510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K220163

B Applicant

Boston Cell Standards, Inc.

C Proprietary and Established Names

HER2/ER/PR IHControls® - Level H
HER2/ER/PR IHControls® - Level M
HER2/ER/PR IHControls® - Level L

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
NJW	Class II	21 CFR 864.1860 - Immunohistochemistry Reagents and Kits	PA - Pathology

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Measurand:

Positive controls to monitor performance of the immunohistochemical (IHC) staining process for HER2, ER and PR IHC assays.

C Type of Test:

Peptide based on-slide controls to monitor the performance of the analytic components (antigen retrieval and immunostaining) of certain human epidermal growth factor receptor, type II (HER2), estrogen receptor (ER) and progesterone receptor (PR) IHC stains.

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

Her2/ER/PR IHControls® - Level H
Her2/ER/PR IHControls® - Level H are peptide based qualitative on-slide controls to monitor the performance of the analytic components (antigen retrieval and immunostaining) of the immunohistochemical (IHC) staining process for certain human epidermal growth factor receptor type II (HER2), estrogen receptor (ER) and progesterone receptor (PR) IHC stains. It is indicated for use with formalin-fixed paraffin-embedded (FFPE) breast tumor samples.

Her2/ER/PR IHControls® - Level H are not intended to be used for scoring HER2, ER, and PR IHC stained slides.

Her2/ER/PR IHControls® - Level H are an additional control to the run controls specified in the HER2, ER, or PR IHC device labeling and are not intended to replace the controls approved or cleared as part of an IHC device.

Her2/ER/PR IHControls® - Level M
Her2/ER/PR IHControls® - Level M are peptide based qualitative on-slide controls to monitor the performance of the analytic components (antigen retrieval and immunostaining) of the immunohistochemical (IHC) staining process for certain human epidermal growth factor receptor type II (HER2), estrogen receptor (ER) and progesterone receptor (PR) IHC stains. It is indicated for use with formalin-fixed paraffin-embedded (FFPE) breast tumor samples.

Her2/ER/PR IHControls® - Level M are not intended to be used for scoring HER2, ER, and PR IHC stained slides.

Her2/ER/PR IHControls® - Level M are an additional control to the run controls specified in the HER2, ER, or PR IHC device labeling and are not intended to replace the controls approved or cleared as part of an IHC device.

Her2/ER/PR IHControls® - Level L
Her2/ER/PR IHControls® - Level L are peptide based qualitative on-slide controls to monitor the performance of the analytic components (antigen retrieval and immunostaining) of the immunohistochemical (IHC) staining process for certain human epidermal growth factor receptor type II (HER2), estrogen receptor (ER) and progesterone receptor (PR) IHC stains. It is indicated for use with formalin-fixed paraffin-embedded (FFPE) breast tumor samples.

Her2/ER/PR IHControls® - Level L are not intended to be used for scoring HER2, ER, and PR IHC stained slides.

Her2/ER/PR IHControls® - Level L are an additional control to the run controls specified in the HER2, ER, or PR IHC device labeling and are not intended to replace the controls approved or cleared as part of an IHC device.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

Staining platform approved or cleared as part of the HER2, ER, or PR IHC devices.

IV Device/System Characteristics:

A Device Description:

HER2/ER/PR IHControls® - Level H, HER2/ER/PR IHControls® - Level M and HER2/ER/PR IHControls® - Level L (HER2/ER/PR IHControls®) are unassayed positive controls for HER2, ER, and PR IHC assays which are provided in vials as a liquid suspension. The suspension contains microscopic glass microbeads that are approximately the same size as cells and coated with purified analyte(s). HER2/ER/PR IHControls® are not biological cells or tissues. The microbead surface bears the molecule(s) being measured. Peptides representing the epitopes of HER2, ER, and PR antibodies used by clinical IHC laboratories are incorporated into the products. The same immunohistochemical reaction that occurs on a tissue or cellular sample also occurs on the HER2/ER/PR IHControls®. As a result of immunostaining, the HER2/ER/PR IHControls® bearing the analyte turn the same color as cells expressing the analyte. The HER2/ER/PR panel includes controls at 3 different analyte concentrations, which allows matching the analyte concentration to the dynamic range (range of staining intensity) of the particular HER2, ER, or PR IHC stain with which it is intended to be used.

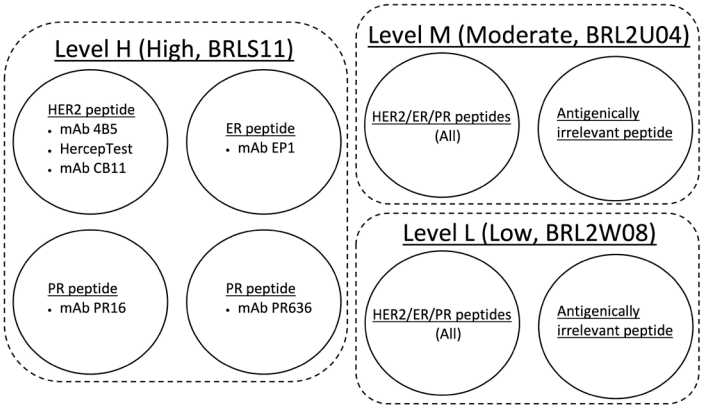


Figure 1. The 3 levels of HER2/ER/PR IHControls® and their microbeads are schematically illustrated. Each circle represents a test microbead, coated with one or more peptide analytes. The primary antibodies immunoreactive with the peptide coatings are listed within the circles. Level H has 4 different test microbeads, each coated with a single peptide. Levels M and L have only two different test microbeads, coated with a cocktail of HER2/ER/PR peptides, although the concentration is lower in Level L.

The 3 different analyte concentrations of the HER2/ER/PR IHControls® panel are provided to allow the user to select a control with the lowest analyte concentration that still produces an easily visible immunostain. The analyte concentrations are as follows:

Level H (high): Includes analytes for HER2, ER, and PR, at approximately 10^6 molecules per microbead. It consists of 4 different microbeads, each coated with a single different (HER2, ER or PR) peptide.
Level M (medium): Includes analytes for HER2, ER, and PR, at approximately 10^5 molecules per microbead. It consists of 2 different types of microbeads in equal numbers, one coated with HER2/ER/PR peptides and the other coated with antigenically irrelevant peptide
Level L (low): Includes analytes for HER2, ER, and PR, at approximately 10^4 molecules per microbead. It consists of two different types of microbeads in equal numbers, one coated with HER2/ER/PR peptides and the other coated with antigenically irrelevant peptide.

These concentrations are approximate; they are not intended as assayed controls.

The configuration of the different levels (high, medium, low) of the device also provides for an internal negative control for each product. For level H, the negative control microbeads comprise those with other HER2/ER/PR analytes. For levels M and L, the negative control microbead bears a peptide that is unrelated to HER2/ER/PR. This arrangement also means that for any single IHC stain, 25% of the microbeads will turn positive for Level H and 50% for Levels M and L.

HER2/ER/PR IHControls® are intended to be placed on the same slide as the patient tissue. The precise location of the HER2/ER/PR IHControls® on each individual slide depends on where the tissue section is and where there is space on the slide. Figure 2 below shows the acceptable positioning of the HER2/ER/PR IHControls® on the slide that has patient tissue.

Figure 2. Examples for Placement of the HER2/ER/PR IHControls® on the Same Slide as Patient Tissue

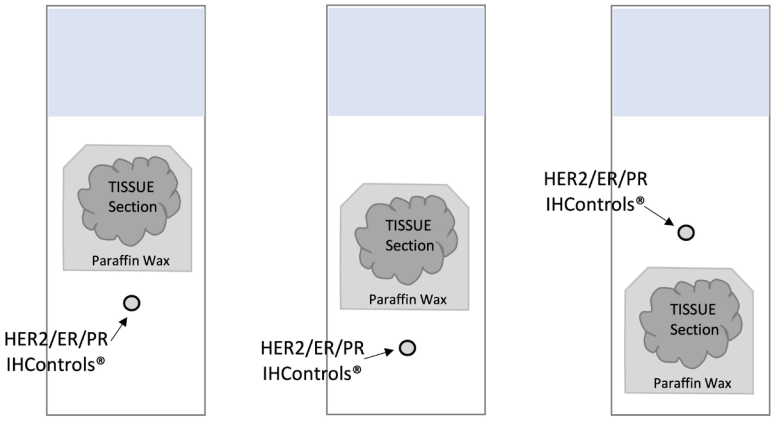


Table 1. IHC Assays Intended to be Used with HER2/ER/PR IHControls®

HER2	ER	PR
• BOND ORACLE HER2 IHC System • PATHWAY Anti-HER-2/Neu (4B5) Rabbit Monoclonal Primary Antibody	• FLEX Monoclonal Rabbit Anti-Human Estrogen Receptor α, Clone EP1, Ready-to-Use Primary Antibody • DAKOCYTOMATION ER/PR pharmDx Kit for the Dako Autostainer: Monoclonal Mouse	• DAKO Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PGR 636, Antibody for Immunoenzymatic Staining • VISION BIOSYSTEMS Progesterone Receptor PGR CLONE 16

HER2	ER	PR
• HercepTest (Dako Autostainer)	Anti-Human Estrogen Receptor Cocktail, clones 1D5 and ER-2-123 • Estrogen Receptor Clone 6F11 Ready-to-Use Primary Antibody for Bond • CONFIRM anti-Estrogen Receptor (SP1) Rabbit Monoclonal Primary Antibody	• BOND Ready-to-Use Primary Antibody Progesterone Receptor (16), Novocastra Liquid Mouse Monoclonal Antibody Progesterone Receptor Clone 16 (Concentrated Liquid Antibody Format) • DAKOCYTOMATION ER/PR pharmDx Kit for the Dako Autostainer: Monoclonal Mouse Anti-Human Progesterone Receptor, Clone: PgR 1294 • CONFIRM anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody

B Principle of Operation:

The HER2/ER/PR IHControls® contains analytes that bind IHC stains. They are on-slide controls and therefore negative staining due to analytic error is readily detectable for each individual slide. Like tissue samples, the HER2/ER/PR IHControls® are formalin fixed during manufacture. Therefore, test microbeads in the HER2/ER/PR IHControls® product may demonstrate improved immunoreactivity after antigen retrieval.

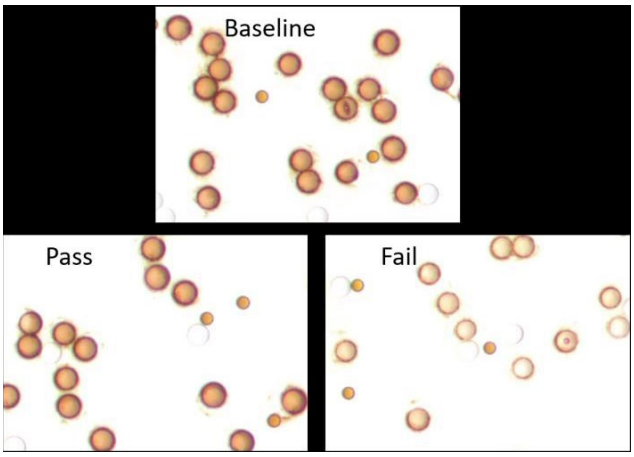
Users pipette a droplet of HER2/ER/PR IHControls® onto a microscope slide that also bears a patient's tissue sample. The droplet hardens upon drying, adheres the analyte-coated microbeads to the microscope slide, and is then processed with the patient sample. The hardened droplet is able to pass through dry heat associated with "baking" of slides, organic solvents associated with deparaffinization, boiling associated with antigen retrieval, and repeated rinses associated with immunostaining. After staining steps, the slide containing both the patient sample and the HER2/ER/PR IHControls®, can be observed by a standard brightfield microscope. Microscopic examination is performed with approximately 400X magnification using Köhler illumination optics, modified by opening the condenser aperture to the maximum.

Interpretation: Approximately one-quarter to one-half of the microbeads on the slide will be stained with the appropriate single HER2, ER or PR IHC stain. Test microbeads with the different analyte remain unstained. Fields with the highest microbead stain intensity without significant background staining of the matrix are chosen for interpretation. Expected stain intensity (baseline) must be initially determined by manual microscope review of the slide containing the HER2/ER/PR IHControls® microbead before placing this product into routine use. This baseline stain intensity may be different for each laboratory depending on the IHC device being used. HER2/ER/PR IHControls® are interpreted by manual microscopic review by comparing their stain intensity to the established baseline slide. Stain intensity for the HER2/ER/PR IHControls® should be similar from day-to-day. If an HER2/ER/PR IHControls stain intensity is visibly lower than the baseline, then that indicates failure of the HER2/ER/PR

IHControls® and should not be used to assess the performance of the analytic components of the IHC staining. HER2/ER/PR IHControls® are interpreted on a Pass/Fail basis. This Pass/Fail readout is different than the scoring system used for patient samples.

HER2/ER/PR IHControls® is not a calibrator; the stain intensity is not intended to be used for scoring HER2, ER, and PR IHC stained slides.

Figure 3. Example showing HER2/ER/PR IHControls® stain intensity – Baseline, Pass, and Fail



V Substantial Equivalence Information:

A Predicate Device Name(s):

QCS HER2 Immunocontrols

B Predicate 510(k) Number(s):

K023335

C Comparison with Predicate

Device & Predicate Device(s):	K220163	K023335
Device Trade Name	HER2/ER/PR IHControls®	QCS HER2 ImmunoControl slides
General Device Characteristic: Similarities		
Intended Use/ Indications For Use	Her2/ER/PR IHControls®-Level H Her2/ER/PR IHControls®-Level H are peptide based qualitative on-slide controls to monitor the performance of the analytic components (antigen retrieval and	QCS HER2 ImmunoControls, are intended for laboratory use to control semi-quantitative immunohistochemistry using different Her2/neu antibodies. This control ensures that

Device & Predicate Device(s):	K220163	K023335
	immunostaining) of the immunohistochemical (IHC) staining process for certain human epidermal growth factor receptor type II (HER2), estrogen receptor (ER) and progesterone receptor (PR) IHC stains. It is indicated for use with formalin-fixed paraffin-embedded (FFPE) breast tumor samples. Her2/ER/PR IHControls®-Level H are not intended to be used for scoring HER2, ER, and PR IHC stained slides. Her2/ER/PR IHControls®-Level H are an additional control to the run controls specified in the HER2, ER, or PR IHC device labeling and are not intended to replace the controls approved or cleared as part of an IHC device. Her2/ER/PR IHControls®-Level M Her2/ER/PR IHControls®-Level M are peptide based qualitative on-slide controls to monitor the performance of the analytic components (antigen retrieval and immunostaining) of the immunohistochemical (IHC) staining process for certain human epidermal growth factor receptor type II (HER2), estrogen receptor (ER) and progesterone receptor (PR) IHC stains. It is indicated for use with formalin-fixed paraffin-embedded (FFPE) breast tumor samples. Her2/ER/PR IHControls®-Level M are not intended to be used for scoring HER2, ER, and PR IHC stained slides.	performance of immunohistochemical staining is consistent in one laboratory over time and also aids in correlation with the results of other laboratories.

Device & Predicate Device(s):	K220163	K023335
	Her2/ER/PR IHControls®-Level M are an additional control to the run controls specified in the HER2, ER, or PR IHC device labeling and are not intended to replace the controls approved or cleared as part of an IHC device. Her2/ER/PR IHControls®-Level L Her2/ER/PR IHControls®-Level L are peptide based qualitative on-slide controls to monitor the performance of the analytic components (antigen retrieval and immunostaining) of the immunohistochemical (IHC) staining process for certain human epidermal growth factor receptor type II (HER2), estrogen receptor (ER) and progesterone receptor (PR) IHC stains. It is indicated for use with formalin-fixed paraffin-embedded (FFPE) breast tumor samples. Her2/ER/PR IHControls®-Level L are not intended to be used for scoring HER2, ER, and PR IHC stained slides. Her2/ER/PR IHControls®-Level L are an additional control to the run controls specified in the HER2, ER, or PR IHC device labeling and are not intended to replace the controls approved or cleared as part of an IHC device.	
Assay compatibility	Polyclonal and monoclonal IHC stains	Polyclonal and monoclonal IHC stains
Analyte concentration	Three different levels of HER2, ER, PR each at different concentrations.	Three different cell lines each expressing different concentrations of HER2.

Device & Predicate Device(s):	K220163	K023335
General Device Characteristic: Differences		
Reagents	Formalin-fixed HER2, ER, PR peptide epitopes covalently attached to glass microbeads in a liquid matrix that adhere to a slide.	Formalin-fixed paraffin embedded breast cancer cell lines expressing HER2 protein, mounted on slides
Slide controls	Controls on every slide (on-slide control).	Separate slides for batch control

VI Standards/Guidance Documents Referenced:

I/LA28-A2: Quality Assurance for Design Control and Implementation of immunohistochemistry Assays; Approved Guideline—Second Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

a) Lot to Lot Reproducibility:
Three independent lots of each level (H, M and L) of HER2/ER/PR IHControls® were used in this study. The reproducibility of the products was evaluated by physical (concentration, pH) as well as functional (stain intensity, microbead retention) criteria.

Peptide analyte concentration: The peptides that represent the analytes have a single fluorescein attached at a location away from the primary antibody epitope. The attachment of the peptide(s) to the microbead was verified by measuring fluorescence intensity. Coefficients of variation (CVs) among three lots were as follows: Level H product – CV ranged from 2.7% - 6.8%, Level M – 9.5% and Level L- 4.5. All of the product lots also met the required minimum threshold concentration criteria that was developed to target the three distinct levels for peptide analyte concentration.

Table 2. Reproducibility of Peptide Analyte Concentration on Microbead

Microbead	Product	CV
Microbead containing Her2 Peptide (3 Lots)	Level H product	2.7%
Microbead containing PR Peptide-1 (3 Lots)	Level H product	6.8%
Microbead containing PR Peptide-2	Level H product	

Microbead	Product	CV
(3 Lots)		4.8%
Microbead containing ER Peptide (3 Lots)	Level H product	5.9%
Microbead containing Her2/ER/PR (all peptides) (3 Lots)	Level M product	9.5%
Microbead containing Her2/ER/PR (all peptides) (3 Lots)	Level L product	4.5%

Stain intensity: This was a functional test to verify that the microbead was immunoreactive to at least a minimal threshold level of stain intensity. Stain intensity was measured after depositing a 1 microliter droplet of product onto a microscope slide, which was then processed with the appropriate IHC stain. Table 3 shows that the CVs among three lots of each of the three assembled products ranged from 6.5% - 22%, depending on the analyte being stained. This variability factors in the peptide analyte reproducibility coupled with the variability associated with IHC assays. It meets the minimum stain intensity requirements for each product lot.

Table 3. Lot to Lot Reproducibility by Stain Intensity

Product	Antibody	CV
Level H product	HER2 4B5	13.9%
	HER2 polyclonal	9.1%
	ER EP1	22%
	PR 636	18.7%
	PR 16	15.5%
Level M product	HER2 polyclonal	9.3%
	ER SP1	6.5%
	ER 6F11	14.6%
	PR 1294	7.6%
	PR1E2	12.2%
Level L product	ER SP1	6.7%

pH: All lots had a pH of 6 +/- 0.3, as per the manufacturing specification.

Microbead retention: The microbead retention was measured after depositing a 1 microliter droplet of the assembled product onto a microscope slide. Three lots of each product (Levels H, M and L) were tested in triplicate (that included with and without antigen retrieval conditions for each). The “without antigen retrieval condition”

represented the baseline for 100% retention. The percent retention was calculated as the number of microbeads on the antigen retrieval slides divided by the number of microbeads on the slides that were untreated. The minimum passing threshold for acceptability was 80%. Retention rates were consistently found to be >90%.

b) Reader Reproducibility:
The purpose of this study was to evaluate the pathologist's ability to reproducibly interpret HER2/ER/PR IHControls®. Thirty slides (10 slides each for HER2, ER, and PR) containing the HER2/ER/PR IHControls® beads were evaluated in this study. In each set of ten, 4 were stained with a diluted primary antibody (2 slides with weak stain) or no primary antibody (2 slides with no stain) to simulate an IHC staining problem. Slides stained sub-optimally were included in this study to avoid bias. All 3 product levels, H, M, and L were tested.

Three pathologists were provided with an HER2/ER/PR IHControls® slide set that included slides demonstrating the expected stain intensity associated with normal staining. Each pathologist evaluated 10 HER2, 10 ER, and 10 PR HER2/ER/PR IHControls® slides in a blinded manner and assessed stain intensity. The pathologists evaluated the slides and scored them as Pass (staining is as expected) or Fail (suboptimal staining due to diluted primary antibody). The pathologists' answers were then compared, to determine if pathologists were able to identify decrements in stain intensity.

There was 100% agreement with the expected results for both the Pass and Fail parameters for all 3 pathologists.

2. Linearity:

Not applicable

3. Analytical Specificity/Interference:

This study evaluated HER2/ER/PR IHControls® immunoreactivity to a panel of 26 antigenically irrelevant antibodies that are commonly used in clinical immunohistochemistry laboratories. HER2/ER/PR IHControls® were pipetted onto slides in duplicate, and a positive tissue control was included on every slide to verify test performance. The slides were stained with the primary antibodies listed in the Table 4 below and reviewed. All 3 product levels, H, M, and L were tested.

Staining for HER2/ER/PR IHControls® and tissue control were expressed as "positive" or "negative" as in Table 4 below.

Table 4. Staining Results when HER2/ER/PR IHControls® are stained with commonly used antigenically irrelevant antibodies

	Marker	Organ	Antibody	Staining in Tissue Control	Staining in HER2/ER/PR IHControls®
1.	Bcl-6	Tonsil	GI191E/A8	Positive	Negative
2.	C4d	Tonsil	SP91	Positive	Negative

3.	CD10	Tonsil	SP67	Positive	Negative
4.	CD138	Tonsil	B-A38	Positive	Negative
5.	CD20	Tonsil	L26	Positive	Negative
6.	CD34	Tonsil	QBEnd/10	Positive	Negative
7.	CD5	Tonsil	SP19	Positive	Negative
8.	CD56	Tonsil	MRQ-42	Positive	Negative
9.	CMV	Placenta	CMV	Positive	Negative
10.	Cyclin D1	Lymphoma	SP4-R	Positive	Negative
11.	Cytokeratin 20	Colon	SP33	Positive	Negative
12.	Cytokeratin 7	Lung	SP52	Positive	Negative
13.	EFGR	Normal Skin	5B7	Positive	Negative
14.	Keratin	Skin	34BE12	Positive	Negative
15.	Ki-67	Tonsil	30-9	Positive	Negative
16.	Mart-1	Melanoma	A103	Positive	Negative
17.	MITF	Melanoma	C5/D5	Positive	Negative
18.	p53	p53	BP53-11	Positive	Negative
19.	p63	Prostate	4A4	Positive	Negative
20.	Pan Keratin	Appendix	AE1/AE3/PCK26	Positive	Negative
21.	Podoplanin	Tonsil	D2-40	Positive	Negative
22.	PSA	Prostate	PSA	Positive	Negative
23.	S100	S100	4C4.9	Positive	Negative
24.	Somatostatin	Pancreas	Somatostatin	Positive	Negative
25.	TAG 72	Colon	B72.3	Positive	Negative
26.	TTF-1	Thyroid	8G7G3/1	Positive	Negative
27.	Breast	Breast ca	ER SP1	Positive	Positive
28.	Breast	Breast ca	HER2 4B5	Positive	Positive
29.	Breast	Breast ca	PR 1E2	Positive	Positive

Results: None of the HER2/ER/PR IHControls® stained with any of the 26 antigenically irrelevant antibodies. All tissue positive controls stained, demonstrating that the IHC assay itself worked appropriately. The HER2/ER/PR IHControls® slides showed appropriate positive and negative staining.

4. Assay Reportable Range:

Not applicable

5. Stability, Expected Values (Controls, Calibrators, or Methods):

The stability study tested the immunoreactivity of 3 different lots of the HER2/ER/PR panel of HER2/ER/PR IHControls® in the final product container under refrigerated conditions (2-8ºC).

For each IHControls®, three vials from each of three different lots were stored at 2 – 8ºC, for a total of nine vials. At each time point, all the vials were removed from the refrigerator and opened. One vial of each set was used until it was depleted, followed by the second vial, then

the third. One microliter of the HER2/ER/PR IHControls® was pipetted onto duplicate slides and tested by IHC staining.

Each slide consisted of nine one microliter spots: three rows of three spots. Each row contained one spot for each of the HER2/ER/PR IHControls® lots. The HER2/ER/PR IHControls®-spotted slides were stained with various HER2, ER, or PR immunostains.

Failure is defined when stain intensity is below moderate intensity, for two sequential evaluations. The failure time point is the first of these two. For visual examination, the data are expressed as Pass (P) or Fail (F). Based on the data, the shelf-life of HER2/ER/PR IHControls® was determined to be at 392 days when stored at 2 – 8ºC.

6. Detection Limit:

   Not applicable

7. Assay Cut-Off:

   Not applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:
   Not applicable

2. Matrix Comparison:
   Not applicable

C Clinical Studies:

1. Clinical Sensitivity:
   Not applicable

2. Clinical Specificity:
   Not applicable

3. Other Clinical Supportive Data:

   a. The performance of the HER2/ER/PR IHControls® as a positive on-slide control was evaluated in 3 clinical sites (immunohistochemistry laboratories). HER2/ER/PR IHControls® was placed on the same slides as patient samples, as per device instructions for use. Also, the laboratory's own tissue controls that are normally used to evaluate the quality of their stains were placed on the same slides. The HER2/ER/PR IHControls® were used for HER2, ER, and PR testing for 37 to 42 days over a period of two months at each site for a total of 442 samples. The pathologist at each site evaluated stain performance using the HER2/ER/PR IHControls® at the same time that the tissue controls were evaluated. Slide review results were recorded as pass or fail, both for the laboratory's existing (comparator) controls as well as for the HER2/ER/PR IHControls®.

The overall concordance rate was 440 out of 442 tests, or 99.5%, from all 3 clinical trial sites, for ER, PR, and HER2 tests combined. Individual site concordance was 100%, 99.5%, and 99.1%. The two discrepancies between HER2/ER/PR IHControls® and the comparator tissue controls were due to operator error: (1) placement of the HER2/ER/PR IHControls® at the slide edge because the patient sample and tissue (comparator) control left no other place, and (2) use of an incorrect HER2/ER/PR IHControls®. In addition, at one of the sites the histotechnologist did not pipette the HER2/ER/PR IHControls® onto the slides on 2 separate days. Therefore, data points from the two days (that included a total of 10 slides) were not included in the analysis.

Table 5. Performance of HER2/ER/PR IHControls® from Three Clinical Sites

Site	Immunostain	Product Tested	# of Slides	Concurrence (%)	Deviations
1	Estrogen Receptor Clone 6F11 Ready-to-Use Primary Antibody for Bond	BRL2U04-001 Level M	39	39/39 (100%)	0
	VISION BIOSYSTEMS Progesterone Receptor PGR CLONE 16	BRLSll-001 Level H	39	39/39 (100%)	0
	BOND ORACLE HER2 IHC System	BRL2U04-001 Level M	39	39/39 (100%)	0
2	DAKO Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PGR 636, Antibody for Immunoenzymatic Staining	BRL2U04-001 Level M	172*	171/172 (99.42%)	1
	PATHWAY Anti-HER-2/Neu (4B5) Rabbit Monoclonal Primary Antibody	BRLSll-003 Level H	42	42/42 (100%)	0
	CONFIRM anti-Estrogen Receptor (SP1) Rabbit	BRL2W08-003 Level L	37	36/37 (97.3%)	1

Site	Immunostain	Product Tested	# of Slides	Concurrence (%)	Deviations
3	Monoclonal Primary Antibody				
	BOND Ready-to-Use Primary Antibody Progesterone Receptor (16)	BRLSll-001 Level H	37	37/37 (100%)	0
	PATHWAY Anti-HER-2/Neu (4B5) Rabbit Monoclonal Primary Antibody	BRLSll-001 Level H	37	37/37 (100%)	0

*Slides from two days, ten (10) slides in total, were deemed uninformative because HER2/ER/PR IHControls® were not applied to the slides and therefore not included in the data analysis

b. An additional study was conducted to demonstrate that HER2/ER/PR IHControls® are comparable to staining failures in conventional tissue controls, under simulated failure (lower levels of primary antibody) conditions.

The study compared the sensitivity of HER2/ER/PR IHControls® and tissue controls in detecting simulated assay failure. Microscope slides bearing both HER2/ER/PR IHControls® and tissue controls were stained as per protocol or after diluting the primary antibody. The HER2/ER/PR IHControls® and tissue controls were then evaluated visually, by 4 pathologists to objectively and quantitatively assess stain intensity. Pass/fail scores were assigned to each slide. A "pass" meant that quality control revealed a normally functioning IHC assay; the stain intensity was not noticeably different than that associated with assay normal mode. A "fail" meant that the quality control reveals the presence of an IHC assay problem showing noticeable lowered stain intensity than baseline. In 48 readouts, both tissue controls and HER2/ER/PR IHControls® provide concordant measures of IHC assay performance. There was 100% agreement in identifying assay failures between HER2/ER/PR IHControls® and tissue controls based on the staining in HER2/ER/PR IHControls® and tissue control slides.

D Clinical Cut-Off:

Not applicable

E Expected Values/Reference Range:

Not applicable

VIII Proposed Labeling:

The labeling is sufficient, and it satisfies the requirements of 21 CFR Part 809.10.

IX Conclusion:

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