WHO Prequalification of In Vitro Diagnostics
PUBLIC ASSESSMENT REPORT

Product: BD Onclarity HPV Assay for the BD Viper LT System
WHO reference number: PQDx 12315-045-00

The BD Onclarity HPV Assay for the BD Viper LT System, with product code 442946, manufactured by Becton, Dickinson and Company, BD Biosciences - MD Site, CE-mark regulatory version, was accepted for the WHO list of prequalified in vitro diagnostics and was listed on 13 October 2025.

Summary of the WHO prequalification assessment for the BD Onclarity HPV Assay for the BD Viper LT System

	Date	Outcome
Prequalification listing	13 October 2025	listed
Dossier assessment	21 May 2025	MR
Product performance evaluation	Waived	MR

MR: Meets Requirements

Intended use

According to the intended use claim from *the manufacturer in the Instructions for Use (version* 8089899(18), 2023-07)), "*The BD Onclarity HPV Assay is an amplified DNA test for the qualitative detection of high risk types of human papillomavirus (HPV).*
The assay detects all high risk HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) and provides the capability for individually genotyping six high risk types (HPV 16,18, 31, 45, 51, and 52) and three genotype groups (33/58, 35/39/68, and 56/59/66).
Cervical specimens that are tested with the BD Onclarity HPV Assay include the BD Onclarity HPV Cervical Brush Collection Kit, BD SurePath Preservative Fluid, and PreservCyt Solution (using an aliquot that is removed prior to or after processing for either the BD SurePath or ThinPrepPap test). Self-collected vaginal specimens can also be tested with the BD Onclarity HPV Assay for cervical cancer screening. The BD Onclarity HPV Assay is indicated for use for routine cervical cancer screening as per professional medical guidelines, including triage of ASC-US cytology, co-testing (or adjunctive screen) with cytology, and HPV primary screening of women to assess the risk for cervical precancer and cancer. Patients should be followed-up in accordance with professional medical guidelines, results from prior screening, medical history, and other risk factors. The BD Onclarity HPV Assay is an automated assay performed with the BD Viper LT System."

Reagents and materials provided

Contents	Quantity
BD Onclarity HPV Assay Reagent Pack Catalog Number 442946	192 Tests
Control Set for the BD Onclarity HPV Assay Catalog Number 441993	24 Sets
BD Onclarity HPV Liquid Based Cytology Specimen (LBC) Diluent Catalog Number 442840	400 Tubes
BD Onclarity HPV Liquid Based Cytology Specimen (LBC) Diluent Catalog Number 444046	48 Tubes
BD Onclarity HPV Self Collection Diluent Tubes Catalog Number 444869	400 Tubes
BD FOX PCR Extraction Tubes Catalog Number 441992	384 Tubes
BD Viper PCR Extraction Reagent Trough with Piercing Tool Catalog Number 442841	384 Tests
BD Viper XTR Neutralization Pouch Catalog Number 441354	12 Pouches
BD Onclarity HPV Cervical Brush Collection Kit Catalog Number 441991	100 Pouches
BD Viper LT Pipette Tips Catalog Number 440330	3,840 Tips
BD Viper Waste Liners Catalog Number 442968	100 Liners
BD Viper LT PCR Accessory Kit Catalog Number 442967	80 Pieces
BD Pierceable Caps Catalog Number 440295	200 Caps
BD Pierceable Caps Pink Catalog Number 440331	400 Caps
BD Viper LT PCR Tube/Tray Kit Catalog Number 442957	20 Pieces
BD Viper LT System Catalog Number 442839	1 System
BD Key Card Catalog Number 443747 1,000	Each

Items required but not provided

Item
Vortex Mixer
Nitrile gloves
Displacement pipettes and polypropylene aerosol-resistant tips capable of delivering 0.5 ± 0.05 mL
0.5% or 1.0% (v/v) sodium hypochlorite
3% (v/v) hydrogen peroxide
Isopropyl alcohol
Molecular biology-grade nuclease free water
BD Syringing Pipettes
Rovers Evalyn Tweezers (Catalog Number 380500135)
Rovers ReMover (Catalog Number 380500170)

Storage Temperature and Stability

Parameter	Condition
Storage Temperature	BD Onclarity HPV Cervical Brush Diluent Tube must be stored at 2–25 °C until the indicated expiration date. All other reagents must be stored at 2–33 °C until the indicated expiration date.
Shelf Life[1]	17 months.

Dossier review

The manufacturer submitted a product dossier as per the "Instructions for compilation of a product dossier" (PQDx_018). The information (data and documentation) submitted in the product dossier was reviewed by WHO staff and external technical experts (assessors) appointed by WHO.

The manufacturer's responses to the discrepancies found during dossier screening and assessment findings were accepted on 21 May 2025.

Based on the screening and assessment of the product dossier, the BD Onclarity HPV Assay for the BD Viper LT System meets WHO prequalification requirements.

Manufacturing site inspection

The inspection of the manufacturing site(s) was conducted to assess whether the manufacturer's quality management system (QMS) and manufacturing practices are in alignment with:
(i) applicable international standards, such as ISO 13485 (Medical devices – Quality management systems – Requirements for regulatory purposes);
(ii) the manufacturer's own documented procedures and quality requirements; and
(iii) other relevant international standards and guidelines applicable to in vitro diagnostic (IVD) medical devices. The WHO's Public Inspection Reports are accessible at:

[1] The assigned device shelf-life is based on stability data generated from the date of manufacture. The finished goods shelf-life, calculated from the date of packaging completion, may be shorter depending on the time elapsed between manufacture and final packaging of the device.

https://extranet.who.int/pqweb/vitro-diagnostics/who-public-inspection-reports

Product performance evaluation

The objective of the performance laboratory evaluation is to assess the performance and operational characteristics of commercially available in-vitro diagnostics for the purpose of advising procurers and the governments of WHO Member States on these issues.

As of October 2025, WHO has taken the executive decision to adopt the fulfilment of Meijer's criteria in independent evaluations as the prequalification independent performance evaluation component for HPV nucleic acid tests.

Based on the risk level associated with the use of this category of product, it was decided that WHO will not conduct a performance evaluation of these categories of in vitro diagnostics as part of the prequalification assessment process.

Consequently, laboratory evaluation of the BD Onclarity HPV Assay for the BD Viper LT System was not conducted.

Labelling review

The labelling submitted for the BD Onclarity HPV Assay for the BD Viper LT System was reviewed by WHO staff and external technical experts appointed by WHO. The review evaluated the labelling for clarity and consistency with the information submitted in the product dossier, alignment with international guidance and standards, and suitability for the intended users and settings in WHO Member States, including low- and middle-income countries.

The table below provides traceability of the labelling documents reviewed during the assessment, including document titles, version numbers, approval dates, and control identifiers.

Controlled Labelling References

Document Type	Document Title	Version / Revision	Date Approved	Controlled Document No.
Instructions for Use (IFU)	BD Onclarity HPV Assay	v18	15-Oct-2024	8089899
Outer box artwork	BD Onclarity HPV Assay Reagent Pack – For use with BD Viper LT System (442946)	V7	10-Mar-2025	8089898
G1 PCR Pouch label	BD Onclarity HPV Assay G1 PCR Tubes	V4	15-Oct-2024	8089897
G2 PCR Pouch label	BD Onclarity HPV Assay G2 PCR Tubes	V4	15-Oct-2024	8089896
G3 PCR Pouch label	BD Onclarity HPV Assay G3 PCR Tubes	V4	15-Oct-2024	8089895

Labels

Artwork Number:	Catalog Number(s):	SAP/Blank Stock Number	Category and Description:	Rev from:	Rev to:	Carton/Label Sheet, 11"x17"
8089898	442946	N/A	Carton Label, BD Onclarity™ HPV Assay Reagent Pack	06	07	ENGLISH

BD Onclarity™ HPV Assay Reagent Pack REF 442946

Σ 192

For use with BD Viper™ LT System.

CE 2797 IVD eifu.bd.com 33 °C 2 °C

Becton, Dickinson and Company
7 Loveton Circle
Sparks, Maryland 21152 USA

EC REP Becton Dickinson Ireland Ltd.
Donore Road, Drogheda
Co. Louth, A92 YW26
Ireland

CH REP BD Switzerland Sàrl
Route de Crassier 17
Business Park Terre-Bonne
Bâtiment A4
1262 Eysins, Switzerland

Australian and New Zealand Sponsors:
Becton Dickinson Pty Ltd., 66 Waterloo Road, Macquarie Park NSW 2113, Australia
Becton Dickinson Limited, 14B George Bourke Drive, Mt. Wellington Auckland 1060, New Zealand

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8089898(07) Made in USA

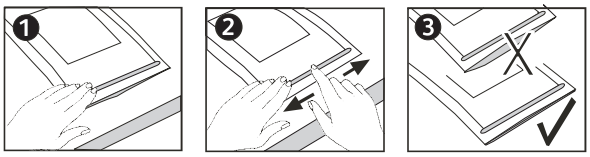
Placement of Customer barcode
(17) YYMMDD (10) LLLLLL

UDI

LOT LLLLLL YYYY-MM-DD

Placement of Device with Check Digit and Production Identifier
(01) 0 038290 442946 1 (17) YYMMDD (10) LLLLLL

Artwork Number: 8089897	Catalog Number(s): HALB - 8088466	Label Sheet, 8.5"x11"
SAP/Blank Stock Number: N/A	Category and Description: Pouch Label, BD Onclarity™ HPV Assay G1 PCR Tubes	Rev from: 03 Rev to: 04
		Job Number: 4667-23



BD 96

BD Onclarity™ HPV Assay G1 PCR Tubes

For use with BD Viper™ LT System.

Becton, Dickinson and Company
7 Loveton Circle
Sparks, Maryland 21152 USA

8089897(04)

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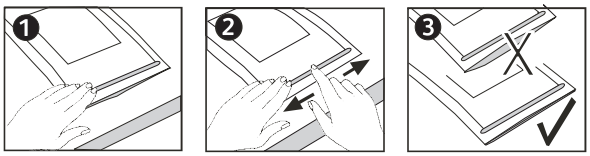
LOT LLLLLLL SSSS
YYYY-MM-DD

Artwork Number: 8089896	Catalog Number(s): HALB - 8088467	Label Sheet, 8.5"x11"
SAP/Blank Stock Number: N/A	Category and Description: Pouch Label, BD Onclarity™ HPV Assay G2 PCR Tubes	Rev from: 03 Rev to: 04
		Job Number: 4667-23



BD 96

BD Onclarity™ HPV Assay G2 PCR Tubes

For use with BD Viper™ LT System.

Becton, Dickinson and Company
7 Loveton Circle
Sparks, Maryland 21152 USA

8089896(04)

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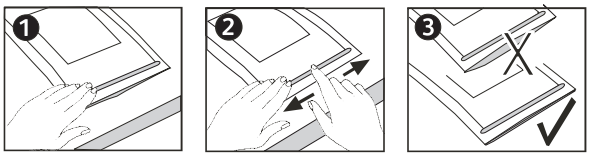
LOT LLLLLLL SSSS
YYYY-MM-DD

Artwork Number: 8089895	Catalog Number(s): HALB - 8088468	Label Sheet, 8.5"x11"
SAP/Blank Stock Number: N/A	Category and Description: Pouch Label, BD Onclarity™ HPV Assay G3 PCR Tubes	Rev from: 03 Rev to: 04
		Job Number: 4667-23



BD 96

BD Onclarity™ HPV Assay G3 PCR Tubes

For use with BD Viper™ LT System.

Becton, Dickinson and Company
7 Loveton Circle
Sparks, Maryland 21152 USA

8089895(04)

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LOT LLLLLLL SSSS
YYYY-MM-DD

Instructions for Use[2]

[2] English version of the IFU was the one that was assessed by WHO. It is the responsibility of the manufacturer to ensure correct translation into other languages.

BD Onclarity™ HPV Assay

CE 2797 IVD bd.com/e-labeling

8089899(18)
2023-07
English

REF 442946

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BD Onclarity™ HPV Assay

CE 2797 IVD bd.com/e-labeling

8089899(18)
2023-07
English

REF 442946

INTENDED USE

The BD Onclarity™ HPV Assay is an amplified DNA test for the qualitative detection of high risk types of human papillomavirus (HPV). The assay detects all high risk HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) and provides the capability for individually genotyping six high risk types (HPV 16,18, 31, 45, 51, and 52) and three genotype groups (33/58, 35/39/68, and 56/59/66). Cervical specimens that are tested with the BD Onclarity™ HPV Assay include the BD Onclarity™ HPV Cervical Brush Collection Kit, BD SurePath™ Preservative Fluid, and PreservCyt® Solution (using an aliquot that is removed prior to or after processing for either the BD SurePath™ or ThinPrep® Pap test). Self-collected vaginal specimens can also be tested with the BD Onclarity™ HPV Assay for cervical cancer screening. The BD Onclarity™ HPV Assay is indicated for use for routine cervical cancer screening as per professional medical guidelines, including triage of ASC-US cytology, co-testing (or adjunctive screen) with cytology, and HPV primary screening of women to assess the risk for cervical precancer and cancer. Patients should be followed-up in accordance with professional medical guidelines, results from prior screening, medical history, and other risk factors. The BD Onclarity™ HPV Assay is an automated assay performed with the BD Viper™ LT System.

WARNING

The BD Onclarity™ HPV Assay is NOT intended:

- For use in determining the need for treatment (i.e., excisional or ablative treatment of the cervix) in the absence of high-grade cervical dysplasia.
- For women who have undergone hysterectomy.
- For use with cervical samples other than those collected by a clinician using the BD Onclarity™ HPV Cervical Brush Collection Kit or an endocervical brush/spatula combination or broom in the BD SurePath™ vial or PreservCyt® Solution.
- For use with self-collected vaginal samples other than those collected with the Rovers® Evalyn® Brush (Catalog Number 380500131), Rovers® Viba-Brush® (Catalog Number 380200331) and Copan FLOQSwabs® (Catalog Number 5E089N).
- For use with other non-gynecological specimens.

HPV-negative cancers of the cervix do occur in rare circumstances.[1-3] Also, no cancer screening test is 100% sensitive. Use of this device for primary cervical cancer screening should be undertaken after carefully considering the performance characteristics put forth in this label, as well as recommendations of professional guidelines.

The use of this test has not been evaluated for the management of women with prior ablative or excisional therapy, or who are pregnant.

SUMMARY AND EXPLANATION OF THE TEST

There are more than 100 different genotypes of human papillomavirus (HPV), of which 14 are considered high-risk for cervical cancer and its precursor lesions. It is one of the most common sexually transmitted viruses in the world: nearly all sexually active men and women will get HPV at some point in their lives.[4] According to the World Health Organization (WHO), cervical cancer is the fourth largest contributor to female cancer mortality worldwide, claiming an estimated 270,000 lives annually.[5] It is estimated that in 2017 there were 12,820 cases of cervical cancer and 4,210 deaths in the United States, which correspond, respectively, to an age-adjusted rate of 7.4 and 2.3 per 100,000 women, annually.[6] In many cases, HPV infections are transient, and the body will clear the virus on its own.

HPV is a double-stranded DNA virus with a circular genome of approximately 8,000 base pairs and encodes 8 open reading frames (ORFs). Its ORFs are divided into early and late genes involved in replication (i.e., E1 and E2) and packaging (i.e., L1 and L2) with the remaining genes (E6, E7, E5, and E4) playing roles in driving cell cycle entry, immune evasion, and virus release.[7] A persistent infection of one of the fourteen sexually transmitted HPV genotypes considered high risk (genotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) can lead to the development of cervical cancer and its precursor lesions.[8]

The identification of the HPV virus' relationship to cervical cancer disease has resulted in a rich volume of scientific activity in this field. These activities range from the development of therapeutic vaccines designed to prevent infection with HPV viruses to in vitro diagnostic tests for use as aids in cervical cancer screening and clinical patient management. Today, Pap tests can inform a clinician if there are changes to the cervical cells. If those cells are abnormal, an HPV test may be done to determine if those cervical changes are due to a high risk strain of HPV which can lead to cervical cancer. Not all molecular assays can distinguish among the different types of HPV. The BD Onclarity™ HPV Assay detects HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, and allows simultaneous, discrete identification of the high-risk types 16, 18, 31, 45, 51, and 52.

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The clinical performance of the BD Onclarity™ HPV Assay has been investigated in multiple published studies, including PreservCyt®, [9-16] BD SurePath™,[17-28] liquid preservative media, and self-collected vaginal specimens.[29-35]

PRINCIPLES OF THE PROCEDURE

The BD Onclarity™ HPV Assay is based on two major processing steps: 1) automated specimen preparation to homogenize the matrix, lyse cells, and extract cellular DNA; and 2) PCR amplification of target DNA sequences using primers and fluorescently-labeled detector probes for both HPV and human beta globin. Human beta globin amplification and detection is included in the BD Onclarity™ HPV Assay to differentiate HPV negative specimens from those that do not exhibit HPV signal due to insufficient cell mass in the specimen. The human beta globin serves as an internal control of the entire test by concurrently assessing specimen processing, extraction, and amplification. The BD Onclarity™ HPV Assay uses HPV target regions for primers and probes (E6/E7 oncogenes) that provide robust detection of HPV genotypes reducing the potential risk for lack of detection due to nucleic acid deletions and/ or mutations.[36-38]

The automated specimen preparation for the BD Onclarity™ HPV Assay is completed by the BD Pre-Warm Heater and the BD Viper™ LT System. Cervical specimens are extracted using BD FOX™ Extraction to release cellular DNA. The purified cellular DNA solution from each extracted specimen is transferred into PCR tubes containing reagents which are then sealed to prevent contamination.

The BD Onclarity™ HPV Assay reagents are dried in three individual PCR tubes that are capable of detecting 14 high risk HPV genotypes and a specimen-derived internal control consisting of a fragment of DNA from the human beta globin gene. These genotypes are reported either individually (16, 18, 31,45, 51, 52) or as a genotype group (33/58, 59/56/66, and 35/39/68). Each of the three PCR tubes contains specific oligonucleotide sets to detect HPV genotype DNA and an oligonucleotide set to detect a region of the human beta globin gene.

The BD Onclarity™ HPV Assay uses real-time PCR technology.[39] The detection of the target DNA is accomplished using TaqMan® DNA probes that include a fluorescent dye at the 5' end and a quenching molecule at the 3' end of the oligonucleotide. The BD Onclarity™ HPV Assay utilizes fifteen probes labeled with one of four fluorescent dyes. Each dye is paired with one of two Black Hole Quencher molecules (BHQ® Dye). Fluorescent detection of amplification occurs in four separate optical channels on the BD Viper™ LT System.

REAGENTS

BD Onclarity™ HPV Assay Reagent Pack (192 tests) Catalog Number 442946		
Components	**Quantity per kit**	**Ingredients**
BD Onclarity™ **G1 PCR tubes**	2 x 96 tests	Tris Buffer Glycerol Trehalose <0.75% Upstream and downstream HPV primers <0.06% Upstream and downstream beta-globin primers <0.37% Fluorescent-labeled HPV probes <0.12% Fluorescent-labeled beta-globin probes <1.97% Hot Gold Star polymerase (microbial)
BD Onclarity™ **G2 PCR tubes**	2 x 96 tests	Tris Buffer Glycerol Trehalose <1.00% Upstream and downstream HPV primers <0.06% Upstream and downstream beta-globin primers <0.62% Fluorescent-labeled HPV probes <0.12% Fluorescent-labeled beta-globin probes <1.97% Hot Gold Star polymerase (microbial)
BD Onclarity™ **G3 PCR tubes**	2 x 96 tests	Tris Buffer Glycerol Trehalose <1.00% Upstream and downstream HPV primers <0.06% Upstream and downstream beta-globin primers <0.50% Fluorescent-labeled HPV probes <0.12% Fluorescent-labeled beta-globin probes <1.97% Hot Gold Star polymerase (microbial)
Safety and Warnings		
N/A		

Control Set for the BD Onclarity™ HPV Assay (24 sets) Catalog Number 441993		
Components	**Quantity per kit**	**Ingredients**
BD Onclarity™ HPV Positive Control	24 x 0.05 mL	<1.178% Nonspecific DNA (biological) <0.077% Non-infectious plasmid DNA (microbial) containing HPV-16, 18, 56 sequences <0.013% Non-infectious plasmid DNA (microbial) containing human beta-globin sequence
BD Onclarity™ HPV Negative Control	24 x 0.05 mL	<1.182% Nonspecific DNA (biological)
Safety and Warnings		
N/A		

BD Onclarity™ HPV Cervical Brush Collection Kit Catalog Number 441991		
Components	**Quantity per kit**	**Ingredients**
Cervical Brush Diluent (CBD)	100 x 2.2 mL	<0.9% Detergent <0.05% Proclin <4.0% Tris HCl <5.0% Tris Base <1.5% Sodium Chloride
Safety and Warnings		

WARNING
H317 May cause an allergic skin reaction.
H319 Causes serious eye irritation.
H411 Toxic to aquatic life with long lasting effects.
P261 Avoid breathing dust/fume/gas/mist/vapors/spray.
P264 Wash face, hands and any exposed skin thoroughly after handling.
P272 Contaminated work clothing should not be allowed out of the workplace.
P280 Wear protective gloves/protective clothing/eye protection/face protection.
P273 Avoid release to the environment.
P302+P352 IF ON SKIN: Wash with plenty of soap and water.
P333+P313 If skin irritation or rash occurs: Get medical advice/attention.
P363 Wash contaminated clothing before reuse.
P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P337+P313 If eye irritation persists: Get medical advice/attention.
P391 Collect spillage.
P501 Dispose of contents/container to an approved facility in accordance with local, regional, national and international regulations.
Contains: CMIT/MIT mixture (3:1) - a mixture of: 5-chloro-2-methyl-4-isothiazolin-3-one [EC No 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC No 220-239-6] (3:1)
Authorization number: REACH/23/8/0 (CAS 9036-19-5)

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BD Onclarity™ HPV Liquid Based Cytology Specimen (LBC) Diluent Catalog Numbers 442840, 444046		
Components	**Quantity per kit**	**Ingredients**
Liquid Based Cytology Specimen (LBC) Diluent **Or** **BD Onclarity™ HPV LBC Diluent Tubes**	Catalog Number 442840 400 x 1.7 mL Or Catalog Number 444046 48 x 1.7 mL	<0.9% Detergent <0.05% Proclin <4.0% Tris HCl <5.0% Tris Base <1.5% Sodium Chloride
Safety and Warnings		

WARNING
H317 May cause an allergic skin reaction.
H319 Causes serious eye irritation.
H411 Toxic to aquatic life with long lasting effects.
P261 Avoid breathing dust/fume/gas/mist/vapors/spray.
P272 Contaminated work clothing should not be allowed out of the workplace.
P273 Avoid release to the environment.
P280 Wear protective gloves/protective clothing/eye protection/face protection.
P302+P352 IF ON SKIN: Wash with plenty of soap and water.
P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P333+P313 If skin irritation or rash occurs: Get medical advice/attention.
P337+P313 If eye irritation persists: Get medical advice/attention.
P363 Wash contaminated clothing before reuse.
P391 Collect spillage.
P501 Dispose of contents/container to an approved facility in accordance with local, regional, national and international regulations.
Contains: CMIT/MIT mixture (3:1) - a mixture of: 5-chloro-2-methyl-4-isothiazolin-3-one [EC No 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC No 220-239-6] (3:1)
Authorization number: REACH/23/8/0 (CAS 9036-19-5)

BD Onclarity™ HPV Self Collection Diluent Tubes Catalog Number 444869		
Components	**Quantity per kit**	**Ingredients**
Self Collection Diluent Tubes	400 x 3.0 mL	<0.9% Detergent <0.05% Proclin <4.0% Tris HCl <5.0% Tris Base <1.5% Sodium Chloride
Safety and Warnings		

WARNING
H317 May cause an allergic skin reaction.
H319 Causes serious eye irritation.
H411 Toxic to aquatic life with long lasting effects.
P261 Avoid breathing dust/fume/gas/mist/vapors/spray.
P273 Avoid release to the environment.
P280 Wear protective gloves/protective clothing/eye protection/face protection.
P302+P352 IF ON SKIN: Wash with plenty of soap and water.
P333+P313 If skin irritation or rash occurs: Get medical advice/attention.
P362+P364 Take off contaminated clothing and wash it before reuse.
P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P337+P313 If eye irritation persists: Get medical advice/attention.
P391 Collect spillage.
P501 Dispose of contents/container to an approved facility in accordance with local, regional, national and international regulations.
Contains: CMIT/MIT mixture (3:1) - a mixture of: 5-chloro-2-methyl-4-isothiazolin-3-one [EC No 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC No 220-239-6] (3:1)
Authorization number: REACH/23/8/0 (CAS 9036-19-5)

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BD FOX™ PCR Extraction Tubes (384 tubes) Catalog Number 441992		
Components	**Quantity per kit**	**Ingredients**
BD FOX™ PCR Extraction Tubes	48 x 8	Iron Oxide in dissolvable film
Safety and Warnings		
N/A		

BD Viper™ PCR Extraction Reagent Trough with Piercing Tool (384 tests) Catalog Number 442841		
Components	**Quantity per kit**	**Ingredients**
PCR Extraction Reagent Trough with Piercing Tool	12 x 32	Sodium Phosphate, Monobasic Proclin 300 <0.109% Detergent <22.0% Sulfuric Acid <38.0% Potassium Hydroxide <0.3% Tris Base <2.9% Tris HCl
Safety and Warnings		

DANGER
EUH208 Contains (CMIT/MIT mixture (3:1) - a mixture of: 5-chloro-2-methyl-4-isothiazolin-3-one [EC No 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC No 220-239-6] (3:1)). May produce an allergic reaction.
EUH210 Safety data sheet available on request.
H314 Causes severe skin burns and eye damage.
H350 May cause cancer.
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe dust/fume/gas/mist/vapors/spray.
P264 Wash face, hands and any exposed skin thoroughly after handling.
P280 Wear protective gloves/protective clothing/eye protection/face protection.
P301+P330+P331 IF SWALLOWED: Rinse mouth. Do NOT induce vomiting.
P303+P361+P353 IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water [or shower].
P304+P340 IF INHALED: Remove person to fresh air and keep comfortable for breathing.
P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P310 Immediately call a POISON CENTER/doctor.
P363 Wash contaminated clothing before reuse.
P405 Store locked up.
P501 Dispose of contents/container to an approved facility in accordance with local, regional, national and international regulations.
Contains: Potassium hydroxide (K(OH)), Sulfuric acid

WARNING AND PRECAUTIONS

1. For in vitro diagnostic use. For Use by Trained Laboratory Personnel.
2. For warnings, precautions and cleaning procedures related to automated instrumentation, consult the BD Viper™ LT System User's Manual.
3. Pathogenic microorganisms, including hepatitis viruses and Human Immunodeficiency Virus, may be present in clinical specimens. "Standard Precautions"[40-43] and institutional guidelines should be followed in handling all items contaminated with blood and other body fluids. For additional specific warnings, cautions and notes specific to the BD Viper™ LT, consult the BD Viper™ LT System User's Manual.

Collect and dispose of all used and unused reagents and any other contaminated disposable materials following procedures for biohazardous or potentially biohazardous waste. It is the responsibility of each laboratory to handle solid and liquid waste according to their nature and degree of hazardousness and to adequately treat and dispose of them (or have them treated and disposed of) in accordance with any applicable regulations. Do not discharge liquid waste down the drain where prohibited.

Specimen

4. Optimal performance of the BD Onclarity™ HPV Assay requires proper specimen collection, handling and testing within the expiration dating of the BD Onclarity™ HPV LBC Diluent and BD Onclarity™ HPV Self Collection Diluent Tubes.
5. Proper labeling should accompany each specimen to the laboratory.
6. Take care to avoid cross-contamination during the specimen handling steps. Ensure that specimen containers do not contact one another, and discard used materials without passing over open containers. If gloves come in contact with specimen, change gloves to avoid contamination.

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7. Cervical specimens that may be tested with the BD Onclarity™ HPV Assay include those collected with the BD Onclarity™ HPV Cervical Brush Collection Kit, or those in BD SurePath™ (using an aliquot that is removed prior to or after processing with the BD SurePath™ Pap test) or PreservCyt® solution (using an aliquot that is removed prior to or after processing for the ThinPrep® Pap test).
8. Vaginal specimens that may be tested with the BD Onclarity™ HPV Assay include those collected with the Rovers® Evalyn® Brush (Catalog Number 380500131), Rovers® Viba-Brush® (Catalog Number 380200331) and Copan FLOQSwabs® (Catalog Number 5E089N).
9. When processing specimens on the BD Viper™ LT, select the appropriate test type from the Rack Login Display dropdown menu. Processing with the incorrect test type may result in downstream processing errors or inaccurate results.

Cytology Specimens (BD SurePath™ and/or PreservCyt®)

10. For liquid-based cytology specimens, use only the BD Onclarity™ HPV LBC Diluent Tubes.
11. Under- or over-dispensing of LBC specimen into the BD Onclarity™ HPV LBC Diluent Tube may affect assay performance. Over filling the tubes may also result in liquid overflow on the BD Viper™ LT deck, and could cause contamination.
12. Use only polypropylene aerosol-resistant pipette tips to transfer specimens to the BD Onclarity™ HPV LBC Diluent Tubes.
13. For automated transfer, only the BD Totalys™ MultiProcessor should be used to transfer BD SurePath™ LBC specimens to the BD Onclarity™ HPV LBC Diluent Tubes.

Cervical Brush Specimens

14. For cervical brush specimens, use only the BD Onclarity™ HPV Cervical Brush Collection Kit.
15. To reduce unnecessary bleeding, do not over-rotate the cervical brush during specimen collection.
16. When breaking the shaft of the cervical brush, take care to avoid splashing, spilling, or creating aerosols. Avoid contamination of the cervical brush head.
17. Do not test the BD Onclarity™ HPV Cervical Brush Diluent Tube if received in the laboratory without the brush present. A false negative test result may occur.

Vaginal Self-Collection Specimens

18. For vaginal self-collection specimens, use only the BD Onclarity™ HPV Self Collection Diluent Tubes.
19. Vaginal specimens may be self-collected at either the clinic or in the home setting.
20. When transferring the Rovers® Evalyn® Brush head from the collection device, use a new Rovers® ReMover® or a new pair of Evalyn® Brush Tweezers for each specimen. Do not reuse tools as this can cause cross contamination during the specimen handling.
21. For the Rovers® Evalyn® Brush and Rovers® Viba-Brush® vaginal brush, ensure the brush head is placed in the BD Onclarity™ Self Collection Diluent Tubes with the bristles pointing up.
22. Do not test the BD Onclarity™ HPV Self Collection Diluent Tubes without a device present. A false negative test result may occur.

Assay/Reagent

23. Use only sample and control tubes with pierceable caps on the BD Viper™ LT System. Do not remove pierceable caps prior to running the instrument. Post pre-warm BD Onclarity™ LBC Diluent Tubes and BD Onclarity™ Self Collection Diluent Tubes with punctured caps are stable at 2–30 °C for 7 days without re-capping. Punctured caps should be replaced for storage outside of the aforementioned claims. For BD Onclarity™ HPV Cervical Brush Diluent Tubes, be sure to replace any previously punctured cap with a new cap prior to retesting or prior to storage.
24. Do not interchange or mix kit reagents from kits with different lot numbers.
25. Reagent pouches containing unused PCR tubes MUST be carefully resealed after opening. Verify that desiccant is present prior to resealing the reagent pouches.
26. Use only the BD Viper™ LT pipette tips as supplied by BD with the BD Viper™ LT System.
27. Use only the BD Viper™ LT Clear Plate Sealers on the PCR tubes with the BD Viper™ LT System.
28. The PCR tubes MUST be properly sealed with the BD Viper™ LT Clear Plate Sealers prior to removing the plate from the BD Viper™ LT System. Sealing ensures a closed reaction for amplification and detection and is necessary to avoid contamination of the instrument and work area with amplification products. Do not remove sealing material from PCR tubes at any time.
29. To prevent contamination of the work environment with amplification products, use the disposal bags provided in the BD Viper™ LT System PCR Accessory Kit to dispose of tested PCR tubes. Make sure the bags are properly closed before disposal.
30. Do not use reagents after their expiration dates.
31. The Positive and Negative Controls are intended to monitor for substantial system failure and ensures reagent functionality. Quality control requirements must be performed in conformance with applicable regulations or accreditation requirements and your laboratory's standard Quality Control procedures.
32. Although dedicated work areas are not required because the BD Viper™ LT design reduces the possibility of amplicon contamination in the testing environment, other precautions for controlling contamination, particularly to avoid contamination of specimens during manipulation, are necessary.
33. CHANGE GLOVES if they come in contact with specimen or appear to be wet, to avoid contaminating other specimens. Change gloves before leaving work area and upon entry into work area.
34. Safety Data Sheets (SDS) are available at bd.com or by contacting BD Technical Service and Support.
35. Contact BD Technical Service and Support in the event of an unusual situation, such as a spill into the BD Viper™ LT System or DNA contamination that cannot be removed by cleaning.

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STORAGE AND HANDLING REQUIREMENTS

1. Do not freeze reagents.
2. The BD Onclarity™ HPV Cervical Brush Diluent Tube should be stored at 2–25 °C until the indicated expiration date.
3. All other reagents may be stored at 2–33 °C until the indicated expiration date.
4. Once a PCR tube pouch is opened, the PCR tubes are stable for 4 weeks at 2–33 °C, if properly sealed or until the expiration date, whichever comes first.

Reagents and Materials Provided

Contents	Quantity
BD Onclarity™ HPV Assay Reagent Pack Catalog Number 442946	192 Tests
Control Set for the BD Onclarity™ HPV Assay Catalog Number 441993	24 Sets
BD Onclarity™ HPV Liquid Based Cytology Specimen (LBC) Diluent Catalog Number 442840	400 Tubes
BD Onclarity™ HPV Liquid Based Cytology Specimen (LBC) Diluent Catalog Number 444046	48 Tubes
BD Onclarity™ HPV Self Collection Diluent Tubes Catalog Number444869	400 Tubes
BD FOX™ PCR Extraction Tubes Catalog Number 441992	384 Tubes
BD Viper™ PCR Extraction Reagent Trough with Piercing Tool Catalog Number 442841	384 Tests
BD Viper™ XTR Neutralization Pouch Catalog Number 441354	12 Pouches
BD Onclarity™ HPV Cervical Brush Collection Kit Catalog Number 441991	100 Pouches
BD Viper™ LT Pipette Tips Catalog Number 440330	3,840 Tips
BD Viper™ Waste Liners Catalog Number 442968	100 Liners
BD Viper™ LT PCR Accessory Kit Catalog Number 442967	80 Pieces
BD Pierceable Caps Catalog Number 440295	200 Caps
BD Pierceable Caps Pink Catalog Number 440331	400 Caps
BD Viper™ LT PCR Tube/Tray Kit Catalog Number 442957	20 Pieces
BD Viper™ LT System Catalog Number 442839	1 System
BD Key Card Catalog Number 443747 1,000	Each

Materials Required but Not Provided

- Vortex Mixer
- Nitrile gloves
- Displacement pipettes and polypropylene aerosol-resistant tips capable of delivering 0.5 ± 0.05 mL
- 0.5% or 1.0% (v/v) sodium hypochlorite
- 3% (v/v) hydrogen peroxide
- Isopropyl alcohol
- Molecular biology-grade nuclease free water
- BD Syringing Pipettes
- Rovers® Evalyn® Tweezers (Catalog Number 380500135)
- Rovers® ReMover® (Catalog Number 380500170)

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SPECIMEN COLLECTION, TRANSPORT, AND STORAGE

PRECAUTION: Handle all specimens as if they are capable of transmitting infectious agents.

Specimen Collection

BD SurePath™ or PreservCyt® specimens must be collected using either an endocervical broom or a brush/spatula combination as described in the BD SurePath™ or PreservCyt® product insert. Specimens in BD Onclarity™ HPV Cervical Brush Diluent must be collected with the cervical brush included in the BD Onclarity™ HPV Cervical Brush Collection Kit as described in the product insert. Do not use the specimen after the expiration date on the tube. Vaginal self-collection specimens should be collected using validated devices per their respective instructions for use.

Specimen Transport and Storage

Specimen transport should comply with applicable regulations for the transport of etiological agents.

For use in the BD Onclarity™ HPV Assay, cervical specimens collected in BD Onclarity™ HPV Cervical Brush Diluent, BD SurePath™, PreservCyt® vials, or vaginal specimens self-collected by the validated self-collection devices, may be stored according to the conditions listed, up to the specified timeframe:

Specimen Type	2–8 °C	2–30 °C	-20 °C
Specimen in BD SurePath™ vial (after collection and prior to dilution)	180 days	30 days	180 days
Specimen in PreservCyt® Solution vial (after collection and prior to dilution)	180 days	30 days	180 days
Self-collected vaginal specimen[a] (after collection dry transport)	30 days	30 days	30 days
Specimen in BD Onclarity™ HPV Cervical Brush Diluent (after collection in CBD diluent tube and prior to pre-warm)	180 days	30 days	180 days
Sample in BD Onclarity™ HPV LBC Diluent (after specimen dilution and prior to pre-warm)	15 days	15 days	90 days
Sample in BD Onclarity™ HPV Self Collection Diluent (after specimen transfer and prior to pre-warm)	15 days	15 days	15 days
Sample in BD Onclarity™ HPV LBC Diluent, capped post pre-warm[b] (after specimen dilution and sample pre-warm)	7 days	7 days	180 days
Sample in BD Onclarity™ HPV Self Collection Diluent, capped post pre-warm[b] (after specimen transfer and sample pre-warm)	7 days	7 days	7 days
Sample in BD Onclarity™ HPV Cervical Brush Diluent, capped post pre-warm[c] (after collection in CBD diluent tube and sample pre-warm)	7 days	7 days	180 days

[a] With up to 6 days exposure at 40 °C.

[b] Post pre-warm samples with punctured caps are stable at 2–30 °C for 7 days without re-capping. Punctured caps should be replaced for storage outside of the aforementioned claims.

[c] For BD Onclarity™ HPV Cervical Brush Diluent Tubes, the cap must be replaced prior to retesting or storage per the aforementioned claims.

Specimen Transfer to BD Onclarity™ HPV LBC Diluent Tubes

NOTE: See the BD Onclarity™ HPV LBC Diluent Tube Package Insert for additional information.

A 0.5 mL aliquot of the LBC specimen must be manually transferred from the original LBC vial to the BD Onclarity™ HPV LBC Diluent Tube. Wear gloves when handling the BD Onclarity™ HPV LBC Diluent Tube and the LBC specimen vial. If gloves come in contact with the specimen, immediately change them to prevent contamination of other specimens and handle one specimen at a time for processing.

A. Manual BD SurePath™ Specimen Transfer Prior to or after Processing for the BD SurePath™ test

NOTE: Refer to the Slide Processor or SlidePrep product insert for instructions on removing an aliquot from the specimen vial prior to performing the liquid-based Pap test.

NOTE: Handle one specimen at a time for processing.

1. Label a BD Onclarity™ HPV LBC Diluent Tube with patient identification information.
2. Remove the cap from the BD Onclarity™ HPV LBC Diluent Tube.
3. In order to ensure a homogenous mixture, vortex the BD SurePath™ specimen vial for 10–20 seconds.
4. Quickly transfer 0.5 mL from the specimen vial using an aerosol-resistant tip to the BD Onclarity™ HPV LBC Diluent Tube within 1 minute of vortexing.
5. Discard pipette tip.
   NOTE: A separate pipette tip must be used for each specimen.
6. Tightly recap the BD Onclarity™ HPV LBC Diluent Tube.

   NOTE: Bubbles may be seen upon recapping. To prevent bubbles, the user may discard the cap removed in Step 2 and replace with a new pierceable cap.
7. Invert the BD Onclarity™ HPV LBC Diluent Tube 3 to 4 times to ensure that the specimen and diluent are well mixed.

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B. Automated BD SurePath™ Specimen Transfer Using BD Totalys™ MultiProcessor, Prior to or after Processing for the BD SurePath™ Test

1. Refer to the BD Totalys™ MultiProcessor User's Manual for instructions on removing an aliquot from the BD SurePath™ Collection Vial.
2. Refer to the BD Onclarity™ HPV LBC Diluent Tube product insert for instructions on loading the BD Onclarity™ HPV LBC Diluent Tube in the MultiProcessor for automated aliquot transfer.

C. Manual PreservCyt® Specimen Transfer Prior to or after Processing for the ThinPrep® Pap Test

NOTE: Refer to the ThinPrep® 2000/5000 System Operator's Manual Addendum for instructions on removing an aliquot from the PreservCyt® specimen vial prior to performing the ThinPrep® test.

NOTE: Handle one specimen at a time for processing.

1. Label a BD Onclarity™ HPV LBC Diluent Tube with patient identification information.
2. Remove the cap from the BD Onclarity™ HPV LBC Diluent Tube.
3. In order to ensure a homogenous mixture, vortex the PreservCyt® specimen vial at high speed for 8–12 seconds.
4. Immediately transfer 0.5 mL from the specimen vial using an aerosol-resistant tip to the BD Onclarity™ HPV LBC Diluent Tube.
5. Discard pipette tip.
   NOTE: A separate pipette tip must be used for each specimen.
6. Tightly recap the BD Onclarity™ HPV LBC Diluent Tube.

   NOTE: Bubbles may be seen upon recapping. To prevent bubbles, the user may discard the cap removed in Step 2 and replace with a new pierceable cap.
7. Invert the BD Onclarity™ HPV LBC Diluent Tube 3 to 4 times to ensure that the specimen and diluent are well mixed.

CERVICAL BRUSH SPECIMEN COLLECTION

1. Insert the BD Onclarity™ HPV Cervical Brush into the endocervix until only the bottom most bristles are exposed at the os. Slowly rotate 1/4 to 1/2 turn in one direction. To reduce unnecessary bleeding, do not over-rotate the brush.
2. Remove cap from the BD Onclarity™ HPV Cervical Brush Diluent Tube and immediately place the brush into the bottom of the tube.
3. Carefully break the shaft at the score line. Avoid splashing of the contents.
4. Tightly recap the tube.

SELF-COLLECTED VAGINAL SPECIMEN

Transfer of Copan FLOQSwabs® to the BD Onclarity™ HPV Self Collection Diluent Tube

1. Uncap a BD Onclarity™ HPV Self Collection Diluent Tube.
2. Hold the test tube in one hand with the test tube opening facing away from your face.
3. Grip the end of the shaft with the thumb and forefinger of the other hand.
4. Align the breakpoint (red area with indent) with the edge of the tube.
5. Bend the swab shaft to an angle of 180° so that it breaks at the breakpoint. If necessary, gently turn the swab shaft until it is completely broken off. Discard the broken off part of the swab.

   NOTE: Breaking or cutting the shaft at the wrong location could result in downstream processing errors, delaying test results.
6. Tightly recap the tube.

   NOTE: Bubbles may be seen upon recapping. To prevent bubbles, the user may discard the cap removed in Step 1 and replace with a new pierceable cap.
7. Use a vortex mixer to vortex the tube at high speed for 5 seconds to ensure that the specimen and diluent are well mixed.

Transfer of Rovers® Evalyn® Brush (Fully Assembled Device) to the BD Onclarity™ HPV Self Collection Diluent Tube

1. Uncap a BD Onclarity™ HPV Self Collection Diluent Tube.
2. Squeeze the sides of the pink cap with your thumb and index finger to remove the pink cap from the Evalyn® Brush.
3. Depress the plunger into the casing to expose the brush head.
4. Ensure that you do not touch the white fibers of the Evalyn® Brush with your hands.
5. If using a ReMover® to transfer the brush head, guide the Evalyn® Brush into the ReMover® until the casing hits the ReMover®. If using Evalyn® Tweezers, position the tweezers over the base of the brush head.

   NOTE: A new Rovers® ReMover® or a new pair of Evalyn® Tweezers must be used for each brush.
6. Squeeze the ReMover® or the Evalyn® Tweezers firmly together and pull off the brush head. Firmly keep the ReMover® or tweezers compressed.
7. Hold the inverted ReMover® or the Evalyn® Tweezers over the mouth of the tube and drop the brush into the tube by releasing your grip.

   NOTE: The brush head must be oriented with the bristles facing up in the tube to avoid downstream processing errors.
8. Tightly recap the tube.

   NOTE: Bubbles may be seen upon recapping. To prevent bubbles, the user may discard the cap removed in Step 1 and replace with a new pierceable cap.
9. Use a vortex mixer to vortex the tube at high speed for 5 seconds to ensure that the specimen and diluent are well mixed.

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Transfer of Rovers® Evalyn® Brush and Viba-Brush® in the ReMover® to the BD Onclarity™ HPV Self Collection Diluent Tube

1. Uncap a BD Onclarity™ HPV Self Collection Diluent Tube.
2. Grip the ReMover® and pull off the cap. Maintain grip on the ReMover®.
3. Hold the inverted ReMover® over the mouth of the tube and drop the brush into the tube by releasing your grip.

   NOTE: The brush head must be oriented with the bristles facing up in the tube to avoid downstream processing errors.
4. Tightly recap the tube.

   NOTE: Bubbles may be seen upon recapping. To prevent bubbles, the user may discard the cap removed in Step 1 and replace with a new pierceable cap.
5. Use a vortex mixer to vortex the tube at high speed for 5 seconds to ensure that the specimen and diluent are well mixed.

QUALITY CONTROL

One BD Onclarity™ HPV Positive and one BD Onclarity™ HPV Negative Control must be included in each assay run and for each new reagent kit lot number. Controls must be positioned according to the BD Viper™ LT System User's Manual. The HPV Positive Control will monitor for substantial reagent failure. The BD Onclarity™ HPV Negative Control monitors for reagent and/or environmental contamination. Additional controls may be tested according to guidelines or requirements of local, state, and/or federal regulations or accrediting organizations.

General QC Information for the BD Viper™ LT System

The location of the PCR tubes is shown in a color-coded plate layout screen on the LCD Monitor. The plus symbol (+) within the tube indicates the positive QC sample. The minus symbol (-) within the tube indicates the negative QC sample. A QC pair must be logged in for each reagent kit lot number. If QC pairs have not been properly logged in, a message box appears that prevents saving the rack and proceeding with the run until complete. Additional (optional) QC tubes for testing may be logged in if desired. These tubes are tested as regular samples and do not affect the Pass/Fail status of the run. Refer to the BD Viper™ LT System User's Manual HPV Addendum for instructions.

NOTE: BD Onclarity™ HPV Controls must be manually hydrated prior to loading them into the BD Viper™ LT Specimen Rack.

INSTRUCTIONS FOR USE

Quality Control Preparation

1. Uncap a BD Onclarity™ HPV Negative Control and a BD Onclarity™ HPV LBC Diluent Tube.
2. Pour the entire contents of the BD Onclarity™ HPV LBC Diluent Tube into the BD Onclarity™ HPV Negative Control.
3. Re-cap the rehydrated BD Onclarity™ HPV Negative Control. Re-cap and discard the empty BD Onclarity™ HPV LBC Diluent Tube.
4. Uncap a BD Onclarity™ HPV Positive Control and a BD Onclarity™ HPV LBC Diluent Tube.
5. Pour the entire contents of the BD Onclarity™ HPV LBC Diluent Tube into the BD Onclarity™ HPV Positive Control.
6. Re-cap the rehydrated BD Onclarity™ HPV Positive Control. Re-cap and discard the empty BD Onclarity™ HPV LBC Diluent Tube.
7. Using the Tube Layout Report, place the rehydrated BD Onclarity™ HPV Positive and Negative Controls into the appropriate positions in the BD Viper™ LT Specimen Rack.
8. Controls are ready to be pre-warmed with the specimens. Once hydrated, unpunctured controls may be stored at 2–33 °C for up to 7 days prior to pre-warming.

Processing Procedure for All Specimens

NOTE: If previously prepared specimens are frozen, make sure they are thawed completely at room temperature and mixed by inversion prior to proceeding. Post pre-warm, unpunctured controls may be stored at 2–33 °C for an additional 7 days prior to testing.

1. Select the appropriate test type for the specimens to be processed in the dropdown menu of the BD Viper™ LT Rack Login Display.

Specimen Type	Test Type
LBC	HPV
Cervical Brush Diluent	HPV
Vaginal Self-Collection	HPV Self Collect

2. In the Rack Login Display, log in specimen accessions in the corresponding rack location.
3. Specimens are ready to be pre-warmed.
4. Change gloves prior to proceeding to avoid contamination.

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Pre-Warm Procedure

NOTE: The pre-warm procedure must be applied to all specimens to ensure that the specimen matrix is homogeneous prior to loading on the BD Viper™ LT System. Failure to pre-warm specimens may have an adverse impact on performance of the BD Onclarity™ HPV Assay and/or BD Viper™ LT System.

1. Insert the BD Viper™ LT Specimen Rack into the BD Pre-Warm Heater and select the BD Onclarity™ HPV Assay pre-warm protocol on the BD Viper™ LT Instrument.
2. The BD Pre-warm heater will automatically pre-warm the specimens and controls according to the BD Onclarity™ HPV Assay pre-warm protocol.
3. After the BD Onclarity™ HPV Assay pre-warm protocol is complete, remove the rack from the heater and load into the BD Viper™ LT instrument.

Test Procedure

NOTE: Refer to the BD Viper™ LT Instrument User's Manual for detailed instructions for operating and maintaining the components of the system.

1. The BD Onclarity™ HPV Assay may be used to run 1 to 30 specimens plus one Positive Control and one Negative Control.
2. Perform the system startup and maintenance procedures by following the instructions in the appropriate BD Viper™ LT User's Manual.
3. Access the Rack Login Display to log in the rack barcode and select the test type to be run.
4. Log in the Positive and Negative Control tubes in the first two positions (A1 and B1) as well as the HPV Diluent Tubes.
5. Log in specimen tubes by typing in or scanning each accession number/barcode in the Specimen Login window.
6. Log in Extraction tube QC information by tapping the "extraction lot" button and load extraction tubes where indicated on the Extraction Tube Lot Login display.
7. Tap the plate layout button to view the Plate Layout Display.
8. Load the PCR tubes into PCR Plate as shown on the display. PCR tubes are color-coded as follows:
   a. Blue=G1
   b. Green=G2
   c. Orange=G3

NOTE: Use empty PCR tubes to completely fill the PCR Plates if less than a full plate of tubes is required/logged in.

9. BD SurePath™ LBC samples and Positive and Negative Control tubes must be pre-warmed prior to extraction on the BD Viper™ LT.
10. To prepare the BD Viper™ LT instrument for specimen processing and testing, follow the steps outlined in the BD Viper™ LT User's Manual.
11. After specimens have been logged in, pre-warmed, and the BD Viper™ LT instrument has been prepared, the run can be initiated by tapping the "start run" button on the Main status display.

INTERPRETATION OF TEST RESULTS

The BD Onclarity™ HPV Assay uses the real-time polymerase chain reaction to detect the presence of Human Papillomavirus (HPV) in clinical specimens. All calculations are performed automatically by the BD Viper™ LT software. The presence or absence of clinically relevant HPV DNA is determined by the PCR cycle (Ct) at which the signal crosses a pre-established threshold. The assay will extract, amplify and detect a fragment of the human beta globin gene as an internal control to assess specimen processing, extraction, amplification, and to indicate the presence of PCR inhibitors. If the HPV-specific signal is greater than a cycle threshold, the internal control is utilized by the algorithm in the interpretation of the result. If the HPV-specific signal is less than or equal to a cycle threshold, the internal control is ignored by the algorithm.

For HPV specimens, an "HR" result (the combination of all genotypes) appears on the Tube Results Report. A positive symbol in this column indicates that the HPV assay detected one or more genotypes.

Specific genotypes and combined genotypes appear in columns. If the results for a genotype have been unmasked, those results are reported as explained below. Unmasked positive results will be accompanied by a Ct value in parentheses below the icon. If any genotype results have not been configured for automatic unmasking, those results are masked by a "key" icon.

The instrument can be configured to unmask/report specific genotypes when the run is complete. See the BD Viper™ LT System User's Manual HPV Addendum for instructions on authorizing automatic genotype reporting.

If assay control results are not as expected, patient results are not reported. See the Quality Control section for expected control values. Reported results are determined as follows.

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Table 1: Interpretation of High Risk HPV Genotype HPV Test Results for the BD Onclarity™ HPV Assay

High Risk HPV Result	Interpretation	Result	Report
HR ⊕←	Positive for High Risk HPV types	HPV HR Positive	HPV DNA detected by PCR.
HR ⊖	Negative for High Risk HPV types	HPV HR Negative	HPV DNA not detected by PCR.
~~IC~~	HPV DNA, if present, is not detectable	Internal Control Failure	Internal Control Failure. Repeat test from initial specimen tube or obtain another specimen for testing.
~~ET~~	HPV DNA, if present, is not detectable	Extraction Transfer Failure	Extraction Transfer Failure. Repeat test from initial specimen tube or obtain another specimen for testing.
~~LL~~	HPV DNA, if present, is not detectable.	Liquid Level Failure	Liquid Level Failure. Repeat test from initial specimen tube or obtain another specimen for testing.

Table 2: Interpretation of Specific HPV Genotype Test Results for the BD Onclarity™ HPV Assay

HPV Genotype Result	Interpretation	Result
16 ⊕←	Positive for HPV type 16	HPV type 16 Positive
16 ⊖	Negative for HPV type 16	HPV type 16 Negative
18 ⊕←	Positive for HPV type 18	HPV type 18 Positive
18 ⊖	Negative for HPV type 18	HPV type 18 Negative
45 ⊕←	Positive for HPV type 45	HPV type 45 Positive
45 ⊖	Negative for HPV type 45	HPV type 45 Negative
P1 ⊕←	Positive for HPV types 33 and/or 58	HPV type 33 and/or 58 Positive
P1 ⊖	Negative for HPV types 33 and/or 58	HPV type 33 and/or 58 Negative
31 ⊕←	Positive for HPV type 31	HPV type 31 Positive
31 ⊖	Negative for HPV type 31	HPV type 31 Negative
P2 ⊕←	Positive for HPV types 56, 59 and/or 66	HPV type 56, 59 and/or 66 Positive
P2 ⊖	Negative for HPV types 56, 59 and/or 66	HPV type 56, 59 and/or 66 Negative
51 ⊕←	Positive for HPV type 51	HPV type 51 Positive
51 ⊖	Negative for HPV type 51	HPV type 51 Negative
52 ⊕←	Positive for HPV type 52	HPV type 52 Positive
52 ⊖	Negative for HPV type 52	HPV type 52 Negative
P3 ⊕←	Positive for HPV types 35, 39 and/or 68	HPV type 35, 39 and/or 68 Positive
P3 ⊖	Negative for HPV types 35, 39 and/or 68	HPV type 35, 39 and/or 68 Negative
	HPV genotype result is available for purchase	Genotype result is locked
- -	HPV genotype result is not available for purchase	HPV Negative result, Internal Control failure, Liquid Level failure or Extraction Transfer failure.

See the BD Viper™ LT System User's Manual HPV Addendum for additional information on results reporting.

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Interpretation of Quality Control Results

If assay control results are not as expected, patient results are not reported. If either of the controls does not provide the expected result, repeat the entire run using a new set of controls. If either of the controls is consistently invalid, contact BD Technical Service and Support for technical assistance.

Table 3: Interpretation of Quality Control Results

Control Type	Tube Result Report Symbol	QC Disposition
BD Onclarity™ HPV Positive Control	OK	QC Pass
BD Onclarity™ HPV Positive Control		QC Failure
BD Onclarity™ HPV Positive Control		QC Failure
BD Onclarity™ HPV Positive Control		QC Failure
BD Onclarity™ HPV Negative Control	OK	QC Pass
BD Onclarity™ HPV Negative Control		QC Failure
BD Onclarity™ HPV Negative Control		QC Failure
BD Onclarity™ HPV Negative Control		QC Failure

Refer to the Interpretation of Test Results for a description of Tube Result Report symbols.

Monitoring for the Presence of DNA Contamination

Consult the BD Viper™ LT System User's Manual for more information on Environmental Monitoring and Cleaning Procedures. If a contamination event does not resolve, contact BD Technical Service and Support for additional information.

PROCEDURAL LIMITATIONS

1. The BD Onclarity™ HPV Assay detects DNA of the high-risk types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68. This test does not detect DNA of HPV low-risk types (e.g., 6, 11, 42, 43, 44) since there is no clinical utility for testing of low-risk HPV types for cervical cancer screening. [23]
2. The BD Onclarity™ HPV Assay is not recommended for evaluation of suspected sexual abuse.
3. Optimal performance of the test requires adequate specimen collection, transport, storage and processing. Follow the procedures in this Package Insert and the BD Viper™ LT System User's Manual.
4. A negative test result does not exclude the possibility of infection because test results may be affected by improper specimen collection, technical error, specimen mix-up, or the number of organisms in the specimen which may be below the sensitivity of the test.
5. The BD Onclarity™ HPV Assay provides qualitative results.
6. Use of the BD Onclarity™ HPV Assay is limited to personnel who have been trained in the assay procedure and the BD Viper™ LT System.
7. The BD Onclarity™ HPV Assay has been validated for use with cervical specimens collected by a clinician using an endocervical brush/spatula combination or broom and placed in a BD SurePath™ vial or PreservCyt® Solutions. In the clinical study, the Cytobrush® Plus GT Gentle Touch and Pap Perfect® Plastic Spatula (CooperSurgical, Inc.) and Rovers® Cervex-Brush® (Rovers Medical Devices B.V.) were used. BD SurePath™ cell pellets obtained after processing on the BD PrepStain™ Slide Processor have not been evaluated with the BD Onclarity™ HPV Assay. For cervical brush specimens, use only the BD Onclarity™ HPV Cervical Brush Collection Kit.
8. The BD Onclarity™ HPV Assay has been validated for use with self-collected vaginal specimens using the Rovers® Evalyn® Brush (Catalog Number 380500131), Rovers® Viba-Brush® (Catalog Number 380200331) and Copan FLOQSwabs® (Catalog Number 5E089N). Use only validated self-collection devices in the home setting in your region.
9. Cervical specimens often show visibly detectable levels of blood as a pink or light brown coloration. If concentrations exceed 4% (v/v) in BD SurePath™ vial or 5% (v/v) in PreservCyt® Solution prior to dilution in the BD Onclarity™ HPV Diluent tube, there is a likelihood of obtaining a false-negative HPV result. If concentrations exceed 1% (v/v) in the cervical brush or in a vaginal self-collected sample, there is also a likelihood of obtaining a false-negative HPV result.
10. False negatives may occur for specimens containing >8% (v/v) mucin, >7% (w/v) Zovirax® (Acyclovir) Cream, and >8% (w/v) clindamycin vaginal cream. Refer to Table 27 for more complete information.
11. The effects of other potential variables such as vaginal discharge, use of tampons, douching, etc. and specimen collection variables have not been evaluated.
12. The BD Onclarity™ HPV Assay was not evaluated in women with acetic acid, iodine, spermicide, douche, or anti-fungal medications applied to the cervical area within 24 hours of specimen collection.
13. Detection of high-risk HPV is dependent on the number of copies present in the specimen and may be affected by specimen collection methods, patient factors, stage of infection and the presence of interfering substances.

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14. Prevalence of HPV infection in a population may affect performance. Positive predictive values decrease when testing populations with low prevalence or individuals with no risk of infection.
15. A negative high-risk HPV result does not exclude the possibility of future cytologic high-grade squamous intraepithelial lesion (HSIL) or underlying CIN2-3 or cancer, but indicates a low likelihood of CIN2-3 or cancer.
16. Infection with HPV is not an indicator of cytologic HSIL or underlying high-grade CIN, nor does it imply that CIN2-3 or cancer will develop. Most women infected with one or more high-risk HPV types do not develop CIN2-3 or cancer.
17. An HPV negative specimen must have a valid beta globin signal within a pre-defined range to generate a negative result on the BD Viper™ LT System. The beta globin control does not differentiate between targeted (cervical) and non-targeted nucleated cell types.
18. In certain regions, self-collected vaginal specimens may also be tested with the BD Onclarity™ HPV Assay for cervical cancer screening. Women who are positive for high-risk HPV by the BD Onclarity™ HPV Assay from a self-collected vaginal specimen should follow-up with a clinician to determine management.

BD Onclarity™ Assay Clinical Study Design with BD SurePath™ Liquid Cytology Specimens

A total of 33,858 women were enrolled in the study across 31 collection sites, and cervical samples were tested at 4 testing sites in the US. Of these, 33,634 (99.3%) women were eligible to participate in the study. Eligible women were ≥21 years, provided informed consent, satisfied study inclusion/exclusion criteria, had not enrolled in a cervical disease diagnostic trial since 2007, and had not withdrawn authorization before undergoing study procedures.

The median age of the eligible women was 37, with 28.0% of women in age group 21–29 years, 28.3% in age group 30–39, and 43.7% of women in age group ≥40 years. A total of 90.6% of women had NILM cytology, 5.8% of women had ASC-US cytology, 3.3% of women had >ASC-US cytology, and only 0.2% of women had unsatisfactory cytology.

The percent of final non-reportable BD Onclarity™ assay results was 0.24% (79/33,570). Not included in this calculation are specimens that did not yield a result (64/33,634) due to specimen labeling, processing and volume issues.

A total of 1,960 ASC-US women ≥21 years were enrolled in the study of which 1,953 were evaluable; evaluable women had an ASC-US cytology result and valid results from the BD Onclarity™ HPV Assay.

A total of 22,383 NILM women ≥30 years were enrolled in the study of which 22,284 were evaluable; evaluable women had a NILM cytology result and valid results from the BD Onclarity™ HPV Assay.

A total of 29,633 women ≥25 years were enrolled in the study of which 29,513 were evaluable; evaluable women had valid cytology and BD Onclarity™ HPV Assay results.

Table 4 shows HPV positivity of the BD Onclarity™ HPV Assay by testing site and study population. HPV prevalence was 39.1% in the ASC-US (≥21 years) population, 7.9% in the NILM (≥30 years) population and 12.7% in the Primary Screening (≥25 years) population.

Table 4: Summary of HPV Positivity of the BD Onclarity™ HPV Assay by Testing Sites and Study Population

BD Onclarity™ HPV HR Positivity Rate			
Testing Site	**ASC-US (≥21 years)**	**NILM (≥30 years)**	**Primary Screening (≥25 years)**
1	39.5% (234/592)	9.3% (644/6,921)	14.2% (1,306/9,167)
2	36.7% (126/343)	7.4% (369/4,962)	12.0% (757/6,300)
3	33.3% (259/778)	7.1% (372/5,219)	12.7% (941/7,434)
4	60.0% (144/240)	7.3% (376/5,182)	11.3% (744/6,612)
Total	39.1% (763/1,953)	7.9% (1,761/22,284)	12.7% (3,748/29,513)

Table 5 shows HPV prevalence by the BD Onclarity™ HPV Assay by age and study population. HPV prevalence decreased with age in each study population.

Table 5: Summary of HPV Positivity of the BD Onclarity™ HPV Assay by Age and Study Population

BD Onclarity™ HPV HR Positivity Rate			
Age Group	**ASC-US (≥21 years)**	**NILM (≥30 years)**	**Screening (≥25 years)**
21–29	54.6% (398/729)	N/A	22.4% (1,216/5,432)
30–39	39.2% (204/521)	10.3% (889/8,663)	13.8% (1,310/9,477)
≥40	22.9% (161/703)	6.4% (872/13,621)	8.4% (1,222/14,604)
Total	39.1% (763/1,953)	7.4% (1,761/22,284)	12.7% (3,748/29,513)

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PERFORMANCE CHARACTERISTICS

Clinical Performance-BD SurePath™

Baseline Phase

A multicenter, prospective study was conducted to evaluate the performance of the BD Onclarity™ HPV Assay as a triage test to stratify women with ASC-US cytology results for referral to colposcopy, as an adjunctive test to cervical cytology to guide management decisions, and also as a primary cervical cancer screening test. The study consisted of a Baseline Phase and a 3 year Follow-up Phase. In the Baseline Phase, women ≥21 years old undergoing routine cervical cancer screening were invited to participate in the study. In total, 33,858 women were enrolled from August 2013 to June 2015 at 31 clinical sites in the Baseline Phase. Following written informed consent, demographic information and gynecologic histories were obtained. Two cervical specimens were collected from each woman and preserved in liquid based cytology (LBC) media. Cytology testing was performed on the first vial collected, at three different laboratories, and results were classified according to the 2001 Bethesda System criteria. HPV testing with the BD Onclarity™ HPV Assay was performed at one of four laboratories from a pre-cytology aliquot of the first vial collected and performance results are shown below. The second cervical specimen collected was tested with the BD Onclarity™ HPV Assay and an FDA-approved HPV test, according to the manufacturer's instructions.

Those women ≥21 years old with ≥ASC-US cytology and women ≥25 years old with unsatisfactory cytology were invited to undergo colposcopy. In addition, all women ≥25 years old with a positive high-risk HPV test result (positive by the BD Onclarity™ HPV Assay and/or the FDA-approved HPV test), as well as a randomly selected subset of women (approximately 5%) with NILM (negative for intraepithelial lesions or malignancy) cytology and negative high-risk HPV DNA (by both the BD Onclarity™ HPV Assay and the FDA-approved HPV DNA test), were invited to proceed to colposcopy. In order to avoid observation bias, both study participants and colposcopists were blinded to all HPV tests and cytology results until after the colposcopy was completed. Colposcopy was conducted according to a standardized protocol in which biopsies were obtained on all visible lesions or acetowhite areas; endocervical curettage was performed in all patients, and a single random cervical biopsy at the squamocolumnar junction was obtained if no lesions or acetowhite areas were visible. All biopsies were examined by a Central Pathology Review Panel (CPR) consisting of three expert pathologists. Discordant results were adjudicated according to a pre-defined protocol. For all analyses, the clinical performance of the BD Onclarity™ HPV Assay was measured against CPR histopathology results using both conventional H&E staining and H&E with p-16 assisted immunohistochemical staining, in alignment with the consensus recommendations of The 2012 Lower Anogenital Squamous Terminology Standardization Project for HPV-Associated Lesions (LAST).[24] Clinical performance for the BD Onclarity™ HPV Assay is expressed using p-16-assisted H&E for purposes of consistency, especially in the histopathologic category of CIN2. Overall, there are no statistically significant differences in clinical performance of the BD Onclarity™ HPV Assay with both histology reference methods for each of the three intended use populations.

Follow-Up Phase

All women who were biopsied at baseline and not treated and approximately 10% of NILM women (≥25 years) with HPV HR negative results and no baseline biopsy or treatment were invited to participate in a 3 year longitudinal study. Approximately 8,900 women were eligible for the follow-up study. All women invited into this 3 year longitudinal study undergo annual visits for cervical sampling for cytology and HPV DNA testing with the BD Onclarity™ HPV Assay. All women with ≥ASC-US are invited to proceed to colposcopy. Colposcopy and biopsies are performed in a standardized manner as described above. All cervical tissue is examined by the Central Pathology Review Panel. An exit colposcopy with biopsy and endocervical curettage (ECC) is collected from all women in Year 3. All women, regardless of histology result, will be followed through the duration of the study with the exception of those who receive treatment procedures; they will exit the study.

STUDY DESIGNS

Study Design to Demonstrate Clinical Sensitivity and Specificity for Screening Patients with ASC-US Cytology Results to Determine the Need for Referral to Colposcopy

Those women ≥21 years old with ASC-US cytology, regardless of HPV results, were invited to undergo colposcopy. Both study participants and colposcopists were blinded to all HPV tests and cytology results until after the colposcopy was completed. Colposcopy was conducted according to a standardized protocol and all biopsies were read by the CPR, as described above. The clinical performance of the BD Onclarity™ HPV Assay was measured against histology results of ≥CIN2 and ≥CIN3 by CPR.

Study Design to Demonstrate Clinical Performance of the BD Onclarity™ HPV Assay as an Adjunct to Cervical Cytology in Women ≥30 Years

All women ≥30 years old with NILM cytology and a positive result for HR HPV DNA (BD Onclarity™ HPV Assay and/or the FDA approved HPV test), as well as a randomly selected subset of women (approximately 5%) with NILM cytology/negative HR HPV DNA (BD Onclarity™ HPV Assay and the FDA approved HPV test), were invited to proceed to colposcopy. The analyses were performed for histology results of ≥CIN2 and ≥CIN3 by CPR.

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Study Design to Demonstrate Clinical Performance of the BD Onclarity™ HPV Assay as a First-Line Primary Test for Cervical Cancer Screening

Women ≥25 years with ≥ASC-US cytology and/or a positive result for HR HPV DNA (BD Onclarity™ HPV Assay and/or the FDA approved HPV test) were invited to proceed to colposcopy in the baseline phase. All women who were invited to colposcopy in the baseline phase and a portion (approximately 10%) of women ≥25 years with NILM cytology and HR HPV negative results, who did not have baseline biopsy and were not treated are eligible to participate in a 3 year longitudinal study for the BD Onclarity™ HPV Assay. All women with follow-up cytology ≥ASC-US are invited to proceed to colposcopy; colposcopy and biopsies are performed in a standardized manner as describe above. All cervical biopsies are examined by the CPR. Exit colposcopy with biopsy and ECC are performed on all women. The objectives of the follow-up phase of the study are to determine the 3-year risk (cumulative incidence rates, CIRs) of developing ≥CIN2 and ≥CIN3 in different study sub-populations defined by baseline HPV status and cytology.

Baseline data were evaluated for all evaluable women 25 years and older. The clinical performance of the primary screening indication for the BD Onclarity™ HPV Assay was measured against histology results of ≥CIN2 and ≥CIN3 by CPR and compared to the performance of cytology alone.

PERFORMANCE CHARACTERISTICS IN THE ASC-US POPULATION (≥21 YEARS)

A total of 1,960 ASC-US women ≥21 years were enrolled in the study of which 1,953 were evaluable. Evaluable women had an ASC-US cytology result and valid results from the BD Onclarity™ HPV Assay. Of the 1,953 evaluable ASC-US women, 1,607 completed the colposcopy procedure with a valid CPR result. The results of the BD Onclarity™ HPV Assay reported as (HPV HR) Positive or (HPV HR) Negative together with the CPR diagnosis are presented in Table 6. Of the 1,607 ASC-US women with a valid CPR panel diagnosis and BD Onclarity™ HPV result, 105 women were ≥CIN2 (prevalence of 6.5%), and 35 women were ≥CIN3 (prevalence of 2.2%).

Table 6: Results of the BD Onclarity™ HPV Assay and Central Pathology Review Panel Diagnosis in the ASC-US Population

	Central Pathology Review Panel Diagnosis					
BD Onclarity™ HPV Assay Result	**NEG**	**CIN1**	**CIN2**	**≥CIN3**	**Unknown Disease Status**	**Total**
Positive	423	116	58	32	134	763
Negative	888	75	12	3	212	1,190
Invalid/Missing*	6	0	0	0	1	7
Total	1,317	191	70	35	347**	1,960

NOTE:

* Invalid/Missing results include mislabeled specimens, instrument errors and non-reportable results.

** 341 women did not return or were no longer eligible for a colposcopy procedure. Three women had unsatisfactory histology results and three women had biopsy specimen collection errors.

The performance of the BD Onclarity™ HPV Assay in detecting high-grade cervical disease (≥CIN2 and ≥CIN3) is presented in Table 7. The sensitivity and the specificity of the test for detecting ≥CIN2 histology were 85.7% (90/105) and 64.1% (963/1,502), respectively. The positive likelihood ratio (PLR) was estimated as 2.4, which indicates a positive BD Onclarity™ HPV Assay result is 2.4 times more likely in women with ≥CIN2 than in women with <CIN2. The negative likelihood ratio (NLR) was estimated as 0.2, which indicates that a negative BD Onclarity™ HPV Assay result is 5 (1/0.2) times more likely in women with <CIN2 than in women with ≥CIN2.

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The sensitivity and specificity of the BD Onclarity™ HPV Assay for detecting ≥CIN3 histology were 91.4% (32/35) and 62.0% (975/1,572), respectively.

Table 7: Performance of the BD Onclarity™ HPV Assay in the ASC-US Population (≥21 years)

Performance	≥CIN2	≥CIN3
	Central Pathology Review Panel Diagnosis	
Sensitivity (%) (95% CI)	85.7 90/105[a] (77.8, 91.1)	91.4 32/35[b] (77.6, 97.0)
Specificity (%) (95% CI)	64.1 963/1,502 (61.7, 66.5)	62.0 975/1,572 (59.6, 64.4)
PPV (%) (95% CI)	14.3 90/629 (13.0, 15.5)	5.1 32/629 (4.3, 5.6)
NPV (%) (95% CI)	98.5 963/978 (97.6, 99.0)	99.7 975/978 (99.2, 99.9)
PLR (95% CI)	2.39 (2.13, 2.63)	2.41 (2.03, 2.64)
NLR (95% CI)	0.22 (0.14, 0.35)	0.14 (0.05, 0.36)
Disease Prevalence (%)	6.5 105/1,607	2.2 35/1,607

[a]12 of the 15 BD Onclarity™ HPV Assay negative, ≥CIN2 subjects were also negative by the FDA approved HPV test. Three of the subjects were positive by the FDA approved HPV test and were identified as low risk HPV types 67 and/or 82 by a sequencing method.
[b]2 of the 3 BD Onclarity™ HPV Assay negative ≥CIN3 subjects were also negative by the FDA approved HPV test. One subject was positive by the FDA approved HPV test and was identified as low risk HPV type 67 by a sequencing method.

The performance of the BD Onclarity™ HPV Assay in detecting high-grade cervical disease (≥CIN2 and ≥CIN3) and the performance of the FDA approved HPV test is presented in Table 8. The sensitivity for detecting ≥CIN2 histology was 85.7% (90/105) for the BD Onclarity™ HPV Assay and 82.9% (87/105) for the FDA approved HPV test. The specificity for detecting ≥CIN2 histology was 64.1% (959/1,496) for the BD Onclarity™ HPV Assay and 61.4% (919/1,496) for the FDA approved HPV test.

The sensitivity for detecting ≥CIN3 histology was 91.4% (32/35) for the BD Onclarity™ HPV Assay and 85.7% (30/35) for the FDA approved HPV test. The specificity for detecting ≥CIN3 histology was 62.0% (971/1,566) for the BD Onclarity™ HPV Assay and 59.5% (932/1,566) for the FDA approved HPV test.

Table 8: Comparison of the Performance of the BD Onclarity™ HPV Assay and an FDA Approved HPV Test in the ASC-US Population (≥21 years)

Performance Metrics	BD Onclarity™ HPV Assay		FDA Approved HPV Test	
	Estimate	95% CI	Estimate	95% CI
≥CIN2; Prevalence 6.6% (105/1,601)				
Sensitivity (%)	85.7 (90/105)	(77.8, 91.1)	82.9 (87/105)	(74.5, 88.9)
Specificity (%)	64.1 (959/1,496)	(61.6, 66.5)	61.4 (919/1,496)	(58.9, 63.9)
PPV (%)	14.4 (90/627)	(13.0, 15.6)	13.1 (87/664)	(11.8, 14.3)
NPV (%)	98.5 (959/974)	(97.6, 99.0)	98.1 (919/937)	(97.2, 98.7)
PLR	2.39	(2.13, 2.63)	2.15	(1.90, 2.37)
NLR	0.22	(0.14, 0.35)	0.28	(0.18, 0.42)
≥CIN3; Prevalence 2.2% (35/1,601)				
Sensitivity (%)	91.4 (32/35)	(77.6, 97.0)	85.7 (30/35)	(70.6, 93.7)
Specificity (%)	62.0 (971/1,566)	(59.6, 64.4)	59.5 (932/1,566)	(57.1, 61.9)
PPV (%)	5.1 (32/627)	(4.3, 5.6)	4.5 (30/664)	(3.7, 5.0)
NPV (%)	99.7 (971/974)	(99.2, 99.9)	99.5 (932/937)	(98.9, 99.8)
PLR	2.41	(2.03, 2.64)	2.12	(1.73, 2.37)
NLR	0.14	(0.05, 0.36)	0.24	(0.11, 0.49)

NOTE: This table is a paired analysis of specimens with a valid BD Onclarity™ HPV Assay and FDA approved HPV test result. Six women (<CIN2) with a BD Onclarity™ result but no FDA approved HPV test result were excluded from this analysis.

The performance of the BD Onclarity™ HPV Assay and the FDA approved HPV test for detecting ≥CIN2 and ≥CIN3 evaluated by age group is presented in Table 9. The sensitivity of the BD Onclarity™ HPV Assay and the FDA approved HPV test ranged from 68.8–93.6% for ≥CIN2. The specificity of the BD Onclarity™ HPV Assay ranged from 49.5–78.2% and from 45.9–76.3% for the FDA approved HPV test.

The sensitivity of the BD Onclarity™ HPV Assay for detecting ≥CIN3 histology ranged from 85.7–92.9% and from 71.4–92.9% for the FDA approved HPV test. The specificity of the BD Onclarity™ HPV Assay ranged from 47.0–77.0% and from 43.7–75.6% for the FDA approved HPV test.

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Table 9: Performance of the BD Onclarity™ HPV Assay and an FDA Approved HPV Test by Age Group in the ASC-US (≥21 years) Population

Performance Metrics	BD HPV	FDA Approved HPV Test	BD HPV	FDA Approved HPV Test	BD HPV	FDA Approved HPV Test
	21–29 Years		30–39 Years		≥40 Years	
≥CIN2						
Sensitivity (%) 95% CI	93.6 44/47 (82.8, 97.8)	91.5 43/47 (80.1, 96.6)	83.3 (35/42) (69.4, 91.7)	78.6 (33/42) (64.1, 88.3)	68.8 (11/16) (44.4, 85.8)	68.8 (11/16) (44.4, 85.8)
Specificity (%) 95% CI	49.5 260/525 (45.3, 53.8)	45.9 241/525 (41.7, 50.2)	63.2 (254/402) (58.4, 67.8)	60.7 (244/402) (55.8, 65.3)	78.2 (445/569) (74.6, 81.4)	76.3 (434/569) (72.6, 79.6)
PPV (%) 95% CI	14.2 44/309 (12.6, 15.6)	13.1 (43/327) (11.5, 14.4)	19.1 (35/183) (16.0, 21.9)	17.3 (33/191) (14.2, 20.0)	8.1 (11/135) (5.3, 10.6)	7.5 (11/146) (4.9, 9.7)
NPV (%) 95% CI	98.9 (260/263) (97.0, 99.6)	98.4 (241/245) (96.2, 99.4)	97.3 (254/261) (95.2, 98.6)	96.4 (244/253) (94.1, 98.0)	98.9 (445/450) (98.0, 99.5)	98.9 (434/439) (98.0, 99.5)
PLR 95% CI	1.85 (1.61, 2.06)	1.69 (1.46, 1.88)	2.26 (1.82, 2.69)	2.00 (1.59, 2.39)	3.15 (1.99, 4.20)	2.90 (1.83, 3.84)
NLR 95% CI	0.13 (0.04, 0.35)	0.19 (0.07, 0.44)	0.26 (0.13, 0.49)	0.35 (0.19, 0.60)	0.40 (0.18, 0.71)	0.41 (0.19, 0.73)
≥CIN3						
Sensitivity (%) 95% CI	92.9 (13/14) (68.5, 98.7)	92.9 (13/14) (68.5, 98.7)	92.9 (13/14) (68.5, 98.7)	85.7 (12/14) (60.1, 96.0)	85.7 (6/7) (48.7, 97.4)	71.4 (5/7) (35.9, 91.8)
Specificity (%) 95% CI	47.0 (262/558) (42.8, 51.1)	43.7 (244/558) (39.7, 47.9)	60.5 (260/430) (55.8, 65.0)	58.4 (251/430) (53.7, 62.9)	77.7 (449/578) (74.1, 80.9)	75.6 (437/578) (71.9, 78.9)
PPV (%) 95% CI	4.2 (13/309) (3.1, 4.7)	4.0 (13/327) (2.9, 4.4)	7.1 (13/183) (5.3, 8.1)	6.3 (12/191) (4.4, 7.4)	4.4 (6/135) (2.5, 5.5)	3.4 (5/146) (1.7, 4.6)
NPV (%) 95% CI	99.6 (262/263) (98.3, 99.9)	99.6 (244/245) (98.2, 99.9)	99.6 (260/261) (98.3, 99.9)	99.2 (251/253) (97.8, 99.8)	99.8 (449/450) (99.2, 100.0)	99.5 (437/439) (99.0, 99.9)
PLR 95% CI	1.75 (1.28, 1.96)	1.65 (1.21, 1.84)	2.35 (1.71, 2.72)	2.06 (1.42, 2.45)	3.84 (2.15, 4.80)	2.93 (1.45, 3.99)
NLR 95% CI	0.15 (0.03, 0.67)	0.16 (0.03, 0.72)	0.12 (0.02, 0.52)	0.24 (0.07, 0.69)	0.18 (0.03, 0.66)	0.38 (0.11, 0.85)

NEGATIVE FOR INTRAEPITHELIAL LESION OR MALIGNANCY (NILM)

NILM (≥30 years) Population

A total of 22,383 NILM women ≥30 years were enrolled in the study. Women with a NILM cytology result and an HPV positive result (1,991) and a random subset of women (1,228) with negative HPV results (from both the BD Onclarity™ HPV Assay and FDA-approved HPV test) were assigned to colposcopy for a histological diagnosis. Of the 3,219 women identified for colposcopy, 2,591 completed the procedure with a valid CPR and BD Onclarity™ HPV result. In order to account for the different rates of selection in the HPV positive and HPV negative groups, verification bias adjusted (VBA) performance estimates were calculated. Adjustment was made by calculating the likely number of diseased cases that would have been found if all women had colposcopy.

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The results of the BD Onclarity™ HPV Assay in the NILM (≥30 years) population reported as HPV HR Positive or HPV HR Negative together with the CPR panel diagnosis are summarized in Table 10.

Table 10: BD Onclarity™ HPV Assay Result and CPR Panel Diagnosis in the NILM Population (≥30 years)

BD Onclarity™ HPV Assay Test Results	Central Pathology Review Panel Diagnosis				Unknown Disease Status	Total
	NEG	CIN1	CIN2	≥CIN3		
Positive	1,198	93	27	43	400	1,761
Negative	1,184	36	7	3	19,293	20,523
Invalid/Missing[a]	5	1	0	0	93	99
Total	2,387	130	34	46	19,786[b]	22,383

[a] Invalid/Missing results include mislabeled specimens, instrument errors and non-reportable results.

[b] 19,164 women were not identified for colposcopy. 609 women did not return or were no longer eligible for a colposcopy procedure. Six women had unsatisfactory histology results and seven women had biopsy specimen collection errors.

NILM (≥30 years) Population-Performance Evaluation

The performance of the BD Onclarity™ HPV Assay in detecting high grade cervical disease is presented in Table 11. The unadjusted estimates of sensitivity and specificity for detection of ≥CIN2 histology are 87.5% (78.5, 93.1) and 48.6% (46.6, 50.5), respectively. The positive likelihood ratio for the detection of ≥CIN2 was 5.86 (adjusted estimates), indicating a strong probability that a positive result is truly positive. The negative likelihood ratio for the detection of ≥CIN2 was 0.26 (crude estimates) and 0.60 (adjusted estimates), indicating a strong likelihood that a negative result was associated with the absence of disease.

Verification bias adjusted (VBA) sensitivity and specificity for ≥CIN2 are 44.4% (27.2, 76.2) and 92.4% (92.1, 92.8), respectively.

Unadjusted estimates of sensitivity and specificity for the detection of ≥CIN3 are 93.5% (82.5, 97.8) and 48.2% (46.3, 50.2), respectively. The positive likelihood ratio for the detection of ≥CIN3 was 9.02 (adjusted estimates) indicating that an HPV positive result is nearly 9 times more likely to occur in a subject with ≥CIN3 histology than in a subject with <CIN3. Negative likelihood ratio was 0.3 (adjusted estimates), indicating a strong likelihood that a negative result was associated with the absence of disease.

VBA sensitivity and specificity for the detection of ≥CIN3 are 69.3% (42.0, 100.0) and 92.3% (92.0, 92.7), respectively.

Table 11: Performance of the BD Onclarity™ HPV Assay in the NILM Population (≥30 years)

Performance	Central Pathology Review Panel Diagnosis			
	≥CIN2		≥CIN3	
	Unadjusted Estimate	Adjusted Estimate (%, 95% CI)	Unadjusted Estimate	Adjusted Estimate (%, 95% CI)
Sensitivity (%) (95% CI)	87.5 70/80 (78.5, 93.1)	44.4 (27.7, 76.2)	93.5 43/46 (82.5, 97.8)	69.3 (42.0, 100.0)
Specificity (%) (95% CI)	48.6 1,220/2,511 (46.6, 50.5)	92.4 (92.1, 92.8)	48.2 1,227/2,545 (46.3, 50.2)	92.3 (92.0, 92.7)
PPV (%) (95% CI)	5.1 70/1,361 (4.6, 5.5)	5.1 (3.9, 6.3)	3.2 43/1,361 (2.8, 3.4)	3.0 (2.1, 3.9)
NPV (%) (95% CI)	99.2 1,220/1,230 (98.6, 99.5)	99.5 (99.0, 99.9)	99.8 1,227/1,230 (99.3, 99.9)	99.9 (99.7, 100.0)
PLR (95% CI)	1.70 (1.52, 1.83)	5.86 (3.63, 10.11)	1.81 (1.59, 1.92)	9.02 (5.48, 13.21)
NLR (95% CI)	0.26 (0.14, 0.44)	0.60 (0.26, 0.78)	0.14 (0.05, 0.36)	0.33 (0.00, 0.63)
Disease Prevalence (%)	3.1 80/2,591	0.9 (0.5, 1.4)	1.8 46/2,591	0.3 (0.2, 0.6)

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The performance of the BD Onclarity™ HPV Assay as well as the FDA approved HPV test for detecting ≥CIN2 and ≥CIN3 is presented in Table 12.

Table 12: Performance of the BD Onclarity™ HPV Assay and an FDA Approved HPV Assay in the NILM Population (≥30 years)

Performance	Central Pathology Review Panel Diagnosis			
	Unadjusted Estimates		Adjusted Estimates	
	BD HPV	FDA Approved HPV test	BD HPV	FDA Approved HPV test
≥CIN2; unadjusted prevalence 3.1%, adjusted prevalence 0.9%				
Sensitivity (%) (95% CI)	87.5 70/80 (78.5, 93.1)	82.5 66/80 (72.7, 89.3)	44.1 (27.7, 77.8)	40.3 (25.2, 69.0)
Specificity (%) (95% CI)	48.6 1,220/2,508 (46.7, 50.6)	52.3 1,312/2,508 (50.4, 54.3)	92.4 (92.1, 92.8)	93.4 (93.1, 93.8)
PPV (%) (95% CI)	5.2 70/1,358 (4.6, 5.5)	5.2 66/1,262 (4.6, 5.7)	5.0 (3.9, 6.1)	5.3 (4.1, 6.5)
NPV (%) (95% CI)	99.2 1,220/1,230 (98.6, 99.5)	98.9 1,312/1,326 (98.4, 99.4)	99.5 (98.9, 99.9)	99.4 (98.9, 99.8)
PLR (95% CI)	1.70 (1.52, 1.84)	1.73 (1.52, 1.90)	5.82 (3.65, 10.19)	6.14 (3.83, 10.59)
NLR (95% CI)	0.26 (0.14, 0.44)	0.33 (0.20, 0.52)	0.61 (0.24, 0.78)	0.64 (0.33, 0.80)
≥CIN3; unadjusted prevalence 1.8%, adjusted prevalence 0.3%				
Sensitivity (%) (95% CI)	93.5 43/46 (82.5, 97.8)	87.0 40/46 (74.3, 93.9)	69.5 (42.8, 100.0)	63.3 (38.7, 94.9)
Specificity (%) (95% CI)	48.3 1,227/2,542 (46.3, 50.2)	51.9 1,320/2,542 (50.0, 53.9)	92.3 (92.0, 92.7)	93.3 (93.0, 93.7)
PPV (%) (95% CI)	3.2 43/1,358 (2.8, 3.4)	3.2 40/1,262 (2.7, 3.5)	3.0 (2.2, 4.0)	3.2 (2.3, 4.2)
NPV (%) (95% CI)	99.8 1,227/1,230 (99.3, 99.9)	99.5 1,320/1,326 (99.1, 99.8)	99.9 (99.7, 100.0)	99.9 (99.7, 100.0)
PLR (95% CI)	1.81 (1.59, 1.92)	1.81 (1.54, 1.98)	9.05 (5.52, 13.19)	9.49 (5.82, 14.42)
NLR (95% CI)	0.14 (0.05, 0.36)	0.25 (0.12, 0.49)	0.33 (0.00, 0.62)	0.39 (0.06, 0.66)

Note: This table is a paired analysis of specimens with a valid BD Onclarity™ HPV Assay and FDA approved HPV test result. Three women with BD Onclarity™ results but without FDA approved test results were not included in the analysis.

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PRIMARY SCREENING POPULATION (≥25 years)

A total of 29,633 women ≥25 years were enrolled in the study of which 29,513 were evaluable. Evaluable women had valid cytology and BD Onclarity™ HPV Assay results.

The median age of enrolled women in the primary screening population was 39 years with 18% of women 25–29, 32% of women 30–39, and 50% of women ≥40 years old. Approximately 79% of women were white and 18% were Black or African American.

A total of 5,534 women ≥25 years completed the colposcopy procedure with a valid CPR and BD Onclarity™ HPV result.

Screening Algorithms

The use of the BD Onclarity™ HPV Assay as a first line screening method was evaluated by comparing the Primary Screening algorithm with the Cytology algorithm, shown in Figures 1 and 2.

Figure 1: Primary Screening Algorithm

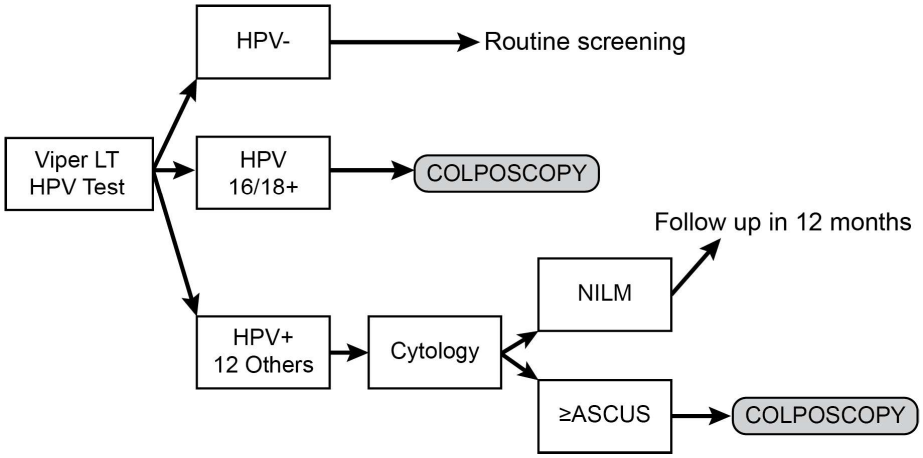
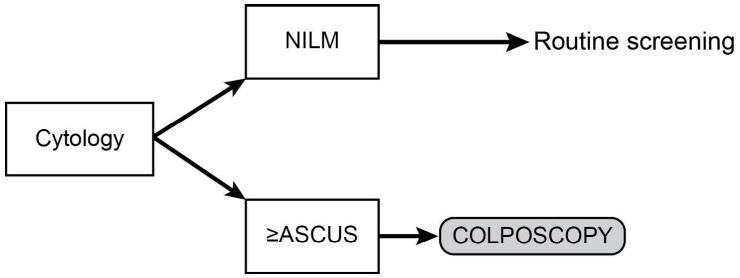


Figure 2: Cytology Algorithm



The performance of the Primary Screening algorithm with HPV 16 and 18 genotyping with reflex to cytology, and the Cytology algorithm (cytology alone) was evaluated and compared in the primary screening population by estimating the sensitivity, specificity, PPV, NPV, PLR, and NLR for the identification of ≥CIN2 and ≥CIN3. Results are presented in Table 13. As compared to cytology alone, the primary screening algorithm improves disease detection, while also reducing the number of colposcopies: 15.0% increase in ≥CIN3 sensitivity, 2.3% reduction in colposcopy rates (27.2% relative reduction).

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Table 13: Performance Comparison of the Primary Screening Algorithm and Cytology Algorithm

Performance Metrics	≥CIN2; Prevalence (Adjusted) = 1.9%			≥CIN3; Prevalence (Adjusted) = 0.8%		
	Primary Screening Algorithm	Cytology Screening Algorithm	Difference	Primary Screening Algorithm	Cytology Screening Algorithm	Difference
Sensitivity (%) (95% CI)	53.72 (44.18, 65.52)	47.42 (39.31, 57.77)	6.30[a] (2.39, 10.51)	64.24 (50.59, 79.65)	49.20 (38.31, 62.64)	15.05[a] (9.12, 22.26)
Specificity (%) (95% CI)	94.80 (94.53, 95.06)	92.36 (92.03, 92.67)	2.45[a] (2.17, 2.74)	94.39 (94.11, 94.66)	91.96 (91.63, 92.27)	2.43[a] (2.15, 2.72)
PPV (%) (95% CI	16.48 (14.58, 18.48)	10.59 (9.34, 12.00)	5.89[a] (4.67, 7.16)	8.98 (7.70, 10.49)	5.00 (4.09, 5.98)	3.97[a] (3.14, 4.88)
NPV (%) (95% CI	99.08 (98.66, 99.41)	98.92 (98.53, 99.27)	0.15[a] (0.07, 0.24)	99.68 (99.44, 99.85)	99.53 (99.28, 99.71)	0.15[a] (0.09, 0.20)
PLR (95% CI)	10.34 (8.36, 12.76)	6.20 (5.06, 7.62)	4.13[a] (3.18, 5.50)	11.46 (8.99, 14.22)	6.12 (4.74, 7.82)	5.34[a] (4.00, 7.09)
NLR (95% CI)	0.49 (0.36, 0.59)	0.57 (0.46, 0.66)	-0.08[a] (-0.12, -0.04)	0.38 (0.22, 0.52)	0.55 (0.41, 0.67)	-0.17[a] (-0.25, -0.11)
Colposcopy Rate (95% CI)	6.11 (5.83, 6.38)	8.39 (8.08, 8.72)	-2.28[a] (-2.58, -2.00)	6.11 (5.83, 6.38)	8.39 (8.08, 8.72)	-2.28[a] (-2.58, -2.00)

[a]Indicates statistically significant difference at the 0.05 level.

Baseline Risk of Disease for Women with NILM Cytology and Negative BD Onclarity™ HPV Test Results

The baseline risk of disease was compared in the primary screening population between women with a NILM cytology result and women with a negative BD Onclarity™ HPV result. Women with a negative BD Onclarity™ HPV result had a 0.20% baseline risk of ≥CIN3 compared to 0.47% for those with NILM cytology. The addition of a NILM cytology result to a negative BD Onclarity™ HPV result marginally decreased the ≥CIN3 risk (0.20 vs 0.19).

Table 14: Baseline Risk of Disease for Women with NILM Cytology and Negative BD Onclarity™ HPV Test Results in the Primary Screening (≥25 Years) Population

Subgroup	Percentage with result	≥CIN3 Risk (95% CI)	≥CIN2 Risk (95% CI)
NILM	91.61	0.47 (0.29, 0.72)	1.08 (0.73, 1.47)
HPV HR NEG	87.30	0.20 (0.03, 0.45)	0.63 (0.29, 1.07)
HPV HR NEG and NILM	82.95	0.19 (0.01, 0.46)	0.56 (0.20, 1.01)

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Performance in Unvaccinated and Vaccinated Women

The clinical sites enrolled both HPV vaccinated and unvaccinated women, with a vaccinated enrollment limit of approximately 10%. The final vaccinated rate in the study was 9.1%, with an additional 1.4% unknown or missing vaccination status; vaccination status was self-reported.

The first HPV vaccine was introduced in 2006 and the clinical study occurred from 2013–2015, thus a majority of the vaccinated women in the study were under the age of 30 (3,064 vaccinated subjects overall, 2,625 under 30). The performance of the BD Onclarity™ HPV Assay in vaccinated and unvaccinated women (excluding women with unknown or missing vaccination status) is shown below for women with ASC-US cytology (21–29 years old) and a subset of the primary screening population (25–29 years old).

Table 15: BD Onclarity™ HPV Assay Performance in Unvaccinated and Vaccinated Women with ASC-US Cytology (21–29 years old)

Performance Metrics	≥CIN2			
	Unvaccinated (prevalence 7.8%)		Vaccinated (prevalence 9.7%)	
	Estimate	95% CI	Estimate	95% CI
Sensitivity	100.0% (31/31)	(89.0%, 100.0%)	80.0% (12/15)	(54.8%, 93.0%)
Specificity	48.9% (180/368)	(43.8%, 54.0%)	52.1% (73/140)	(43.9%, 60.2%)
PPV	14.2% (31/219)	(13.3%, 15.5%)	15.2% (12/79)	(10.7%, 18.8%)
NPV	100.0% (180/180)	(98.1%, 100.0%)	96.1% (73/76)	(91.3%, 98.6%)
PLR	1.96	(1.82, 2.17)	1.67	(1.11, 2.16)
NLR	0	(0.00, 0.23)	0.38	(0.13, 0.89)
Performance Metrics	**≥CIN3**			
	Unvaccinated (prevalence 2.0%)		Vaccinated (prevalence 3.2%)	
	Estimate	95% CI	Estimate	95% CI
Sensitivity	100.0% (8/8)	(67.6%, 100.0%)	80.0% (4/5)	(37.6%, 96.4%)
Specificity	46.0% (180/391)	(41.2%, 51.0%)	50.0% (75/150)	(42.1%, 57.9%)
PPV	3.7% (8/219)	(3.6%, 4.0%)	5.1% (4/79)	(2.4%, 6.6%)
NPV	100.0% (180/180)	(98.6%, 100.0%)	98.7% (75/76)	(95.9%, 99.8%)
PLR	1.85	(1.82, 2.04)	1.60	(0.74, 2.12)
NLR	0	(0.00, 0.71)	0.40	(0.07, 1.28)

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Table 16: BD Onclarity™ HPV Assay Performance in Unvaccinated and Vaccinated Women in the Primary Screening Population (25–29 years old)

Performance	Unadjusted Estimate		Adjusted Estimate	
	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
≥CIN2				
Sensitivity (%) (95% CI)	67.05 59/88 (56.69, 75.97)	60.00 15/25 (40.74, 76.60)	58.85 (41.92, 76.31)	59.26 (39.57, 76.83)
Specificity (%) (95% CI)	68.86 690/1,002 (65.93, 71.65)	79.64 223/280 (74.54, 83.94)	89.39 (88.39, 90.33)	93.78 (92.35, 95.43)
PPV (%) (95% CI)	15.90 59/371 (13.54, 18.15)	20.83 15/72 (14.46, 27.29)	15.97 (12.11, 19.79)	20.18 (10.83, 30.54)
NPV (%) (95% CI)	95.97 690/719 (94.75, 97.03)	95.71 223/233 (93.74, 97.45)	98.45 (97.00, 99.27)	98.86 (98.07, 99.44)
PLR (95% CI)	2.15 (1.78, 2.53)	2.95 (1.89, 4.20)	5.54 (3.80, 7.43)	9.53 (6.04, 14.24)
NLR (95% CI)	0.48 (0.35, 0.63)	0.50 (0.29, 0.75)	0.46 (0.26, 0.65)	0.43 (0.25, 0.65)
Colpo Rate (95% CI)			12.21 (11.24, 13.23)	7.59 (5.84, 9.11)
Prevalence (95% CI)			3.31 (2.39, 4.67)	2.58 (1.65, 3.69)
≥CIN3				
Sensitivity (%) (95% CI)	81.58 31/38 (66.58, 90.78)	61.54 8/13 (35.52, 82.29)	58.48 (31.62, 92.66)	61.35 (34.93, 86.50)
Specificity (%) (95% CI)	67.68 712/1,052 (64.79, 70.44)	78.08 228/292 (72.99, 82.45)	88.59 (87.57, 89.54)	93.17 (91.77, 94.93)
PPV (%) (95% CI)	8.36 31/371 (6.83, 9.54)	11.11 8/72 (6.51, 15.54)	8.12 (5.43, 11.07)	11.20 (4.58, 19.77)
NPV (%) (95% CI)	99.03 712/719 (98.24, 99.51)	97.85 228/233 (96.44, 99.00)	99.20 (97.80, 99.90)	99.42 (98.87, 99.88)
PLR (95% CI)	2.52 (2.03, 2.92)	2.81 (1.57, 4.13)	5.12 (2.68, 8.28)	8.98 (4.86, 14.76)
NLR (95% CI)	0.27 (0.14, 0.49)	0.49 (0.23, 0.83)	0.47 (0.08, 0.77)	0.41 (0.14, 0.69)
Colpo Rate (95% CI)			12.21 (11.24, 13.23)	7.59 (5.84, 9.11)
Prevalence (95% CI)			1.70 (0.92, 2.97)	1.39 (0.68, 2.25)

Comparison of Results from the BD Onclarity™ HPV Assay for PreQuot vs. PostQuot BD SurePath™ Clinical Samples

An equivalence study design was employed to compare the performance of the BD Onclarity™ HPV Assay with a cervical specimen tested prior to (PreQuot) or after (PostQuot) normal cytology processing.

A total of 3,879 subjects were enrolled in the PreQuot vs. PostQuot study. During the Baseline Study, 0.5 mL of the cervical specimen stored in BD SurePath™ was manually transferred into a BD Onclarity™ HPV LBC Diluent tube (PreQuot). After normal processing per the BD PrepMate™ labeling, 0.5 mL of the residual specimen in BD SurePath™ was manually transferred into a BD Onclarity™ HPV LBC Diluent Tube (PostQuot). The comparative performance of the PreQuot to the PostQuot sample when tested with the BD Onclarity™ HPV Assay is shown in Tables 17 and 18.

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Table 17: Agreement Results of the BD Onclarity™ HPV Assay PreQuot vs. PostQuot

Population	Positive Percent Agreement (95%CI)	Negative Percent Agreement (95%CI)	Overall Percent Agreement (95%CI)
NILM ≥30 yrs (%)	86.0	99.3	98.3
	(80.3, 90.3)	(98.8, 99.5)	(97.8, 98.8)
ASC-US ≥21 yrs (%)	100.0	97.7	98.5
	(95.0, 100.0)	(93.5, 99.2)	(95.8, 99.5)
>ASC-US ≥21 yrs (%)	97.6	100.0	98.1
	(91.8, 99.4)	(83.2, 100.0)	(93.3, 99.5)
Screening Population ≥25 yrs (%)	91.0	99.0	98.1
	(87.7, 93.4)	(98.6, 99.3)	(97.6, 98.5)

Table 18: BD Onclarity™ HPV Assay PreQuot vs. PostQuot Results

BD Onclarity™ HPV Assay PostQuot Result	BD Onclarity™ HPV Assay PreQuot Result							
	ASC-US ≥21		>ASC-US ≥21		NILM ≥30		All Subjects ≥25	
	POS	NEG	POS	NEG	POS	NEG	POS	NEG
Positive	73	3	83	0	160	18	353	30
Negative	0	129	2	19	26	2,431	35	3,052
Total	73	132	85	19	186	2,449	388	3,082

Clinical Performance-PreservCyt® and BD Onclarity™ HPV Cervical Brush Specimens

BD Onclarity™ HPV Cervical Brush specimens and PreservCyt® specimens, were collected from 836 protocol compliant women who were referred for follow-up due to abnormal Pap test or HPV infection, or women attending a clinic for a routine visit at two geographically diverse clinical sites in Europe. Two specimens were collected from each enrolled subject in the following order: PreservCyt® specimen and a BD Onclarity™ HPV Cervical Brush specimen (transported in a BD Onclarity™ HPV Cervical Brush Diluent Tube). For each cytology vial collected, 0.5 mL was aliquoted into a BD Onclarity™ HPV LBC Diluent Tube. Cytology, HPV DNA results (digene® Hybrid Capture 2 [hc2] High-Risk HPV DNA Test), and Roche LINEAR ARRAY® HPV Genotyping Test (RLA) results were available for most of the specimens. Histology results were available for most of the subjects attending a high-risk clinic. Each site also enrolled residual specimens (PreservCyt®) with associated cytology results, HPV DNA results (digene® Hybrid Capture 2 High-Risk HPV DNA Test), Roche LINEAR ARRAY® HPV Genotyping Test results, and where applicable, histology results. For each specimen enrolled, 0.5 mL was aliquoted into a BD Onclarity™ HPV LBC Diluent Tube. There were 510 compliant retrospective specimens enrolled, with histology results available for 234 women.

All specimens were tested on the BD Viper™ LT System in accordance with the assay package insert and user's manual. For each media type, the clinical sensitivity and specificity for detection of disease, which is defined as (1) Cervical Intraepithelial Neoplasia (CIN2) or greater histology result or (2) Cervical Intraepithelial Neoplasia (CIN3) or greater histology result, was calculated. Final data analysis includes BD Onclarity™ HPV Assay results 361 PreservCyt® specimens and a total of 515 BD Onclarity™ HPV Cervical Brush specimens. The performance estimates for the detection of high grade cervical disease for the BD Onclarity™ HPV Assay and the hc2 assay are presented in Tables 19 and 20 for PreservCyt® media, and Tables 22 and 23 for the BD Onclarity™ HPV Cervical Brush specimens.

BD Onclarity™ HPV Assay results were also compared to HPV DNA results from the digene® Hybrid Capture 2 High-Risk HPV DNA Test and Roche LINEAR ARRAY® HPV Genotyping Test (composite comparator). A positive result from both the hc2 and RLA (high risk) assays is defined as composite comparator positive, a negative result from both the hc2 and RLA (high risk) assays is defined as composite comparator negative, and when the two assays disagree (or results were not available; for both tests), the composite comparator result is defined as unresolved. Positive, negative, and overall percent agreement was calculated for each media type versus the composite comparator. Final data analysis includes BD Onclarity™ HPV Assay and composite comparator results (regardless of histology status) from 674 PreservCyt® specimens (Table 21).

Table 19: Performance of the BD Onclarity™ HPV Assay with PreservCyt® Media Compared to Histology Results (CIN2+)

	BD Onclarity™ HPV Assay		hc2 HPV DNA Test	
	Estimate	95% Confidence Interval	Estimate	95% Confidence Interval
Sensitivity	96.4% (163/169)	(92.5, 98.4)	97.0% (160/165)	(93.1, 98.7)
Specificity	49.0% (94/192)	(42.0, 56.0)	40.8% (75/184)	(33.9, 48.0)

Table 20: Performance of the BD Onclarity™ HPV Assay with PreservCyt® Media Compared to Histology Results (CIN3+)

	BD Onclarity™ HPV Assay		hc2 HPV DNA Test	
	Estimate	95% Confidence Interval	Estimate	95% Confidence Interval
Sensitivity	95.6% (86/90)	(89.1, 98.3)	97.7% (85/87)	(92.0, 99.4)
Specificity	35.4% (96/271)	(30.0, 41.3)	29.8% (78/262)	(24.6, 35.6)

Table 21: Performance of the BD Onclarity™ HPV Assay with PreservCyt® Media Compared to Composite Comparator

BD Onclarity™ HPV Assay	Composite Comparator Result						
	Positive	Negative	Unresolved*	Total	Positive Percent Agreement (95% Confidence Interval)	Negative Percent Agreement (95% Confidence Interval)	Overall Percent Agreement (95% Confidence Interval)
Positive	249	10	20	279	97.3% (94.5%, 98.7%)	97.3% (95.1%, 98.5%)	97.3% (95.7%, 98.3%)
Negative	7	361	27	395			
Total	256	371	47	674			

* hc2 and RLA results do not agree or results were not available for both tests.

Table 22: Performance of the BD Onclarity™ HPV Assay with the BD Onclarity™ HPV Cervical Brush Compared to Histology Results (CIN2+)

Site		BD Onclarity™ HPV Assay		hc2 HPV DNA Test	
		Estimate	95% Confidence Interval	Estimate	95% Confidence Interval
A	Sensitivity	97.2% (104/107)	(92.1%, 99.0%)	99.1% (106/107)	(94.9%, 99.8%)
	Specificity	17.1% (24/140)	(11.8%, 24.2%)	21.4% (30/140)	(15.4%, 28.9%)
B	Sensitivity	100.0% (121/121)	(96.9%, 100.0%)	97.5% (116/119)	(92.8%, 99.1%)
	Specificity	37.4% (55/147)	(30.0%, 45.5%)	43.0% (61/142)	(35.1%, 51.2%)

Table 23: Performance of the BD Onclarity™ HPV Assay with the BD Onclarity™ HPV Cervical Brush Compared to Histology Results (CIN3+)

Site		BD Onclarity™ HPV Assay		hc2 HPV DNA Test	
		Estimate	95% Confidence Interval	Estimate	95% Confidence Interval
A	Sensitivity	97.3% (72/74)	(90.7%, 99.3%)	98.6% (73/74)	(92.7%, 99.8%)
	Specificity	14.5% (25/173)	(10.0%, 20.5%)	17.3% (30/173)	(12.4%, 23.7%)
B	Sensitivity	100.0% (60/60)	(94.0%, 100.0%)	98.3% (57/58)	(90.9%, 99.7%)
	Specificity	26.4% (55/208)	(20.9%, 32.8%)	31.0% (63/203)	(25.1%, 37.7%)

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Analytical Performance

Analytical Sensitivity at the Clinical Cutoff

The limit of detection (LOD) at the HPV clinical cutoff was determined for the BD Onclarity™ HPV Assay using HPV positive cell lines: SiHa (HPV16), HeLa (HPV18) and MS751 (HPV45) and cloned plasmid DNA containing the sequences for the following HPV genotypes: HPV31, 33, 35, 39, 51, 52, 56, 58, 59, 66, and 68 in BD SurePath™ Preservative Fluid, PreservCyt® Solution and BD Onclarity™ HPV Cervical Brush Diluent containing a HPV-negative cell line (C33A). The HPV cell lines were tested individually whereas the HPV plasmids were tested collectively in three groups: 1) HPV31, 33, 51, 52, and 59; 2) HPV56, 58, 68; and 3) HPV35 and 66. A minimum of forty-five replicates of each of six target levels for the HPV cell lines and twenty replicates of each of six target levels for the HPV plasmids were tested across a minimum of three lots of reagents and a minimum of three BD Viper™ LT Systems. The LOD is the level of HPV DNA in the undiluted specimen that has positive results above the clinical cutoff at least 95% of the time. The maximum LOD value for each of the HPV genotypes and media is described in Table 24. The cells/mL nomenclature refers to the target concentration in the BD Onclarity™ HPV LBC Diluent Tube, BD Onclarity™ HPV Cervical Brush Diluent, or BD Onclarity™ HPV Self Collection Diluent Tube.

Table 24: Analytical Sensitivity

Target	BD SurePath™ Media (95% Confidence Interval)	PreservCyt® Media (95% Confidence Interval)	BD Onclarity™ HPV Cervical Brush Diluent and Vaginal Self-Collection Devices* (95% Confidence Interval)
SiHa (HPV16) cells/mL	50 (37–67)	163 (117–228)	9.7 (7.7–13.4)
HeLa (HPV18) cells/mL	199 (154–256)	395 (261–597)	51 (46–56)
MS751 (HPV45) cells/mL	862 (669–1,111)	1,233 (947–1,606)	305 (284–343)
HPV31 copies/mL	830 (718–879)	936 (886–961)	692 (650–817)
HPV33 copies/mL	1,665 (1,495-2,030)	1,880 (1,806–1,987)	1,376 (1,272–1,451)
HPV35 copies/mL	1,550 (1,472–1,655)	1,655 (1,567–1,744)	1,552 (1,317–1,780)
HPV39 copies/mL	1,794 (1,617–1,862)	1,880 (1,775–2,136)	1,531 (1,419–1,685)
HPV51 copies/mL	1,522 (1,315–1,613)	1,343 (1,262–1,551)	1,229 (1,155–1,353)
HPV52 copies/mL	814 (776–951)	951 (850–1,082)	833 (744–934)
HPV56 copies/mL	1,090 (937–1,185)	1,085 (1,018–1,363)	836 (737–911)
HPV58 copies/mL	2,369 (2,231–6,631)	2,611 (2,043–2,809)	2,990 (2,656–7,818)
HPV59 copies/mL	1,000 (942–1,152)	994 (933–1,246)	772 (722–899)
HPV66 copies/mL	862 (823–916)	1,014 (911–1,101)	701 (646–767)
HPV68 copies/mL	2,392 (2,227–2,646)	2,383 (2,231 –2,746)	2,079 (1,995–2,125)

*LOD values for BD Onclarity™ HPV Cervical Brush Diluent were confirmed to generate a positive result above the clinical cutoff at least 95% of the time with vaginal self-collection devices.

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Cross-Reactivity

A panel of bacteria, yeast and cultured viruses along with cloned plasmid DNA containing high-risk and low-risk HPV target sequences was used to evaluate the analytical specificity of the BD Onclarity™ HPV Assay on the BD Viper™ LT System. Each potential cross-reactant was tested individually in BD SurePath™ Preservative Fluid and PreservCyt® Solution containing a HPV-negative cell line (C33A). The microorganisms are described in Tables 25 and 26. The BD Onclarity™ HPV Assay did not cross-react with any of the microorganisms tested.

Table 25: Microorganisms Tested for Analytical Specificity

Bacteria*	Bacteria*	Viruses**
Actinomyces israelii	*Mycoplasma genitalium*	Adenovirus, type 5
Atopobium vaginae	*Neisseria gonorrhoeae*	EBV-1, B95-8 Strain
Bacteroides fragilis	*Peptostreptococcus anaerobius*	HCMV, AD169 Strain
Bacteroides ureolyticus ureolyticus	*Prevotella bivia*	HIV-1
Bifidobacterium adolescentis	*Prevotella disiens*	HSV1
Bifidobacterium breve	*Proteus mirabilis*	HSV2
Bifidobacterium longum ssp. *longum*	*Proteus vulgaris*	**High risk HPV*** **
Chlamydia trachomatis	*Providencia stuartii*	HPV16
Clostridium perfringens	*Pseudomonas aeruginosa*	HPV18
Corynebacterium genitalium	*Staphylococcus aureus*	HPV31
Enterobacter cloacae ssp. *cloacae*	*Staphylococcus epidermidis*	HPV33
Enterococcus faecalis	*Streptococcus agalactiae*	HPV35
Enterococcus faecium	*Streptococcus pyogenes*	HPV39
Escherichia coli	*Ureaplasma urealyticum*	HPV45
Fusobacterium nucleatum ssp. *nucleatum*	**Yeast/Protozoa****	HPV51
Gardnerella vaginalis	*Candida albicans*	HPV52
Klebsiella pneumoniae ssp. *ozaenae*	*Trichomonas vaginalis*	HPV56
Lactobacillus acidophilus		HPV58
Mycobacterium smegmatis		HPV59
		HPV66
		HPV68

*Bacteria tested at approximately 1.0 x 10^7 CFU/mL except for the following: *Chlamydia trachomatis* (1.0 x 10^7 EB/mL), *Mycobacterium smegmatis* (2.5 x 10^6 CFU/mL), and *Ureaplasma urealyticum* (8.0 x 10^6 CFU/mL).

**Viruses tested at 1.0 x 10^6 VP/mL.

***High risk HPV plasmid DNA tested at 1.0 x 10^6 copies/mL.

**** Yeast (*Candida albicans*) tested at approximately 1.0 x 10^7 CFU/mL; Protozoa (*Trichomonas vaginalis*) tested at 1.4 x 10^6 CFU/mL.

Table 26: Low Risk HPV Plasmids Tested for Analytical Specificity

HPV6	HPV69
HPV11	HPV70
HPV26	HPV73
HPV30	HPV82
HPV34	HPV97
HPV53	HPVc85
HPV67	

* Low-risk HPV plasmid DNA tested at 1.0 x 10^6 copies/mL.

Interfering Substances

The potential for interference in the BD Onclarity™ HPV Assay on the BD Viper™ LT System was determined with exogenous and endogenous substances that may be present in clinical cervical specimens. Contrived HPV negative specimens and HPV positive specimens (co-spiked with SiHa, HeLa and MS751 cells at 3 x LOD) were tested in the presence or absence of each potential interfering substance. Substances used in these studies are described in Table 27. The concentrations represent the highest level of substance that did not result in any interference in the BD Onclarity™ HPV Assay.

Table 27: Potential Interfering Substances

	BD SurePath™ Media	PreservCyt® Media	BD Onclarity™ HPV Cervical Brush Diluent	Vaginal Self-Collection Devices
Potential Interfering Substance	**Concentration tested**	**Concentration tested**	**Concentration tested**	**Concentration tested**
KY® Vaginal Lubricant	6% (w/v)	10% (w/v)	10% (w/v)	8% (w/v)
VCF® Vaginal Contraceptive Film	10% (w/v)	10% (w/v)	3% (w/v)	3% (w/v)
VCF® Vaginal Contraceptive Foam	10% (w/v)	10% (w/v)	10% (w/v)	10% (w/v)
Nonoxynol-9 Contraceptive Gel, 4%	10% (w/v)	10% (w/v)	1% (w/v)	1% (w/v)
Monistat® 3*	2.0% (w/v)	1.4% (w/v)	1.8% (w/v)	1.8% (w/v)
Clotrimazole 7	10% (w/v)	10% (w/v)	10% (w/v)	10% (w/v)
Tioconazole Ointment, 6.5%	2% (w/v)	2% (w/v)	1% (w/v)	1% (w/v)
Clindamycin Vaginal Cream	8% (w/v)	10% (w/v)	9% (w/v)	9% (w/v)
Summer's Eve® Douche	10% (v/v)	10% (v/v)	10% (v/v)	10% (v/v)
Zovirax® (Acyclovir) Cream	7% (w/v)	10% (w/v)	10% (w/v)	10% (w/v)
Vandazole™ Gel (Metronidazole Vaginal Gel, 0.75%)	10% (w/v)	10% (w/v)	10% (w/v)	10% (w/v)
Summer's Eve Deodorant	3% (w/v)	2% (w/v)	2% (w/v)	1% (w/v)
Replens™ Moisturizer	10% (w/v)	10% (w/v)	3% (w/v)	3% (w/v)
Bovine Mucin	8% (v/v)	8% (v/v)	8% (v/v)	8% (w/v)
Progesterone	20 ng/mL	20 ng/mL	20 ng/mL	20 ng/mL
Estradiol	1.2 ng/mL	1.2 ng/mL	1.2 ng/mL	1.2 ng/mL
Whole Blood	4% (v/v)	5% (v/v)	1% (v/v)	1% (v/v)
Leukocytes	$1x10^6$ cells/mL	$1x10^6$ cells/mL	$1x10^6$ cells/mL	$1x10^6$ cells/mL
Semen	10% (v/v)	10% (v/v)	10% (v/v)	10% (v/v)
Acetic Acid Wash**		5% (v/v)		
Blood +Acetic Acid Wash		5% Blood (v/v), 2.5% Acetic Acid Wash (v/v)		

*Concentrations higher than those listed resulted in liquid level failures during extraction on the BD Viper™ LT System.
**Acetic Acid Wash consists of 1 part Glacial Acetic Acid: 9 parts CytoLyt® solution.

Competitive Target Interference

The potential for the inhibition of HPV detection due to one target present at a high level and another target present at low levels during a mixed infection was evaluated in the BD Onclarity™ HPV Assay. SiHa, HeLa and MS751 cells were tested individually or collectively at 3 x LOD in the presence or absence of competitive HPV target(s) at 1.0 x 10^6 copies/mL in BD SurePath™ Preservative Fluid, PreservCyt® Solution and BD Onclarity™ HPV Cervical Brush Diluent containing a HPV negative cell line (C33A) (Table 28).

Table 28: Competitive Target Interference

HPV Assay Tube Type	Individual HPV Cellular Targets at 3 x	HPV Plasmids at 1 x 10^6 copies/mL	HPV Cellular Target Detection in the Presence or Absence of Competing Genotypes (HPV Plasmids)
G1 Genotypes with G1 co-amplified targets	SiHa (HPV16)	HPV18 + HPV45	Yes
	HeLa (HPV18)	HPV16 + HPV45	Yes
	HPV45 (MS751)	HPV16 + HPV18	Yes
G1 Genotypes with G2 co-amplified targets	SiHa + HeLa + MS751	HPV31 + HPV33 + HPV56 + HPV58 + HPV59 + HPV66	Yes
G1 Genotypes with G3 co-amplified targets	SiHa + HeLa + MS751	HPV35 + HPV39 + HPV51 + HPV52 + HPV68	Yes

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Reproducibility

The reproducibility of the BD Onclarity™ HPV Assay was evaluated on the BD Viper™ LT instrument using a four-member panel consisting of negative, high negative, low positive, and moderate positive specimens. The positive panel members were composed of SiHa, HeLa and MS751 cells spiked collectively into pools of HPV negative clinical BD SurePath™ specimens and BD Onclarity™ HPV Cervical Brush Diluent containing a HPV negative cell line (C33A). The panel was tested across an equal distribution of three lots of reagents and three instruments over 12 days. The data are summarized in Table 29.

Table 29: Summary of Reproducibility Data for the BD Onclarity™ HPV Assay on the BD Viper™ LT System

							Within Run		Between Run		Total	
Sample Type	**Cell Line (Genotype)**	**Panel Level (Cells/mL)**	**Expected Result**	**% Correct (Correct/Total)**	**95% Confidence Interval**	**Mean Ct**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
BD SurePath™	SiHa (HPV16)	Negative (0)	>95% Negative	100% (216/216)	[98.3%, 100%]	NA	NA	NA	NA	NA	NA	NA
		High Negative (8.8)	>94% Negative	95.8% (205/214)	[92.2%, 97.8%]	38.42	0.40	1.04	0.23	0.59	0.54	1.41
		Low Positive (220)	>94% Positive	95.8% (207/216)	[92.3%, 97.8%]	36.59	0.65	1.78	0.00	0.00	0.67	1.84
		Moderate Positive (660)	>98% Positive	99.1% (213/215)	[96.7%, 99.7%]	34.98	0.55	1.56	0.17	0.50	0.59	1.68
	HeLa (HPV18)	Negative (0)	>95% Negative	100% (216/216)	[98.3%, 100%]	NA	NA	NA	NA	NA	NA	NA
		High Negative (102)	>94% Negative	98.6% (213/216)	[96.0%, 99.5%]	35.89	0.75	2.09	0.24	0.68	0.85	2.37
		Low Positive (914)	>94% Positive	99.5% (215/216)	[97.4%, 99.9%]	32.70	0.30	0.92	0.16	0.50	0.37	1.14
		Moderate Positive (2,742)	>98% Positive	100% (216/216)	[98.3%, 100%]	30.68	0.22	0.72	0.13	0.43	0.30	0.98
	MS-751 (HPV45)	Negative (0)	>95% Negative	100% (216/216)	[98.3%, 100%]	NA	NA	NA	NA	NA	NA	NA
		High Negative (395)	>94% Negative	100% (216/216)	[98.3%, 100%]	35.77	0.52	1.45	0.00	0.00	0.55	1.53
		Low Positive (3,793)	>94% Positive	100% (216/216)	[98.3%, 100%]	32.71	0.26	0.80	0.20	0.60	0.36	1.10
		Moderate Positive (11,378)	>98% Positive	99.5% (215/216)	[97.4%, 99.9%]	31.33	0.35	1.10	0.18	0.57	0.41	1.31
BD Onclarity™ HPV Cervical Brush Diluent	SiHa (HPV16)	Negative (0)	>95% Negative	100% (100/100)	[96.3%, 100%]	NA	NA	NA	NA	NA	NA	NA
		High Negative (1.2)	>94% Negative	63.0% (63/100)	[53.2%, 71.8%]	38.00	0.41	1.07	0.00	0.00	0.44	1.14
		Low Positive (12.6)	>94% Positive	94.0% (94/100)	[87.5%, 97.2%]	36.77	0.77	2.09	0.00	0.00	0.77	2.09
		Moderate Positive (37.8)	>98% Positive	100% (100/100)	[98.4%, 100%]	35.45	0.58	1.64	0.00	0.00	0.58	1.64
	HeLa (HPV18)	Negative (0)	>95% Negative	100% (100/100)	[96.3%, 100%]	NA	NA	NA	NA	NA	NA	NA
		High Negative (16)	>94% Negative	44.0% (44/100)	[34.7%, 53.8%]	34.20	0.47	1.38	0.05	0.14	0.48	1.39
		Low Positive (51)	>94% Positive	100% (100/100)	[96.3%, 100%]	33.08	0.38	1.15	0.00	0.00	0.38	1.15
		Moderate Positive (153)	>98% Positive	99.0% (99/100)	[94.6%, 99.8%]	31.65	0.40	1.27	0.00	0.00	0.40	1.27
	MS-751 (HPV45)	Negative (0)	>95% Negative	100% (100/100)	[96.3%, 100%]	NA	NA	NA	NA	NA	NA	NA
		High Negative (70)	>94% Negative	80.0% (80/100)	[71.1%, 86.7%]	34.66	0.00	0.00	0.07	0.21	0.58	1.68
		Low Positive (305)	>94% Positive	99.0% (99/100)	[94.6%, 99.8%]	33.14	0.34	1.03	0.00	0.00	0.34	1.03
		Moderate Positive (915)	>98% Positive	100% (100/100)	[96.3%, 100%]	31.49	0.33	1.04	0.00	0.00	0.33	1.04

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							Within Run		Between Run		Total	
Sample Type	Cell Line (Genotype)	Panel Level (Cells/mL)	Expected Result	% Correct (Correct/Total)	95% Confidence Interval	Mean Ct	SD	%CV	SD	%CV	SD	%CV
Self-Collection	SiHa (HPV16)	Negative (0)	>95% Negative	100% (432/432)	[99.1%, 100%]	N/A	N/A	N/A	N/A	N/A	N/A	N/A
		High Negative (1.2)	>94% Negative	71.5% (309/432)	[67.1%, 75.6%]	38.05	0.59	1.54	0.05	0.12	0.59	1.56
		Low Positive (9.7)	>94% Positive	96.3% (416/432)	[94.1%, 97.7%]	36.41	0.71	1.95	0.04	0.10	0.71	1.96
		Moderate Positive (29.1)	>98% Positive	100% (432/432)	[99.1%, 100%]	34.67	0.50	1.44	0.00	0.00	0.51	1.48
	HeLa (HPV18)	Negative (0)	>95% Negative	100% (432/432)	[99.1%, 100%]	N/A	N/A	N/A	N/A	N/A	N/A	N/A
		High Negative (16)	>94% Negative	85.6% (370/432)	[82.0%, 88.6%]	34.72	0.50	1.43	0.00	0.00	0.51	1.47
		Low Positive (51)	>94% Positive	100% (431/432)	[98.7%, 100%]	33.10	0.31	0.93	0.01	0.03	0.31	0.95
		Moderate Positive (153)	>98% Positive	100% (432/432)	[99.1%, 100%]	31.66	0.39	1.23	0.00	0.00	0.39	1.24
	MS-751 (HPV45)	Negative (0)	>95% Negative	100% (432/432)	[99.1%, 100%]	N/A	N/A	N/A	N/A	N/A	N/A	N/A
		High Negative (70)	>94% Negative	79% (342/432)	[75.1%, 82.7%]	34.65	0.54	1.56	0.02	0.07	0.55	1.59
		Low Positive (305)	>94% Positive	100% (432/432)	[99.1%, 100%]	32.59	0.31	0.95	0.07	0.22	0.36	1.10
		Moderate Positive (915)	>98% Positive	100% (432/432)	[99.1%, 100%]	30.93	0.22	0.71	0.03	0.11	0.26	0.85

Cross-Contamination

A study was performed to evaluate the risk of producing a false positive result in either the same run (within run cross-contamination) or in a subsequent run (between run carryover contamination) on the BD Viper™ LT System. Multiple runs were performed across three instruments comprising a total of 225 HPV negative replicates. Each run consisted of specimens containing a HPV negative cell line (C33A) with and without CaSki cells spiked at a target level higher than 95% of HPV16 target levels observed clinically. HPV positive and negative specimens were arranged in an alternating checkerboard pattern. The overall contamination rate with both BD SurePath™ Preservative Fluid and vaginal self-collection devices was 0.44%, and the overall contamination rate with PreservCyt® Solution and BD Onclarity™ HPV Cervical Brush Diluent was 0.00%.

Neat (In-vial) Specimen Stability

Analytical studies were performed to support the storage claims for the stability of neat cervical specimens. BD SurePath™ Preservative Fluid and PreservCyt® Solution specimens containing HPV clinical positives targeting 3 x LOD or clinical matrix spiked with HPV-positive cell lines at 3 x LOD were stored at 2–8 °C, 30 °C, and -20 °C for multiple time points. BD Onclarity™ HPV Cervical Brush Diluent specimens containing an HPV negative cell line (C33A) were spiked with HPV-positive cell lines at 3 x LOD and stored at 2–8 °C, 30 °C, and -20 °C for multiple time points. At each time point, the specimens were removed from storage and tested with the BD Onclarity™ HPV Assay for the BD Viper™ LT System or the BD COR™ System (BD Catalog Number 443982). Refer to the "Specimen Collection, Transport, and Storage" section for stability durations.

Dry Vaginal Self-Collection Device Specimen Stability

Analytical studies were performed to support the storage claims for the stability of dry vaginal self-collection device specimens. Specimens were prepared with HPV16 an HPV18 negative vaginal matrix spiked with SiHa and HeLa cells at 3 x LOD and stored at 2–8 °C, 30 °C, and -20 °C for multiple time points. Specimens stored at 30°C were exposed to 40 °C for 6 days prior to transfer to 30 °C to simulate elevated shipping temperatures. At each time point, the specimens were removed from storage and tested with the BD Onclarity™ HPV Assay on the BD Viper™ LT System. Refer to the "Specimen Collection, Transport, and Storage" section for the stability durations.

Diluted Specimen Stability

Analytical studies were performed to support the storage claims for the stability of diluted cervical specimens. BD SurePath™ Preservative Fluid and PreservCyt® Solution Specimens were prepared as described in the "Neat (In-vial) Specimen Stability" section and then diluted in a BD HPV LBC Diluent Tube. Vaginal self-collection devices were prepared as described in the "Dry Vaginal Self-Collection Device Specimen Stability" section and then diluted in a BD HPV Self Collection Diluent Tube. Diluted specimens were then stored at 2–8 °C, 30 °C, and -20 °C for multiple time points. At each time point, the specimens were removed from storage and tested with the BD Onclarity™ HPV Assay on the BD Viper™ LT System or BD COR™ System (BD Catalog Number 443982). Refer to the "Specimen Collection, Transport, and Storage" section for stability durations.

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Post Pre-warm Specimen Stability

Analytical studies were performed to support the storage claims for the stability of post pre-warm cervical, and vaginal self-collection specimens. Diluted specimens were prepared as described in the "Diluted Specimen Stability" section (for BD SurePath™ Preservative Fluid, PreservCyt® Solution, and vaginal self-collection device specimens) or in the "Neat (In-vial) Specimen Stability" section (BD Onclarity™ HPV Cervical Brush Diluent specimens) and then pre-warmed with the BD Viper™ LT Pre-warm Heater. The pre-warmed specimens were stored at 2–8 °C, 30 °C, and -20 °C for multiple time points. At each time point, the specimens were removed from storage and tested with the BD Onclarity™ HPV Assay on the BD Viper™ LT System or BD COR™ System (BD Catalog Number 443982). Refer to the "Specimen Collection, Transport, and Storage" section for stability durations.

Punctured Post Pre-warm Specimen Stability (for BD Onclarity™ LBC Diluent Tubes and BD Onclarity™ Self-Collection Diluent Tubes Only)

Analytical studies were performed to support the storage claims for the stability of punctured post pre-warm cervical and vaginal self-collection specimens. Diluted specimens were prepared as described in the "Post Pre-warm Specimen Stability" section then punctured with a pipette tip. The punctured post pre-warm specimens were stored at 2–8 °C and 30 °C for multiple time points. At each time point, the specimens were removed from storage and tested with the BD Onclarity™ HPV Assay for the BD Viper™ LT System or BD COR™ System (BD Catalog Number 443982). Refer to the "Specimen Collection, Transport, and Storage" section for stability durations.

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EU Only: Users shall report any serious incident related to the device to the Manufacturer and National Competent Authority.

Outside EU: Contact your local BD representative for any incident or inquiry related to this device.

Refer to the Eudamed website: https://ec.europa.eu/tools/eudamed for Summary of Safety and Performance.

Change History

Revision	Date	Change Summary
16	2023-01	Updated GHS information. Added option to recap BD Onclarity™ HPV LBC Diluent Tubes and BD Onclarity™ HPV Self Collection Diluent Tubes after manually adding a sample in order to prevent potential bubbles around cap. Added instruction to replace punctured caps prior to storage or prior to repeating instrument runs for BD Onclarity™ HPV Cervical Brush Diluent Tubes. In Table 27, corrected the concentration of Zovirax tested in PreservCyt® Media from 7% to 10%. Added additional symbol definitions. Added EU Importer address. Made typographical and formatting updates.
17	2023-05	Removed 441992 and 442841 from header. Updated GHS information. Replaced catalog number 441996 with 440330. Added BD catalog number 440331, BD Pierceable Caps Pink, in Materials Required but not Provided. Clarified note regarding option to recap BD Onclarity™ LBC Diluent Tubes and BD Onclarity™ Self Collection Tubes. Updated Symbols Glossary. Made typographical and formatting updates.
18	2023-07	Added CE notified body number 2797 for IVDR 2017/746. Removed discontinued catalog number 443748 from Reagents and Materials Provided. Added Eudamed website link. Updated EC REP address. Added CH REP symbol with address. Added Switzerland importer address with symbol. Added Australian and New Zealand sponsor address.

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SYMBOLS GLOSSARY

Please refer to product labeling for applicable symbols.

Symbol	Meaning
	Manufacturer
	Authorized representative in the European Community
	Authorised representative in Switzerland
	Date of manufacture
	Use-by date
	Batch code
	Catalogue number
	Serial number
	Sterile
	Sterilized using aseptic processing techniques
	Sterilized using ethylene oxide
	Sterilized using irradiation
	Sterilized using steam or dry heat
	Do not resterilize
	Non-sterile
	Do not use if package is damaged and consult *instructions for use*
	Sterile fluid path
	Sterile fluid path (ethylene oxide)
	Sterile fluid path (irradiation)
	Fragile, handle with care
	Keep away from sunlight
	Keep dry
	Lower limit of temperature
	Upper limit of temperature
	Temperature limit
	Humidity limitation
	Biological risks
	Do not re-use
	Consult *instructions for use* or consult electronic *instructions for use*
	Caution
	Contains or presence of natural rubber latex
	In vitro diagnostic medical device
	Negative control
	Positive control
	Contains sufficient for <*n*> tests
	For IVD performance evaluation only
	Non-pyrogenic
	Patient number
	This way up
	Do not stack

Symbol	Meaning
	Single sterile barrier system
	Contains or presence of phthalate: combination of bis(2-ethylhexyl) phthalate (DEHP) and benzyl butyl phthalate (BBP)
	Collect separately Indicates separate collection for waste of electrical and electronic equipment required.
	CE marking; Signifies European technical conformity
	Device for near-patient testing
	Device for self-testing
	This only applies to US: "Caution: Federal Law restricts this device to sale by or on the order of a licensed practitioner."
	Country of manufacture "CC" shall be replaced by either the two letter or the three letter country code.
	Collection time
	Cut
	Peel here
	Collection date
	Keep away from light
	Hydrogen gas is generated
	Perforation
	Start panel sequence number
	End panel sequence number
	Internal sequence number
	<Box #> / <Total Boxes>
	Medical device
	Contains hazardous substances
	Ukrainian conformity mark
	Meets FCC requirements per 21 CFR Part 15
	UL product certification for US and Canada
	Unique device identifier
	Importer
	Place patient label in framed area only
	Magnetic resonance (MR) safe
	Magnetic resonance (MR) conditional
	Magnetic resonance (MR) unsafe
	For use with
	This Product Contains Dry Natural Rubber
	For Export Only
	Instruments

Note: Text layout in symbols is determined by label design.

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