scoring (95.7% vs. 89.1%), difference=6.5% with 95%CI: (0.1%; 13.3%), statistically significant improvement)

Table 8. "IA-Assisted" and Manual Scoring Agreement for GT = 2+ (All Sites Pooled)

GT=2+					
		Manual			Total
		0/1+	2+	3+	
"IA-assisted"	0/1+	15	3	0	18
	2+	8	56	0	64
	3+	0	3	0	3
	Total	23	62	0	85

- Percent of 2+ by Manual= 72.9% (62/85) with 95%CI: (62.7%; 81.2%)
- Percent of 2+ by "IA- assisted" = 75.3% (64/85) with 95%CI: (65.2%; 83.2%)
- Across pooled Ground Truth 2+ cases, both methods demonstrated variability consistent with the equivocal nature of HER2 2+ interpretation, with IA-assisted scoring demonstrating slightly higher retention within the Ground Truth 2+ category compared to Manual scoring (75.3% vs. 72.9%), difference=2.4% with 95%CI: (-6.6%; 11.3%), not statistically significant).

Table 9. "IA-Assisted" and Manual Scoring Agreement for GT = 3+ (All Sites Pooled)

GT=3+					
		Manual			Total
		0/1+	2+	3+	
"IA-assisted"	0/1+	0	1	0	1
	2+	0	9	1	10
	3+	0	10	56	66
	Total	0	20	57	77

- Percent of 3+ by Manual= 74.0% (57/77) with 95%CI: (63.3%; 82.5%)
- Percent of 3+ by "IA- assisted" = 85.7% (66/77) with 95%CI: (76.2%; 91.8%)
- Across pooled Ground Truth 3+ cases, IA-assisted scoring demonstrated higher alignment with the Ground Truth positive category compared to Manual scoring (85.7% vs. 74.0%), difference=11.7% with 95%CI: (3.2%; 20.6%), statistically significant improvement).
- The three-way tables stratified by Ground Truth category provide a detailed view of how both IA-assisted and Manual scoring classify slides within each true HER2 stratum. When considered in aggregate, the pooled analysis demonstrates stable and comparable performance of the IA-assisted method relative to Manual scoring across all clinically relevant categories. No systematic pattern of clinically significant multi-category misclassification was observed.

Overall, the study results support the conclusion that the system performs within the expected range of clinical variability and does not introduce additional diagnostic risk relative to standard manual interpretation.

Other studies

Electrical safety and electromagnetic compatibility (EMC) testing were performed, and the results were acceptable.

Software and cybersecurity documentation was reviewed and found to be acceptable.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.