SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	In vitro diagnostic immunohistochemistry (IHC) for detection of PD-L1 protein in formalin-fixed, paraffin-embedded (FFPE) human tissue sections
Device Trade Name:	VENTANA PD-L1 (SP263) Assay
Device Product Code:	PLS
Applicant's Name and Address:	Ventana Medical Systems, Inc. (Roche Tissue Diagnostics) 1910 E Innovation Park Drive Tucson, AZ 85755
Date of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P160046/S010
Date of Notice of Approval:	October 15, 2021

The VENTANA PD-L1 (SP263) Assay was approved on May 1, 2017 for the qualitative detection of PD-L1 protein in formalin-fixed, paraffin-embedded (FFPE) urothelial carcinoma tissue with OptiView DAB IHC Detection Kit on a VENTANA BenchMark ULTRA instrument.

However, the urothelial indication was withdrawn as a consequence of the withdrawal of the corresponding drug indication.

The current supplement was submitted to expand the indication for the VENTANA PD-L1 (SP263) Assay to include non-small cell lung carcinoma (NSCLC) PD-L1 ≥ 1% TC for treatment with TECENTRIQ.

II. INDICATIONS FOR USE

VENTANA PD-L1 (SP263) Assay is a qualitative immunohistochemistry assay using rabbit monoclonal anti-PD-L1 clone SP263 intended for use in the assessment of the programmed death ligand-1 (PD-L1) protein in formalin-fixed, paraffin-embedded (FFPE) non-small cell lung carcinoma (NSCLC) tissue specimens by light microscopy. The VENTANA PD-L1 (SP263) Assay is used with the OptiView DAB IHC Detection Kit for staining on the BenchMark ULTRA instrument.

PD-L1 protein expression in NSCLC is determined by the percentage of tumor cells (% TC) with any membrane staining above background.

VENTANA PD-L1 (SP263) assay is indicated as an aid in identifying patients eligible for treatment with the therapy listed in Table 1 for the indication and PD-L1 status in accordance with the approved therapeutic product labeling.

Table 1. VENTANA PD-L1 (SP263) Assay Companion Diagnostic Indication

Indication for Use	PD-L1 Cut-off	Therapy
NSCLC	≥ 1% TC	TECENTRIQ (atezolizumab)

Results of the VENTANA PD-L1 (SP263) Assay should be interpreted by a qualified pathologist in conjunction with histological examination, relevant clinical information, and proper controls.

This product is intended for in vitro diagnostic (IVD) use.

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

Warnings and precautions can be found in the VENTANA PD-L1 (SP263) Assay product labeling.

V. DEVICE DESCRIPTION

A. Device Kit Components

VENTANA PD-L1 (SP263) Assay contains optimized reagents required to complete an immunohistochemical staining procedure for FFPE specimens on the BenchMark ULTRA automated staining instrument visualized using the OptiView DAB IHC Detection Kit. VENTANA PD-L1 (SP263) Assay includes a recombinant rabbit monoclonal antibody produced as purified cell culture supernatant and contains sufficient reagent for 50 tests. The antibody and detection reagents are provided as ready-to-use dispensers. Table 1 below provides an overview of the VENTANA PD-L1 (SP263) Assay Components.

Table 1. Overview of the VENTANA PD-L1 (SP263) Assay Components

Device Components	Packaged Form	Description
VENTANA anti-PD-L1 (SP263) Rabbit Monoclonal Primary Antibody	Dispenser: 50 tests	One 5 mL dispenser of VENTANA PD-L1 (SP263) contains approx. 8.05 µg of a rabbit monoclonal antibody. The antibody is diluted in 0.05 M Tris-HCI with 1% carrier protein, and 0.10% ProClin 300, a preservative. Total protein concentration of the reagent is approx. 10 mg/mL. Specific antibody concentration is approximately 1.61 µg/mL.

Device Components	Packaged Form	Description
OptiView DAB IHC Detection Kit	Set of 6 dispensers packaged in a kit: 250 tests	**OptiView Peroxidase Inhibitor** contains 3.0% hydrogen peroxide solution.
		OptiView HQ Universal Linker contains a cocktail of HQ-labeled (HQ is a proprietary hapten covalently attached to the goat antibodies) antibodies (goat anti-mouse IgG, goat anti-mouse IgM, and goat anti-rabbit) (<50 µg/mL) in a buffer containing protein with ProClin 300, a preservative.
		OptiView HRP Multimer contains a mouse monoclonal anti-HQ-labeled HRP tertiary antibody (<40 µg/mL) in a buffer containing protein with ProClin 300, a preservative.
		OptiView H_2O_2 contains 0.04% hydrogen peroxide in a phosphate buffer solution.
		OptiView DAB contains 0.2% 3, 3'-diaminobenzidine tetrahydrochloride (DAB) in a proprietary stabilizer solution with a proprietary preservative.
		OptiView Copper contains copper sulfate (5.0 g/L) in an acetate buffer with a proprietary preservative.
BenchMark ULTRA (IHC/ISH) automated staining instrument and VSS system software	Instrument installed with the VSS host system software	A PC that runs on Microsoft Windows controls and monitors the BenchMark ULTRA instrument via the host operating software. The BenchMark ULTRA software has been developed per FDA's guidance on the development of Medical Device Software.
Rabbit Monoclonal Negative Control Ig	1 dispenser packaged as 250 test kit	Intended for laboratory use as a control for nonspecific binding of rabbit immunoglobulin (Ig) in sections of FFPE tissue. One 25 mL dispenser contains approximately 250 µg of a rabbit monoclonal antibody. The antibody is diluted in 0.08 M PBS with 3% carrier protein and 0.05% ProClin 300, a preservative.

Ancillary reagents required for the assay are listed below:

- Hematoxylin II
- Bluing Reagent
- Reaction Buffer (10x)
- EZ Prep Reagent (10x)
- ULTRA Cell Conditioning (CC1) (Pre-dilute)
- ULTRA Liquid Cover Slip (LCS) (Pre-dilute)

B. Device Instrumentation and Software

The VENTANA PD-L1 (SP263) Assay is performed on the BenchMark ULTRA automated staining instrument using the VSS Software versions 12.3 to 12.5.3. The VENTANA PD-L1 (SP263) Assay protocol is assay specific. The software has been designed to recognize and group VENTANA PD-L1 (SP263) Assay, requiring that all system reagents are used together.

C. Specimen Preparation

Routinely processed, FFPE tissues are suitable for use with this VENTANA PD-L1 (SP263) Assay. Ventana recommends tissue fixation in 10% neutral buffered formalin (NBF) for a period of at least 6 hours and for a maximum of 72 hours. Acceptable fixatives for use with VENTANA

PD-L1 (SP263) are Zinc Formalin and Z-5 fixatives when used with at least 6 hours of fixation time. The amount used should be 15 to 20 times the volume of tissue. Fixation can be performed at 15°C - 25°C. Other fixatives, including 95% alcohol, AFA and PREFER, are not acceptable for use with the VENTANA PD-L1 (SP263) Assay.

Tissue sections approximately 4-5 µm thick mounted on positively-charged slides are used for this assay. Slides should be stained promptly, as antigenicity of cut tissue sections may diminish over time and is compromised within 12 months after cutting from the paraffin block for NSCLC specimens and 9 months for placenta specimens. See device package insert for additional details.

D. Quality Control Procedures

Run controls are included in each staining run to establish the validity of the test results. The device labeling instructs that the following controls to be run with the assay.

1. Placenta Tissue Control

   A tissue control must be included with each staining run. Qualified normal human term placental tissue is to be used as the control. Control tissue should be fixed as soon as possible and processed in a manner identical to patient tissues. Such tissue may monitor all steps of the analysis, from tissue preparation through staining. Placental tissue contains positive and negative staining elements for the PD-L1 protein and is therefore suitable for use as a tissue control. The positive and negative staining tissue components are used to confirm that the assay functioned properly.

   Placental tissue shows moderate to strong uniform staining of the membrane and weak to strong uniform staining of the cytoplasm of trophoblast-lineage cells. Placental stromal tissue and vasculature can be used for assessment of any background staining.

2. Rabbit Monoclonal Negative Control IG

   A matched negative reagent control slide must be run for every specimen to aid in the interpretation of results. Rabbit Monoclonal Negative Control Ig a negative reagent control antibody, is specifically matched for this assay and is used in place of the primary antibody to evaluate nonspecific staining that may result from reaction with detection chemistry and not the anti PD-L1 primary antibody. The staining procedure for the negative reagent control should equal the primary antibody incubation period. Use of a different negative control reagent, or failure to use the recommended negative control reagent, may cause false results.

E. Principles of Operation

The VENTANA PD-L1 (SP263) Assay is fully automated for use on the BenchMark ULTRA automated slide stainer from deparaffinization through counterstaining. Patient FFPE tissue specimens are cut to approximately 4-5 µm thick and mounted on positively charged glass slides. These slides are loaded into the Benchmark ULTRA instrument. This system first removes the paraffin wax from the tissue, and then subjects the tissue to heated antigen retrieval (cell conditioning). Antigen retrieval is the process by which the ability of antibodies to bind to the epitopes is restored to formalin-fixed tissues. Endogenous peroxidases that could potentially

react with the horseradish peroxidase conjugates (HRP) are blocked with OptiView Inhibitor (3% H2O2). After the endogenous peroxidase block, the VENTANA PD-L1 (SP263) Rabbit Monoclonal Primary Antibody is dispensed during the antibody incubation step and allowed to bind to its antigen. The slides are then incubated with the reagents in the OptiView DAB IHC Detection Kit, which is an indirect, biotin-free system for detecting mouse IgG, mouse IgM, and rabbit primary antibodies which produces a visible dark brown precipitate (3,3'-Diaminobenzidine) via a horseradish peroxidase (HRP) enzymatic reaction at the antigen site. Tissues are then counterstained blue using Hematoxylin II and Bluing Reagent to create brown/blue contrast to aid the pathologist when reviewing the slides using bright field microscopy. The staining protocol is shown in Table 2 below.

Table 2. Staining Protocol for VENTANA PD-L1 (SP263) Assay

Staining Procedure: VENTANA PD-L1 (SP263) Assay	
Procedure Parameter	**Selection**
Deparaffinization	Selected
Baking	Optional 60ºC 12 minutes
Cell Conditioning	CC1 Cell Conditioning 64 minutes
Pre-primary Antibody Peroxidase	Selected
Antibody (Primary)	VENTANA PD-L1 (SP263) Selected 16 minutes, 36ºC or Negative Control Selected 16 minutes, 36ºC
OptiView HQ Linker	8 minutes (default)
OptiView HQ Multimer	8 minutes (default)
Counterstain	Hematoxylin II, 4 minutes
Post Counterstain	Bluing Reagent, 4 minutes

F. Interpretation of PD-L1 Staining

The VENTANA automated immunostaining procedure causes a brown colored DAB reaction product to precipitate at the antigen sites localized by the VENTANA PD-L1 (SP263) Assay. The stained slide(s) are interpreted by a qualified pathologist using light microscopy. A qualified pathologist experienced in IHC procedures must evaluate tissue controls and qualify the stained product before interpreting results.

1. Placenta Tissue Control Interpretation

   The placenta tissue control should be examined for appropriate staining. The stained positive and negative staining elements of the placenta tissue control should be examined to ascertain that all reagents are functioning properly. Examples of positive and negative staining elements of the placenta tissue control can be found in the VENTANA PD-L1 (SP263) Assay Interpretation Guide for NSCLC. Placental Tissue Control Evaluation Criteria are described in Table 3.

Table 3. Placenta Tissue Control Evaluation Criteria for the VENTANA PD-L1 (SP263) Assay

Interpretation	Staining Description
Acceptable	Moderate to strong uniform membrane staining of trophoblast-lineage cells, and placental stroma and vasculature with no staining.
Unacceptable	No to weak uniform membrane staining of trophoblast lineage cells and/or specific staining within placental stromal and vascular tissue.

If the positive or negative tissue controls fail to demonstrate appropriate staining or demonstrate a change in interpretation, any results with the test specimens should be considered invalid.

2. Negative Reagent Control Interpretation

Non-specific staining, if present, will have a diffuse appearance and can be evaluated using the negative reagent control slide stained with Rabbit Monoclonal Negative Control Ig. Intact cells should be used for interpretation of staining results, as necrotic or degenerated cells often stain nonspecifically. If background staining is excessive, results from the test specimen should be considered invalid. Examples of background staining for this assay can be found in the VENTANA PD-L1 (SP263) Assay Interpretation Guide for Non-Small Cell Lung Carcinoma.

3. Patient Tissue Interpretation

Patient tissue must be evaluated according to the VENTANA PD-L1 (SP263) Assay scoring algorithm for NSCLC provided in Table 4 and the non-specific background scoring criteria provided in Table 5. Refer to the VENTANA PD-L1 (SP263) Assay Method Sheet and VENTANA PD-L1 (SP263) Assay Interpretation Guide for non-small cell lung carcinoma for additional details.

Table 4. VENTANA PD-L1 (SP263) Assay Scoring Algorithm for NSCLC

PD-L1 Interpretation	Staining Description
≥ 1%	≥ 1% of tumor cells with membrane positivity for PD-L1 at any intensity above background staining as noted on the corresponding negative control.
< 1%	< 1% of tumor cells with membrane positivity for PD-L1 at any intensity above background staining as noted on the corresponding negative control.

Table 5. Non-specific Background Scoring Criteria for VENTANA PD-L1 (SP263) Assay

Interpretation	Staining Description
Acceptable	Non-specific staining that is not obtrusive to interpretation of specific staining.
Unacceptable	Non-specific staining that is obtrusive to interpretation of specific staining.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There is currently no alternative FDA-cleared or approved assay available for detection of PD-L1 in non-small cell lung carcinoma FFPE tissues to estimate the likelihood of response for patients treated with TECENTRIQ (atezolizumab).

VII. MARKETING HISTORY

The VENTANA PD-L1 (SP263) Assay for NSCLC is not currently marketed in any country with the intended use to identify patients for treatment with TECENTRIQ.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Failure of the device to perform as expected or failure to correctly interpret test results may lead to incorrect PD-L1 test results, and an inaccurate estimate of a patient's benefit from TECENTRIQ and subsequently improper interpretation of the benefit/risks for patients with NSCLC who are considering treatment with TECENTRIQ.

For the specific adverse events that occurred in the TECENTRIQ clinical study in NSCLC, please see the TECENTRIQ FDA approved package insert which is available at Drugs@FDA.

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

Preclinical studies were performed using the VENTANA PD-L1 (SP263) Assay to establish analytical performance of the device. This assay was run using a VENTANA BenchMark ULTRA instrument, using NSCLC tissue samples that had a range of PD-L1expression levels. These studies were conducted to characterize the assay, demonstrate the impact of pre-analytical variables on assay performance, verify precision and robustness of the assay, and establish assay stability. The study results detailed below establish sensitivity, specificity, precision and reproducibility of the device.

1. Analytical Sensitivity

   The VENTANA PD-L1 (SP263) assay was used to assess the prevalence of PD-L1 staining for the 1% TC cutoff on 733 NSCLC specimens. The prevalence of PD-L1 positive cases based on the tumor cell expression ≥ 1% cutoff was 60% (441/733).

2. Analytical Specificity

   The antibody used in the VENTANA PD-L1 (SP263) Assay is Rabbit Anti-Human PD-L1/CD274 Monoclonal Antibody (Clone SP263). The molecular weight of the antibody's target (PD-L1) is 32 kDa, and the SP263 clone specifically targets a 19 amino acid sequence at the cytoplasmic tail of PD-L1. The following studies were conducted with PD-L1 (SP263) antibody to establish antibody specificity.

a. Western Blot Studies

Western blot analysis was performed on whole cell lysates from 4 cell lines with varying expression levels of PD-L1. The 4 cell lines were H820 (Lung), MDA-231 (Breast), H1975 (Lung) and Calu-3 (Lung). The cell lines were chosen for this study based on IHC staining for PD-L1 (SP263). Independent confirmation of the relative expression levels was based on assessment of mRNA expression levels for PD-L1. No unexpected staining or background was observed in any of the whole cell lysates, that resulted in the ~45-50kD band corresponding to the expected molecular weight of endogenous PD-L1 protein in H820, MDA-MB-231, and H1975. Results were consistent with the anti-SP263 clone reacting as expected with the ~35kD band containing purified recombinant PD-L1 protein that served as the positive control, and it did not react with the recombinant BCL-2 protein used as the negative control.

b. Blast Results for SP263 Epitope

PD-L1 is a member of the B7 family of ligands. PD-L1 (SP263) targets 7 amino acids in the cytoplasmic tail of PD-L1. NCBI BLASTp was used to search for sequence similarity using the SP263 epitope and no significant similarity was found to any other B7 family members.

c. Peptide Inhibition Studies

The specificity of primary antibody binding to PD-L1 was assessed by pre-incubating the antibody with four different concentrations of the specific peptide containing the antibody binding epitope, or a non-specific peptide. The antibody was diluted 1:1 with either the peptide solution under investigation or buffer with no peptide. One lot of antibody was used for this study. In the presence of high molar concentrations of this peptide, the PD-L1 SP263 antibody was completely inhibited from binding to tissue expressing PD-L1 protein as determined by the absence of IHC staining. The non- specific peptide had no effect on PD-L1 staining.

d. Immunoreactivity in Human Tissues

One lot of VENTANA PD-L1 (SP263) Assay and Rabbit Monoclonal Negative Control Ig were used to stain slides of a commercially available multi-tissue array of normal and neoplastic tissue and evaluated by a PD-L1 (SP263) trained qualified reader for presence of positive staining, staining intensity, and background in tumor cells, tumor infiltrating immune cell, and normal cells.

A total of 93 normal tissues and 54 neoplastic tissues were analyzed in this study. The normal formalin-fixed, paraffin-embedded (FFPE) tissues included 25 common types of normal human organs which represent three cases per organ type from three unique individuals. Results for normal tissues are shown in Table 6 and results for neoplastic tissues are shown in Table 7.

Table 6. VENTANA PD-L1 (SP263) Assay Staining of FFPE Normal Tissues

Tissue	No. positive / total cases	Tissue	No. positive / total cases
Adrenal gland	0/3*	Mesothelium	0/3†
Bladder	0/3	Myeloid (bone marrow)	0/4*,†
Breast	0/3	Nerve (sparse)	0/3
Cerebellum	0/3	Ovary	0/3
Cerebrum	0/3	Pancreas	0/3*
Cervix	0/3	Parathyroid gland	0/4
Colon	0/3†	Prostate	0/3
Endometrium	0/3	Salivary gland	0/3†
Esophagus	1/3*,†	Skeletal muscle	0/3
Heart	0/3	Skin	0/4§
Hypophysis	0/3*,†	Spleen	0/3†
Intestine, small	0/3†	Stomach	0/3*,†
Kidney	0/3†	Testis	0/3
Larynx	0/3†	Thymus gland	0/3†
Liver	0/3	Thyroid	0/3*,†
Lung	0/3†	Tonsil	3/3†
Lymph node	0/3†		

Additional staining observed: * Cytoplasmic staining, † Immune cell staining, § Melanocyte staining. Percent of IC present above background cannot be evaluated in this study because there is no tumor area for which to score tumor infiltrating immune cells.

Table 7. VENTANA PD-L1 (SP263) Assay Staining of Formalin-fixed, Paraffin-embedded Neoplastic Tissues for any Tumor Cell or Immune Cell Staining

Tissue Origin	Pathology	No. Positive / Total Cases	
		Tumor Cells	Immune Cells
Cerebrum	Glioblastoma	0/1	1/1
Cerebrum	Atypical meningioma	0/1	0/1
Cerebrum	Malignant ependymoma	0/1	1/1
Cerebrum	Oligodendroglioma	0/1	0/1
Ovary	Serous adenocarcinoma	0/1	1/1
Ovary	Adenocarcinoma	1/1	0/1
Pancreas	Islet cell carcinoma	0/1	0/1
Pancreas	Adenocarcinoma	0/1	1/1
Testis	Seminoma	0/1	0/1
Testis	Embryonal carcinoma	0/1	0/1
Thyroid	Medullary carcinoma	0/1	0/1
Thyroid	Papillary carcinoma	1/1	0/1
Breast	Intraductal carcinoma	0/1	1/1
Breast	Invasive ductal carcinoma	0/2	0/2
Spleen	Diffuse B-cell lymphoma	0/1	1/1
Lung	Small cell undifferentiated carcinoma	1/1	1/1

Tissue Origin	Pathology	No. Positive / Total Cases	
		Tumor Cells	Immune Cells
Lung	Squamous cell carcinoma	1/1	1/1
Lung	Adenocarcinoma	0/1	0/1
Esophagus	Neuroendocrine carcinoma	0/1	0/1
Esophagus	Adenocarcinoma	0/1	0/1
Stomach	Signet-ring cell carcinoma	0/1	0/1
Intestine	Adenocarcinoma	0/1	0/1
Intestine	Stromal sarcoma	0/1	0/1
Colon	Adenocarcinoma	0/1	1/1
Colon	Interstitialoma	0/1	0/1
Rectum	Adenocarcinoma	0/1	0/1
Rectum	Moderate malignant interstitialoma	0/1	0/1
Liver	Hepatocellular carcinoma	0/1	0/1
Liver	Hepatoblastoma	0/1	0/1
Kidney	Clear cell carcinoma	0/1	0/1
Prostate	Adenocarcinoma	0/2	0/2
Uterus	Leiomyoma	0/1	0/1
Uterus	Adenocarcinoma	0/1	0/1
Uterus	Clear cell carcinoma of endometrium	1/1	0/1
Uterine cervix	Squamous cell carcinoma	0/2	2/2
Striated muscle	Embryonal rhabdomyosarcoma	0/1	0/1
Rectum	Malignant melanoma	0/1	0/1
Skin	Basal cell carcinoma	0/1	0/1
Skin	Squamous cell carcinoma	0/1	0/1
Back	Neurofibroma	0/1	1/1
Retroperitoneum	Neuroblastoma	0/1	0/1
Abdominal cavity	Malignant mesothelioma	0/1	0/1
Mediastinum	Diffuse B-cell lymphoma	1/1	1/1
Lymph node	Hodgkin's lymphoma	1/1	1/1
Lymph node	Diffuse B-cell lymphoma	1/1	1/1
Pelvic cavity	Anaplastic large cell lymphoma	1/1	1/1
Bladder	Low grade malignant leiomyosarcoma	0/1	0/1
Bone	Osteosarcoma	0/1	1/1
Retroperitoneum	Spindle cell rhabdomyosarcoma	0/1	0/1
Smooth muscle	Moderate malignant leiomyosarcoma	0/1	0/1
Bladder	Transitional cell carcinoma (bladder)	1/1	1/1

3. Precision

The repeatability and intermediate precision of VENTANA PD-L1 (SP263) Assay was evaluated on the BenchMark ULTRA instrument in combination with OptiView DAB IHC Detection Kit by staining 24 unique cases of human NSCLC.

The sample distribution was as follows:

There were 13 positive cases (including 2 at borderline positive), and 11 negative cases (including 4 at borderline negative). The borderline ranges were, "<1% but not 0%" as borderline negative, and "1% to 9%" as borderline positive.

For within-day repeatability, 5 replicate slides from each of NSCLC specimens were stained on a single BenchMark ULTRA instrument within one day.

For between-day precision, 2 replicate slides from each of NSCLC specimens were stained with VENTANA PD-L1 (SP263) Assay on a single BenchMark ULTRA instrument across 5 non-consecutive days in a span of at least 20 days.

For between-instrument and between-lot precision, 27 slides each from 24 unique NSCLC specimens (11 PD-L1 ≥ 1% and 13 PD-L1 < 1%) were stained with VENTANA PD-L1 (SP263) Assay using three lots of VENTANA PD-L1 (SP263) antibody and three lots of OptiView DAB IHC Detection Kit on three BenchMark ULTRA instruments.

All slides were blinded, randomized, and evaluated using the VENTANA PD-L1 (SP263) Assay scoring algorithm.

Analyses included evaluation of overall percent agreement (OPA), positive percent agreement (PPA), and negative percent agreement (NPA).

A summary of the results can be found in Table 8.

Table 8. Repeatability and Intermediate Precision Study of VENTANA PD-L1 (SP263) Assay Staining on Individual NSCLC Specimens at ≥ 1% TC

Repeatability/Intermediate Precision Parameter	Agreement % (n/N), (95% CI)*
Within-day Repeatability (within a single day)	PPA: 100.0 (65/65/), (94.4-100.0) NPA: 100.0 (55/55), (93.5-100.0) OPA: 100.0 (120/120), (96.9-100.0)
Between-day Precision (5 non-consecutive days)	PPA: 100.0 (130/130), (97.1-100.0) NPA: 100.0 (110/110), (96.6-100.0) OPA: 100.0 (240/240), (98.4-100.0)
Between-instrument and Between-lot Precision (3 instruments, 3 antibody lots, and 3 detection kit lots)	PPA: 100.0 (378/378), (99.0-100.0) NPA: 100.0 (270/270), (98.6-100.0) OPA: 100.0 (648/648), (99.4-100.0)

* 2-sided 95% confidence intervals (CI) were calculated using the Wilson Score method.

4. Reader Precision

To assess between- and within-reader precision, three pathologists evaluated a total of 114 unique cases. The cases were blinded and randomized prior to evaluation for PD-L1 expression per the VENTANA PD-L1 (SP263) Assay scoring algorithm. The reader precision results are provided in Table 9.

The sample distribution was as follows:

There were 63 positive cases (including 9 at borderline positive), and 51 negative cases (including 6 at borderline negative).

Table 9. Between- and Within-reader Precision of VENTANA PD-L1 (SP263) Assay staining NSCLC Specimens at ≥ 1% TC

Reader Precision	Agreement % (n/N), (95% CI)*
Between-reader precision (average of reader-to-reader pairwise comparisons from first read)	APA: 94.3 (362/384), (90.5-97.4) ANA: 92.6 (274/296), (87.8-96.5) OPA: 93.5 (318/340), (89.9-97.1)
Within-reader precision (average of all three readers' agreement rates between first and second reads)	APA: 96.7 (376/389), (94.7-98.3) ANA: 95.6 (280/293), (92.9-97.8) OPA: 96.2 (328/341), (94.1-98.0)

* 2-sided 95% confidence intervals (CI) were calculated using the percentile bootstrap method from 2000 bootstrap samples.

5. External Reproducibility

An inter-laboratory reproducibility study for VENTANA PD-L1 (SP263) Assay staining was conducted to demonstrate reproducibility of the assay in determining PD-L1 protein expression in NSCLC tissue specimens. Twenty-eight unique NSCLC specimens with a range of PD-L1 expression (14 < 1% and 14 ≥ 1%, including 2 borderline positive and 2 borderline negative cases) were stained at 3 external laboratories on each of 5 non-consecutive days over a period of at least 20 days. The specimens were randomized before evaluation by 6 readers (2 readers/site) blinded to the sample identity. At each site, the stained slides were independently evaluated using the VENTANA PD-L1 (SP263) Assay scoring algorithm for NSCLC. Results are summarized in Table 10.

Table 10. Inter-laboratory Reproducibility of VENTANA PD-L1 (SP263) Assay Staining of NSCLC Specimens at ≥ 1% TC

Inter-laboratory Reproducibility[a]	Agreement % (n/N), (95% CI)[b]
Overall agreement [c] (compared to a consensus score, across sites, days and readers)	PPA: 99.5 (418/420), (98.6-100.0) NPA: 100.0 (419/419), (99.1-100.0) OPA: 99.8 (837/839), (99.3-100.0)
Between-site agreement [d] (average of site-to-site pairwise comparisons)	APA: 99.5 (8320/8360), (98.6-100.0) ANA: 99.5 (8360/8400), (98.6-100.0) OPA: 99.5 (8340/8380), (98.6-100.0)
Between-reader agreement [d] (average of reader-to-reader pairwise comparisons within each site)	APA: 100.0 (418/418), (99.1-100.0) ANA: 100.0 (420/420), (99.1-100.0) OPA: 100.0 (419/419), (99.1-100.0)

a n = 839 PD-L1 slide observations

b Note: 95% CI = Confidence interval

For PPA/NPA/OPA 95% CIs were calculated using the Wilson Score method for agreements of 100% or using the percentile bootstrap method for agreements less than 100%

For APA/ANA, 95% CIs were calculated using the transformed Wilson Score method for agreements of 100% or using the percentile bootstrap method for agreements less than 100%

c Agreement of study results with the case-level modal PD-L1 status.

d Pairwise agreement rates.

6. Impact of Tissue Specimen Preparation and Treatment Studies

a. Ischemia Study (Time to Fixation)

The objective of this study was to evaluate the effects of ischemic time on PD-L1 antigenicity as detected by staining with VENTANA PD-L1 (SP263) Assay. This study examined the effects of delay to fixation (Ischemia) for mouse xenografts at zero hour, 0.5 hours, 1 hour, 2 hours, 6 hours and 24 hours post excision, under refrigeration at 2-8°C. All samples were fixed in 10% NBF for 24 hours after being delayed for fixation at their various ischemia time points. The Assay demonstrated no significant change in staining intensity from hour zero to up to 24 hours using a xenograft tissue model.

b. Fixation Study

The objective of this study was to evaluate the effects of fixative type and fixation time on PD-L1 antigenicity as detected by staining with VENTANA PD-L1 (SP263) Assay. Two tonsil tissue cases were fixed for 1, 6, 12, 24, and 72 hours in six fixatives: 10% NBF, Zinc formalin, 95% alcohol, AFA, Z-5 and PREFER for a total of 12 tissues. The data was then compared to the reference standard of 10%NBF for 24 hours.

Tissues fixed for one hour in 10% NBF, Zinc formalin and Z-5 were unacceptable when stained with PD-L1 (SP263). All other time points (6, 12, 24 and 72 hour) in 10% NBF, Zinc formalin and Z-5 were acceptable with the VENTANA PD-L1 (SP263) Assay. The VENTANA PD-L1 (SP263) Assay demonstrated poor performance on the following fixatives at all time points: PREFER, AFA, and 95% alcohol. PREFER, AFA, and 95% alcohol should not be used as a fixative for anti-PD-L1.

7. Impact of Tissue Thickness

Tissue thickness was evaluated using 7 unique NSCLC specimens (2 PD L1 ≥ 1% and 5 PD-L1 < 1%). Duplicate sections at 2, 3, 5, 6, and 7 microns were tested for each case. Four microns thickness was used as reference. Two- and 5-microns thickness demonstrated concordant PD-L1 protein expression and acceptable background levels for VENTANA PD-L1 (SP263) Assay staining when compared to the reference of 4 microns. 3, 6, and 7 microns exhibited a change in PD-L1 protein expression compared to the reference. Specimens should be sectioned at 4-5 microns for staining with VENTANA PD L1 (SP263) Assay.

8. Impact of Cut Slide (section) Stability

This study evaluated the stability of PD-L1 antigen in formalin-fixed, paraffin-embedded (FFPE) tissue sections stored under two different storage conditions, 5±3°C and 30±5°C. Cut slide stability was evaluated on NSCLC tissues from 7 cases with TC staining that spanned a range of PD-L1 expression. Slides sectioned and stained at the Day 0 time point served as the baseline comparator for the remainder of the time points tested. Tissue

was sectioned from each of the seven cases onto glass slides and separated into two different storage conditions for the duration of the study. One box (set of slides) was stored at refrigerated temperature condition (5±3°C) and one at the incubator temperature condition (30±5°C). Slides were stained at each pre-defined designated time and staining results for each time point were compared to the Day 0 baseline slides.

Based on the study results, the recommended cut slide stability is 45 days at both the 5±3ºC and 30±5ºC storage conditions.

9. Real Time Stability Studies

The objective of this study was to assess the stability dating (shelf-life and in-use) and shipping category of the PD-L1 (SP263) Assay. Three production lots of VENTANA-PD-L1 (SP263) Assay were subjected to different stress conditions and then placed at the intended storage condition (2-8°C). Four NSCLC, 4 urothelial carcinoma and 4 squamous cell carcinomas of head and neck tissue were used in this study. Specimens were tested in triplicate at multiple time points. All lots passed the tested conditions to support a 24-month stability claim.

The conditions tested were as follows:

Ship Stress

Intended Storage (2-8°C)

Hot Ship Stress Cat. A (30°C±5ºC 192±5 hours)

Hot Ship Stress Cat. B (15°C±5ºC 192±5 hours)

Cold Ship Stress Freeze/Thaw (-20°C±5ºC 192±5 hours)

B. Additional Studies

1. Primary versus Metastatic

This study evaluated the concordance of PD-L1 status between FFPE matched primary and metastatic NSCLC tumors when stained with the VENTANA-PD-L1 (SP263) Assay on the BenchMark ULTRA instrument.

The concordance of PD-L1 expression level between 48 commercially sourced patient matched Primary and Metastatic tumor NSCLC samples demonstrated an overall concordance of 89.6% (43 /48) for PD-L1 expression level with 88.2% (15/17) positive percent agreement and 90.3% (28/31) negative percent agreement.

2. Tissue Heterogeneity

This study evaluated the prevalence of case heterogeneity in various NSCLC tissue blocks from the same case (multiple blocks from the same case, as well as heterogeneity within a block) when stained with VENTANA-PD-L1 (SP263) Assay on the BenchMark ULTRA instrument.

a. Intra-Block Heterogeneity

The intent of this study was to characterize the intra-block heterogeneity in NSCLC tissue blocks by evaluating the PD-L1 expression level for tumor cells of multiple slide cuts from the same tissue block when stained with VENTANA PD-L1 (SP263) Assay. Ten FFPE NSCLC cases encompassing the PD-L1 expression range from negative to positive were enrolled in the study. The case distribution consisted of 7 positive cases (including 2 borderline positive cases) and 3 negative cases (including 1 borderline negative case). For each block, approximately every 10th section was stained with VENTANA PD-L1 (SP263) Assay. Cases were sectioned to exhaustion. Eight out of the 10 cases maintained the PD-L1 expression level throughout the block. Both cases with inconsistent PD-L1 expression level were borderline cases, 1 borderline positive and 1 borderline negative.

b. Intra-case heterogeneity

The intent of this study was to characterize NSCLC case heterogeneity when multiple blocks from the same patient case were stained with the VENTANA PD-L1 (SP263) Assay. Twenty-four cases with two blocks per case were evaluated in this study. Twenty-two of the 24 cases (92%) maintained the same PD-L1 expression level between blocks.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The clinical performance of VENTANA PD-L1 (SP263) Assay was evaluated in IMpower010 clinical trial.

A. Study Design

IMpower010 is a Phase III, open-label, randomized study to investigate the efficacy and safety of TECENTRIQ (anti−PD L1 antibody) compared with best supportive care following adjuvant cisplatin-based chemotherapy in patients with completely resected stage IB-IIIA NSCLC (IMpower010). A total of 1280 enrolled patients had complete tumor resection and were eligible to receive up to 4 cycles of cisplatin-based chemotherapy. A total of 1005 patients were randomized (1:1) to receive TECENTRIQ 1200 mg by intravenous infusion every 3 weeks for 16 cycles unless disease recurrence or unacceptable toxicity, or Best Supportive Care (BSC), following recovery from surgery. Randomization was stratified by sex, stage of disease, histology, and PD-L1 expression.

Tumor specimens from 1169 of the 1280 enrolled patients (including 985 of the 1005 randomized patients) were tested with VENTANA PD-L1 (SP263) Assay to determine their PD-L1 expression level (the study was an all-comers study and patients were enrolled regardless of PD-L1 status; enrolled subjects were tested with VENTANA PD-L1 (SP263) Assay). The percentage of patients who had tumors with PD-L1 expression on ≥ 1% of tumor cells as determined by VENTANA PD-L1 (SP263) Assay was 55%.

1. Clinical Inclusion and Exclusion Criteria

Patients were included in the study if the following key efficacy-related inclusion/exclusion criteria were met:

Key Inclusion criteria for enrollment phase:

- Histological or cytological diagnosis of Stage IB (tumors ≥ 4 cm)–IIIA (T2–3 N0, T1–3 N1, T1-3 N2, T4 N0-1) NSCLC (per the UICC/AJCC staging system, 7th edition)
- A complete resection of NSCLC 4-12 weeks (≥ 28 days and ≤ 84 days) prior to enrollment and adequately recovered from surgery
- Accepted types of resection include any of the following: lobectomy, sleeve lobectomy, bilobectomy, or pneumonectomy. Patients must also have had a protocol-defined mediastinal lymph node evaluation.
- Eligible to receive a cisplatin-based chemotherapy regimen

Key Exclusion criteria for enrollment phase:

- Treatment with prior systemic chemotherapy, with exceptions
- Hormonal cancer therapy or radiation therapy as prior cancer treatment within 5 years before enrollment
- Treatment with any other investigational agent with therapeutic intent within 28 days prior to enrollment
- Prior treatment with CD137 agonists or immune checkpoint blockade therapies, anti-PD-1, and anti-PD-L1 therapeutic antibodies
- Malignancies other than NSCLC within 5 years prior to enrollment, with the exception of those with a negligible risk of metastasis or death (e.g., expected 5-year OS > 90%) treated with expected curative outcome
- Known tumor PD-L1 expression status as determined by an IHC assay from other clinical studies (e.g., patients whose PD-L1 expression status was determined during screening for entry into a study with anti-PD-1 or anti-PD-L1 antibodies but were not eligible)
- Patients with squamous cell histology (specific for pemetrexed treatment)

Key Exclusion criteria for randomized phase:

- Treatment with systemic immunostimulatory agents (including, but not limited to, interferons or interleukin-2) within 4 weeks or 5 drug-elimination half-lives of the drug, whichever was longer, prior to randomization
- Treatment with systemic corticosteroids or other immunosuppressive medications within 14 days prior to randomization

2. Follow-up Schedule

The median follow-up time was approximately 32 months.

3. Clinical Endpoints

a. Primary Clinical Efficacy Endpoints

A primary objective of the study was to evaluate the efficacy of TECENTRIQ monotherapy treatment compared with best supportive care (BSC) as measured by disease free survival (DFS) as assessed by the investigator in the PD-L1 subpopulation (defined as ≥1% tumor cell [TC] expression level by VENTANA PD L1 [SP263] Assay) within the Stage II-IIIA population, in all randomized patients with Stage II-IIIA non-small cell lung cancer (NSCLC), and in the intent-to-treat (ITT) population.

DFS was defined as the time from the date of randomization to the date of occurrence of any of the following: first documented recurrence of disease, new primary NSCLC, or death due to any cause, whichever occurred first.

b. Secondary Clinical Efficacy Endpoints:

- Overall Survival in the ITT population
- 3-year and 5-year Disease Free Survival rates in the PD-L1 subpopulation (defined as ≥ 1% TC expression by the SP263 IHC assay) within the Stage II–IIIA population, in all randomized patients with Stage II–IIIA NSCLC, and in the ITT population
- DFS in the PD-L1 subpopulation (defined as ≥ 50% TC expression by the SP263 IHC assay) in patients with Stage II–IIIA NSCLC

B. Accountability of PMA Cohort

A total of 1600 patients were screened for, and a total of 1280 patients were enrolled into IMpower010. Of the 1280 enrolled patients, 1269 received adjuvant chemotherapy. Of those, 1005 patients proceeded to the randomization phase (ITT population), which included 882 patients with Stage II-IIIA NSCLC.

Of the 882 patients within the Stage II-IIIA population within the ITT population, 383 cases had PD L1 (SP263) expression levels <1%, and for 23 cases the PD-L1 expression level could not be determined. Thus, the subpopulation of patients with Stage II-IIIA NSCLC and PD-L1 (SP263) ≥ 1% TC expression level comprised a total of 476 patients.

Table 11. Accountability of IMpower010 PMA Cohort

	Number of Study subjects
Efficacy population (ITT/Stage2-3a)	882

Tumor sample collected at baseline	882 Note: All randomized patients provided a sample at baseline, since that was a key inclusion criterion for the IMpower010 study.
PD-L1 Not Determined	23 (5 non-evaluable + 18 not tested)
Non-evaluable	5 (due to unacceptable background or morphology, or tissue wash-off)
Not Tested	18 (tissue blocks not available)
Total evaluable PD-L1 expression	859
PD-L1 positive ≥ 1%	476
PD-L1 negative <1%	383
Tumor Site of Collection: (N= Specimens tested with SP263)	
Primary Site	859 (per IMpower010 inclusion criteria)
Metastatic Site	0
Specimen type (N= Specimens tested with SP263)	
Newly Obtained	0
Archival [1]	859
Sample Procedure (N= Specimens tested with SP263)	
Biopsy	0
Resection	859
Unknown	0

C. Study Population Demographics and Baseline Parameters

Study population included predominantly White (73%) or Asian (24%) men (67%) and had a median age of 62 years (range: 26-84 years). Per IMpower010 study protocol, all patients had a high baseline functional status (ECOG PS 0: 55% vs. 1: 44%), resected Stage IB (tumors ≥4 cm)-IIIA NSCLC, and the majority (78%) had a history of tobacco use.

Note: The inclusion criteria for Impower010 is "patients with Stage IB-IIIA NSCLC". However, there were no Stage IB patients included in the efficacy population, because coincidently, there was no stage 1B patient selected during enrollment. Therefore, the final efficacy population comprised of Stage II-IIIA NSCLC with a PD-L1 (SP263) ≥ 1% TC expression level.

D. Safety and Effectiveness Results

1. Safety Results

No adverse events associated with use of PD-L1 (SP263) assay under the IMPower010 protocol occurred during the course of the clinical study.

2. Effectiveness Results

In the primary analysis, DFS showed a statistically significant and clinically meaningful improvement in the TECENTRIQ arm compared to the BSC arm in the subpopulation of patients with Stage II-IIIA NSCLC and PD L1 (SP263) ≥ 1% TC expression level. At the time of the IMpower010 clinical data cutoff date, a higher proportion of patients in the BSC arm (46.1%) compared to the TECENTRIQ arm (35.5%) had experienced disease recurrence or death. The stratified hazard ratio (HR) was 0.66 (95% CI: 0.50, 0.88; p-value = 0.0039), which corresponds to a 34% relative risk reduction of a DFS event with TECENTRIQ compared to BSC. Results are summarized in Table 12.

Table 12: Efficacy Results from IMpower010 in Patients with Stage II-IIIA NSCLC with PD L1 (SP263) Expression ≥ 1%TC.

	Arm A (TECENTRIQ) n = 248	Arm B (Best Supportive Care) n = 228
DFS events (%)	88 (35.5)	105 (46.1)
Median DFS, months (95% CI)	NR (36.1, NE)	35.3 (29.0, NE)
Hazard ratio [1] (95% CI)	0.66 (0.50, 0.88)	
p-value	0.004	

DFS = Disease-free survival; CI = confidence interval; NE = Not estimable; NR = Not reached

[1] Stratified by stage, sex, and histology

3. Subgroup Analyses

There was no subgroup analysis performed in this trial.

4. Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included one investigator who was a

full-time employee of the sponsor and had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: [None]
- Significant payment of other sorts: [None]
- Proprietary interest in the product tested held by the investigator: [None]
- Significant equity interest held by investigator in sponsor of covered study: [One]

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. The information provided does not raise any questions about the reliability of the data.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Hematology and Pathology Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA did not raise any new safety and effectiveness questions compared with information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The primary efficacy data in conjunction with the staining performance support the reasonable assurance of safety and effectiveness of use of VENTANA PD-L1 (SP263) Assay as a companion diagnostic device for TECENTRIQ treatment in the target NSCLC patient population.

The IMpower010 primary efficacy endpoint was met with a statistically significant and clinically meaningful improvement in DFS for the TECENTRIQ arm compared to the BSC arm for patients with NSCLC whose tumors have PD-L1 expression on ≥ 1%TC as determined by the VENTANA PD-L1 (SP263) Assay.

In addition, the staining performance of VENTANA PD-L1 (SP263) Assay demonstrated a high overall staining acceptability rate where the initial and final staining acceptability rates (overall, background and morphology) were all above 99.3%.

The data therefore supports the performance of this device in identifying patients eligible for treatment with the therapeutic when used in accordance with the instructions for use.

The performance of the VENTANA PD-L1 (SP263) Assay was also supported by the analytical performance validation studies.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory study data as well as data collected in the clinical study conducted to support PMA approval as described above.

The VENTANA PD-L1 (SP263) Assay is an in vitro diagnostic device, which tests FFPE tumor specimens collected from patients with NSCLC. The risks of the device are based on data collected in the clinical study. No adverse events associated with the diagnostic testing procedure were reported during this study. Failure of the device to perform as expected may lead to a failure to correctly interpret test results. The process of testing on FFPE tumor specimens does not present additional significant safety concerns, as these samples are routinely removed for diagnosis. As VENTANA PD-L1 (SP263) Assay is intended for use to identify patients for TECENTRIQ therapy, if incorrect, or false, results are reported, then patients may not receive the proper treatment. Patients with false positive results may undergo treatment with TECENTRIQ without much clinical benefit and may experience adverse reactions associated with TECENTRIQ therapy. Patients with false negative results may not be considered for treatment with TECENTRIQ, and therefore, may receive other treatment options. There is also a risk of delayed results, which may lead to a delay in treatment with TECENTRIQ.

C. Benefit-Risk Determination

Summary of Benefits

The probable benefits of the device are based on data collected in the clinical study IMpower010 conducted to support the supplemental PMA approval as described above.

The clinical performance of the VENTANA PD-L1 (SP263) Assay was demonstrated in the IMpower010 trial. Per the primary analyses, DFS (disease-free survival) showed a statistically significant and clinically meaningful improvement in the atezolizumab arm compared to the BSC (best supportive care) arm in the subpopulation of patients with Stage II-IIIA NSCLC and PD-L1 (SP263) ≥ 1% TC expression level. A higher proportion of patients in the BSC arm (46.1%) compared to the atezolizumab arm (35.5%) had experienced disease recurrence or death. The stratified hazard ratio was 0.66 (95% CI: 0.50, 0.88; p-value = 0.0039), which corresponds to a 34% relative risk reduction of a DFS event with atezolizumab compared to BSC. The Kaplan-Meier estimated median DFS was not reached in the atezolizumab arm due to the low number of events and was 35.3 months in the BSC arm.

Summary of Risks

The probable risks of the device are also based on data collected in the clinical study IMpower010 conducted to support the supplemental PMA approval as described above.

The risks of the use of the device relate to false positive and false negative results. A false positive result could lead to treatment with atezolizumab without the possibility of benefit. This could unnecessarily expose the patient to toxicity of the drug (see below). This is mitigated by the possibility that the patient could nonetheless experience some benefit from the drug even with a result of PD-L1<1%. A false negative result could deprive a patient of the potential benefit of atezolizumab treatment.

Regarding the toxicity profile of atezolizumab, the use of this agent is associated with a wide variety of immune-mediated inflammatory conditions which may be severe or fatal. These

include pneumonitis, colitis, hepatitis, endocrinopathies, dermatological adverse reactions, nephritis and renal dysfunction, and solid organ transplant rejection. In addition, there are infusion-related reactions, fatal and other serious complications of allogeneic hematopoietic stem cell transplant, and embryo-fetal toxicity. The most common adverse reactions are fatigue/asthenia, nausea, cough, dyspnea and decreased appetite, alopecia, constipation, and diarrhea.

Benefit-Risk Balance

The data provided demonstrate that, in the context of this population, there is reasonable assurance that the use of the VENTANA PD-L1 (SP263) Assay to identify an appropriate patient population with stage II-IIIA non-small cell lung cancer to be treated with atezolizumab in the adjuvant setting after platinum-based therapy is safe and effective. More specifically, there is reasonable assurance that the benefits of use of this device, shown by a statistically significant and clinically meaningful improvement in disease-free survival in patients treated with atezolizumab, outweigh the risks of use of the device, which are generally manifested by the toxicity of this agent.

Patient Perspective

This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The provided studies support the use of the VENTANA PD-L1 (SP263) Assay as a companion diagnostic to identify patients with Stage II-IIIA NSCLC following complete resection and adjuvant chemotherapy, for treatment with TECENTRIQ as the probable benefits outweigh the probable risks.

XIII. CDRH DECISION

CDRH issued an approval order on October 15, 2021.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.