WHO Prequalification of In Vitro Diagnostics
PUBLIC REPORT

Product: Abbott RealTime High Risk HPV
WHO reference number: PQDx 0455-180-00

Abbott RealTime High Risk HPV with product codes **02N09-092 and 02N09-080**, manufactured by **Abbott GmbH (formerly called Abbott GmbH & Co.KG)**, **CE Mark regulatory version**, was accepted for the WHO list of prequalified in vitro diagnostics and was listed on 10 October 2019.

Summary of the WHO prequalification assessment for the Abbott RealTime High Risk HPV

	Date	Outcome
Prequalification listing	10 October 2019	listed
Dossier review	N/A	N/A
Site inspection(s) of the quality management system	23 September 2019	MR
Product performance evaluation	N/A	N/A

MR: Meet Requirements
N/A: Not Applicable

Report amendments and/or product changes

This public report has since been amended. Amendments may have arisen because of changes to the prequalified product for which WHO has been notified and has undertaken a review. Amendments to the report are summarised in the following table, and details of each amendment are provided below.

Version	Summary of the amendment	Date of report amendment
2.0	Updated the labelling to refer to its new legal entity Name, Abbott GmbH.	20 October 2021
3.0	Administrative changes to the labels to meet the requirements of the new IVDR 2017/746/EU.	27 October 2025

Intended use:

According to the claim of intended use from Abbott GmbH & Co.KG "*The Abbott RealTime High Risk HPV is a qualitative in vitro test for the detection of DNA from 14 high risk human papillomavirus (HPV) genotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68 in clinical specimens. The assay specifically identifies HPV genotypes 16 and 18 while concurrently detecting the other high risk genotypes at clinically relevant infection levels.*
The Abbott RealTime High Risk HPV is indicated:
a) To screen patients with ASC-US (atypical squamous cells of undetermined significance) cervical cytology results to determine the need for referral to colposcopy. The results of this test are not intended to prevent women from proceeding to colposcopy.
b) To be used with cervical cytology to adjunctively screen to assess the presence or absence of high risk HPV genotypes.
c) To be used as a first-line primary screening test to identify women at increased risk for the development of cervical cancer or the presence of high-grade disease.
d) To assess the presence or absence of HPV genotypes 16 and 18 to identify women at increased risk for the development of cervical cancer or the presence of high-grade disease with or without cervical cytology.
The results from the Abbott RealTime High Risk HPV, together with the physician's assessment of cytology history, other risk factors, and professional guidelines, may be used to guide patient management.

INTENDED USER
The intended users for the Abbott RealTime High Risk HPV assay are laboratory and healthcare professionals."

Assay description:
According to the claim of assay description from Abbott GmbH & Co.KG "*The Abbott RealTime HR HPV assay uses the Abbott m2000sp instrument, the Abbott m24sp instrument, or the manual sample preparation method for processing samples and the Abbott m2000rt instrument for amplification and detection. A primer mix consisting of 3 forward primers and 2 reverse primers targeting a conserved L1 region is used to amplify HPV targets. Signal for 14 HR HPV genotypes (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) is generated with the use of fluorescent labeled probes. Internal Control (IC) amplicons are generated with a primer set targeting an endogenous human beta globin sequence and are detected with the IC specific probe. The Abbott RealTime HR HPV assay detects the endogenous human beta globin sequence as sample validity control for cell adequacy, sample extraction and amplification efficiency. Probes for HPV 16, HPV 18, non-HPV 16/18 genotypes (Other HR HPV) and IC are labeled with different fluorophores allowing their signals to be distinguishable in a single reaction.*

Test kit contents:

Component	**96 tests (product code 2N09-092)**
Abbott RealTime High Risk HPV Amplification Reagent Kit	
Amplification reagent pack	4 packs x 24 tests/ pack
DNA polymerase in a Buffered solution with stabilizers	0.070 mL x 1 bottle
HPV oligonucleotide reagent	0.502 mL x 1 bottle
Activation reagent	0.778 mL x 1 bottle

Items required but not provided:

Component	**Description**
Abbott RealTime High Risk HPV Control Kit	**Product code 2N09-80**
Abbott RealTi*me* High Risk HPV Negative Control	0.5 mL x 12 vials
Abbott RealTime High Risk HPV Positive Control	0.5 mL x 12 vials
Materials for manual sample preparation (Assay Protocol I)	
Abbott *m*Sample Preparation System$_{DNA}$ for RealTime High Risk HPV	3N92
Abbott Optical Adhesive Covers	04J71-75
Abbott Adhesive Cover Applicator	9K32-01
Abbott 96-Well Optical Reaction Plate	04J71-70
Abbott Splash-Free Support Base	09K31-01
Calibrated precision pipettes	10 µL to 1 000 µL
Aerosol barrier pipette tips	20 µL to 1 000µL
Single-use DNase-free tube or container	General laboratory material
Materials for Abbott m24sp (Assay Protocol II)	

Abbott m24sp instrument containing the scripts necessary to run the Abbott RealTime HR HPV assay (m24sp Database v 3.0 or higher)	50-148470 or higher
Abbott *m*Sample Preparation System$_{DNA}$	06K12-24
Calibrated precision pipettes	10 µL to 1 000 µL
Aerosol barrier pipette tips	20 µL to 1 000µL
Sample input tubes	General laboratory equipment
1000 µL disposable tips	04J71-10
200 µL disposable tips	04J71-17
Vortex mixer	General laboratory equipment
USP grade 190 to 200 proof ethanol (95 to 100% ethanol: **Do not use ethanol that contains denaturants.**	General laboratory material
Abbott Optical Adhesive Covers	04J71-75
Abbott Adhesive Cover Applicator	9K32-01
Abbott 96-Deep-Well Plate	04J71-30
Abbott Splash-Free Support Base	09K31-01
13 mm Sample Racks	04J72-82
1.5 mL Reaction Vessels and Output Tubes (1.5 mL screw top microfuge tubes and caps	4J71-50
Abbott 96-Well Optical Reaction Plate	04J71-70
Abbott Splash-Free Support Base	09K31-01
Calibrated precision pipettes	10 µL to 1 000 µL
Aerosol barrier pipette tips	20 µL to 1 000µL
Single-use DNase-free tube or container	
Materials for Abbott m2000sp (Assay Protocol III)	
Abbott m2000sp instrument with Software Version 3.0 or higher	50-148393 or higher
Abbott *m*Sample Preparation System$_{DNA}$	06K12-24
5 mL Reaction Vessels	4J71-20
Calibrated precision pipettes	10 µL to 1 000 µL
Aerosol barrier pipette tips	20 µL to 1 000µL
Sample input tubes	General laboratory material
1000 µL disposable tips	04J71-10
200 µL disposable tips	04J71-17
Vortex mixer	

USP grade 190 to 200 proof ethanol (95 to 100% ethanol: **Do not use ethanol that contains denaturants.**	General laboratory material
Abbott Optical Adhesive Covers	04J71-75
Abbott Adhesive Cover Applicator	9K32-01
Abbott Splash-Free Support Base	09K31-01
Master Mix Tube	04J71-80
200 mL Reagent Vessels	4J71-60
Abbott 96-Deep-Well Plate	04J71-30
Abbott 96-Well Optical Reaction Plate	04J71-70
Materials for Abbott m2000rt	
Abbott m2000rt instrument with Software Version 3.0 or higher	50-148392 or higher
Abbott m2000rt Optical Calibration Kit	4J71-93

Other materials

- Biological safety cabinet approved for working with infectious materials
- Sealable plastic bags
- DNase-free water†
- Microcentrifuge Tubes†
- Cotton Tip Applicators (Puritan or equivalent) †

NOTE: † These three items are used in the procedure for Monitoring the Laboratory for the presence of Contamination. Refer to the QUALITY CONTROL PROCEDURES section of the package insert.

Storage:

- Abbott RealTime High Risk HPV Amplification Reagent Kit (product code 02N09-092) must be stored at -25 to -15°C when not in use.
- Abbott RealTime High Risk HPV Control Kit (product code 2N09-80) must be stored at -10°C or colder.
- Reagents and controls must be shipped on dry ice.

Shelf-life upon manufacture:

18 months.

Warnings/limitations:

Refer to the latest version of the instructions for use attached to this public report.

Prioritisation for prequalification
Based on the established prioritisation criteria, Abbott RealTime High Risk HPV was given priority for the WHO prequalification assessment.

Product dossier assessment

In accordance with the WHO procedure for abridged prequalification assessment, Abbott GmbH & Co.KG was not required to submit a product dossier for the Abbott RealTime High Risk HPV as per the *"Instructions for compilation of a product dossier"* (PQDx_018 version 3). Notwithstanding, certain aspects of the product dossier previously submitted for stringent regulatory review were reviewed by an assessor during the site inspection.

Manufacturing site inspection

In accordance with the WHO procedure, an inspection of a manufacturing site(s) may be waived by WHO in writing under defined circumstances such as; a recent inspection with appropriate scope by a WHO-recognized national regulatory authority or by a Medical Devices Single Audit Program (MDSAP) participating Auditing Organisation as per the "*Information for manufacturers on prequalification inspection procedures for the sites of manufacture of diagnostics*" (PQDx_014 version 4)..

The Abbott GmbH & Co. KG site located at Max-Planck-Ring 2, Wiesbaden, 65205, Germany was inspected by the Medical Device Single Audit Program (MDSAP), audit report (dated 4-7 June 2018). The site was found compliant and meet all requirements of ISO 13485: 2016.

An inspection of the site was waived in light of the MDSAP inspection.

Based on the MDSAP report, the quality management system for Abbott RealTime High Risk HPV meets WHO prequalification requirements.

Product performance evaluation

In accordance with the WHO procedure for prequalification assessment at the date of prioritisation and given the fact that the Abbott RealTime High Risk HPV assay is used as the benchmark assay in the WHO evaluation protocol for HPV core antigen assays, it was

decided that WHO will not conduct the performance evaluation of this assay as part of the prequalification assessment process.

Consequently, the laboratory evaluation of Abbott RealTime High Risk HPV was waived.

Labelling

1. **Labels**
2. **Instructions for use**

1. Labels

1.1 Abbott RealTime High Risk HPV Amplification Reagent Kit Label

List Number: 02N09-092

Top Edge

Abbott RealTi*me* High Risk HPV

Amplification Reagent Kit

(en) In Vitro Test.

Contents:

AMPLIFICATION REAGENT PACK Abbott Real*Time* High Risk HPV Amplification Reagent Pack (4 packs, 24 tests/pack)

Each Reagent Pack contains:

- 1 Bottle (0.070 mL) AmpliTaq Gold Enzyme (5.4 to 5.9 Units/µL) in a buffered solution with stabilizers.
- 1 Bottle (0.502 mL) HPV Oligonucleotide Reagent. <0.1% synthetic oligonucleotides and <1% dNTPs, in a buffered solution with a reference dye. Preservatives: sodium azide and 0.16% ProClin 950.
- 1 Bottle (0.778 mL) Activation Reagent. 38mM magnesium chloride in a buffered solution. Preservatives: sodium azide and 0.15% ProClin 950.

ProClin and AmpliTaq Gold are property of their respective owners.

(pt) Teste *in vitro*.

Conteúdo:

AMPLIFICATION REAGENT PACK Abbott Real*Time* High Risk HPV Amplification Reagent Pack (4 embalagens, 24 testes/embalagem)

Cada embalagem de reagentes contém:

- 1 Frasco (0,070 ml) de enzima AmpliTaq Gold (5,4 a 5,9 unidades/µl) numa solução tamponada com estabilizadores.
- 1 Frasco (0,502 ml) de reagente de oligonucleótidos do HPV. <0,1% de oligonucleótidos sintéticos e <1% de dNTPs, numa solução tamponada com um corante de referência. Conservantes: azida sódica e 0,16% de ProClin 950.
- 1 Frasco (0,778 ml) de reagente de ativação. 38mM de cloreto de magnésio numa solução tamponada. Conservantes: azida sódica e 0,15% de ProClin 950.

ProClin e AmpliTaq Gold são propriedade dos respetivos titulares.

CE 0123

REF 02N09-092

IVD

-15°C

-25°C

51-602801/R4

GTIN

LOT

REF

(de) In-vitro-Test.

Inhalt:

AMPLIFICATION REAGENT PACK Abbott Real*Time* High Risk HPV Amplification Reagent Pack (4 Packungen, 24 Tests/Packung)

Jede Reagenzpackung enthält:

- 1 Fläschchen (0,070 ml) AmpliTaq Gold Enzym (5,4 bis 5,9 Einheiten/µl) in einer gepufferten Lösung mit Stabilisatoren.
- 1 Fläschchen (0,502 ml) HPV Oligonukleotidreagenz. < 0,1 % synthetische Oligonukleotide und < 1 % dNTPs, in einer gepufferten Lösung mit einem Referenzfarbstoff. Konservierungsmittel: Natriumazid und 0,16 % ProClin 950.
- 1 Fläschchen (0,778 ml) Aktivierungsreagenz. 38 mmol/l Magnesiumchlorid in einer gepufferten Lösung. Konservierungsmittel: Natriumazid und 0,15 % ProClin 950.

ProClin und AmpliTaq Gold sind Eigentum der Rechteinhaber.

(fr) Test *in vitro*.

Composition :

AMPLIFICATION REAGENT PACK Abbott Real*Time* High Risk HPV Amplification Reagent Pack (4 coffrets, 24 tests/coffret)

Chaque coffret-réactifs contient :

- 1 flacon (0,070 ml) d'enzyme AmpliTaq Gold (5,4 à 5,9 unités/µl) dans une solution tampon avec des stabilisants.
- 1 flacon (0,502 ml) de réactif d'oligonucléotides HPV. < 0,1 % d'oligonucléotides synthétiques et < 1 % de dNTPs, dans une solution tampon avec un fluorochrome de référence. Conservateurs : azide de sodium et ProClin 950 à 0,16 %.
- 1 flacon (0,778 ml) de réactif d'activation. 38 mmol/l de chlorure de magnésium dans une solution tampon. Conservateurs : azide de sodium et ProClin 950 à 0,15 %.

ProClin et AmpliTaq Gold sont la propriété de leurs détenteurs respectifs.

(es) Análisis *in vitro*.

Contenido:

AMPLIFICATION REAGENT PACK Abbott Real*Time* High Risk HPV Amplification Reagent Pack (4 envases, 24 pruebas/envase)

Cada equipo de reactivos contiene:

- 1 frasco (0,070 ml) AmpliTaq Gold Enzyme (5,4 unidades/µl a 5,9 unidades/µl) en solución tamponada con estabilizantes.
- 1 frasco (0,502 ml) HPV Oligonucleotide Reagent (reactivo de oligonucleótidos del VPH). <0,1% de oligonucleótidos sintéticos y <1% de dNTPs, en solución tamponada con fluoróforo de referencia. Conservantes: azida sódica y ProClin 950 al 0,16%.
- 1 frasco (0,778 ml) Activation Reagent (reactivo de activación). 38 mmol/l de cloruro de magnesio en solución tamponada. Conservantes: azida sódica y ProClin 950 al 0,15%.

ProClin y AmpliTaq Gold están a nombre de su propietario.

(it) Test *in vitro*.

Contenuto:

AMPLIFICATION REAGENT PACK Abbott Real*Time* High Risk HPV Amplification Reagent Pack (4 confezioni, 24 test/confezione)

Ciascuna confezione di reagente contiene:

- 1 flacone (0,070 ml) di AmpliTaq Gold Enzyme (enzima AmpliTaq Gold, da 5,4 a 5,9 unità/µl) in una soluzione tamponata con stabilizzanti.
- 1 flacone (0,502 ml) di HPV Oligonucleotide Reagent (reagente di oligonucleotidi dell'HPV). Oligonucleotidi sintetici < 0,1% e dNTP < 1% in una soluzione tamponata con un colorante di riferimento. Conservanti: sodio azoturo e ProClin 950 allo 0,16%.
- 1 flacone (0,778 ml) di Activation Reagent (reagente di attivazione). 38 mM di cloruro di magnesio in una soluzione tamponata. Conservanti: sodio azoturo e ProClin 950 allo 0,15%.

ProClin e AmpliTaq Gold sono proprietà dei relativi titolari.

Abbott RealTi*me* High Risk HPV

Amplification Reagent Kit

H317, EUH032
P261, P272, P280, P302+P352,
P333+P313, P362+P364, P501

Product of Germany / Produkt aus Deutschland / Produit en Allemagne / Producto de Alemania / Prodotto della Germania / Produto da Alemanha

Abbott GmbH
Max-Planck-Ring 2
65205 Wiesbaden, Germany

www.abbottmolecular.com

Abbott

1.2 Abbott RealTime High Risk HPV Control Kit Label

List Number: 2N09-80

Abbott RealTi*me* High Risk HPV

Control Kit

(en) For *In Vitro* Diagnostic Use. The Abbott RealTi*me* High Risk HPV Controls are used to establish run validity of the Abbott RealTi*me* High Risk HPV assay when used for the detection of high risk human papillomavirus (HPV) DNA in clinical specimens.

Contents:

1. **CONTROL –** Abbott RealTi*me* High Risk HPV Negative Control (12 vials, 0.5 mL per vial). <0.01% noninfectious DNA with Beta Globin sequence in a buffered solution with carrier DNA. Preservatives: sodium azide and 0.15% ProClin 950.
2. **CONTROL +** Abbott RealTi*me* High Risk HPV Positive Control (12 vials, 0.5 mL per vial). <0.01% noninfectious DNA with HPV and Beta Globin sequences in a buffered solution with carrier DNA. Preservatives: sodium azide and 0.15% ProClin 950.

ProClin is property of its owner.

(pt) Para utilização em diagnóstico *in vitro*. Os Abbott RealTi*me* High Risk HPV Controls destinam-se a estabelecer a validade do ensaio Abbott RealTi*me* High Risk HPV quando utilizado para a deteção de ADN do papilomavírus humano de alto risco (HPV) em amostras clínicas.

Conteúdo:

1. **CONTROL –** Abbott RealTi*me* High Risk HPV Negative Control (12 frascos, 0,5 ml por frasco). <0,01% de ADN não infecioso com sequência de betaglobulina numa solução tamponada com ADN transportador. Conservantes: azida sódica e ProClin 950 a 0,15%.
2. **CONTROL +** Abbott RealTi*me* High Risk HPV Positive Control (12 frascos, 0,5 ml por frasco). <0,01% de ADN não infecioso com sequências de HPV e de betaglobulina numa solução tamponada com ADN transportador. Conservantes: azida sódica e ProClin 950 a 0,15%.

ProClin é propriedade do respetivo titular.

REF 2N09-80

IVD

CE 0123

-10°C

51-602329/R4

GTIN

LOT

REF

Abbott RealTi*me* High Risk HPV

Control Kit

H317, EUH032
P261, P272, P280, P302+P352,
P333+P313, P362+P364, P501

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Max-Planck-Ring 2
65205 Wiesbaden, Germany

www.abbottmolecular.com

Abbott

(de) In-vitro-Diagnostikum. Die Abbott RealTi*me* High Risk HPV Kontrollen dienen zur Sicherstellung der Testgültigkeit des Abbott RealTi*me* High Risk HPV Assays beim Nachweis von DNA des humanen Hochrisiko-Papillomavirus (HPV) in Patientenproben.

Inhalt:

1. **CONTROL –** Abbott RealTi*me* High Risk HPV Negative Control (12 Fläschchen, je 0,5 ml). < 0,01 % nicht infektiöse DNA mit Beta-Globin-Sequenz in einer gepufferten Lösung mit Träger-DNA. Konservierungsmittel: Natriumazid und 0,15 % ProClin 950.
2. **CONTROL +** Abbott RealTi*me* High Risk HPV Positive Control (12 Fläschchen, je 0,5 ml). < 0,01 % nicht infektiöse DNA mit HPV und Beta-Globin-Sequenzen in einer gepufferten Lösung mit Träger-DNA. Konservierungsmittel: Natriumazid und 0,15 % ProClin 950.

ProClin ist Eigentum des Rechteinhabers.

(fr) Pour diagnostic *in vitro*. Les Abbott RealTi*me* High Risk HPV Controls sont utilisés pour établir la validité du test Abbott RealTi*me* High Risk HPV lors de la détection de l'ADN du virus du papillome humain (VPH) à haut risque dans les échantillons cliniques.

Composition :

1. **CONTROL –** Abbott RealTi*me* High Risk HPV Negative Control (12 flacons de 0,5 ml chacun). < 0,01 % d'ADN non infectieux avec une séquence bêta-globine dans une solution tampon contenant de l'ADN entraîneur. Conservateurs : azide de sodium et ProClin 950 à 0,15 %.
2. **CONTROL +** Abbott RealTi*me* High Risk HPV Positive Control (12 flacons de 0,5 ml chacun). < 0,01 % d'ADN non infectieux avec du VPH et des séquences bêta-globine dans une solution tampon contenant de l'ADN entraîneur. Conservateurs : azide de sodium et ProClin 950 à 0,15 %.

ProClin est la propriété de son détenteur.

(es) Para uso en diagnóstico *in vitro*. Abbott RealTi*me* High Risk HPV Controls se utilizan para establecer la validez del procesamiento de los ensayos Abbott RealTi*me* High Risk HPV en la detección del DNA del papilomavirus humano (VPH) de alto riesgo, en muestras clínicas.

Contenido:

1. **CONTROL –** Control negativo Abbott RealTi*me* High Risk HPV (12 frascos, 0,5 ml por frasco). <0,01% de DNA no infeccioso con secuencia de beta-globina en solución tamponada con DNA portador. Conservantes: azida sódica y ProClin 950 al 0,15%.
2. **CONTROL +** Control positivo Abbott RealTi*me* High Risk HPV (12 frascos, 0,5 ml por frasco). <0,01% de DNA no infeccioso con secuencias de beta-globina y VPH en solución tamponada con DNA portador. Conservantes: azida sódica y ProClin 950 al 0,15%.

ProClin está a nombre de su propietario.

(it) Per uso diagnostico *in vitro*. Gli Abbott RealTi*me* High Risk HPV Controls vengono utilizzati per stabilire la validità della seduta analitica del dosaggio Abbott RealTi*me* High Risk HPV nella rilevazione del DNA di papillomavirus umano (HPV) ad alto rischio in campioni clinici.

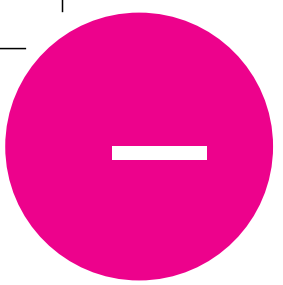
Contenuto:

1. **CONTROL –** Abbott RealTi*me* High Risk HPV Negative Control (12 flaconi, 0,5 ml per flacone). DNA non infettivo < 0,01% con sequenza di gene umano della Beta-globina in una soluzione tamponata con DNA carrier. Conservanti: sodio azoturo e ProClin 950 allo 0,15%.
2. **CONTROL +** Abbott RealTi*me* High Risk HPV Positive Control (12 flaconi, 0,5 ml per flacone). DNA non infettivo < 0,01% con sequenza di HPV e gene umano della Beta-globina in una soluzione tamponata con DNA carrier. Conservanti: sodio azoturo e ProClin 950 allo 0,15%.

ProClin è proprietà dei suoi titolari.

1.2.1 Abbott RealTime High Risk HPV Negative Control Vial Label

List Number: 2N09Z



REF 2N09Z

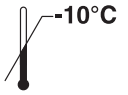
IVD

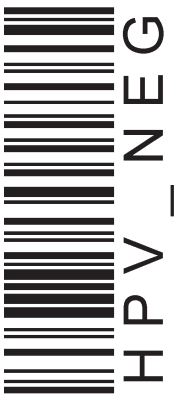
0.5mL

Abbott RealTi*me*

High Risk HPV

CONTROL –





LOT

51-602332/R3

Abbott GmbH
Max-Planck-Ring 2
65205 Wiesbaden, Germany

1.2.2 Abbott RealTi*m*e High Risk HPV Positive Control Vial Label

List Number: 2N09A

REF 2N09A

IVD

0.5mL

Abbott RealTi*me*

High Risk HPV

CONTROL +

-10°C

HPV_POS

LOT

51-602333/R3

Abbott GmbH
Max-Planck-Ring 2
65205 Wiesbaden, Germany

Abbott

2 Instructions for use[1]

[1] 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

Abbott RealTi*me* High Risk HPV

en

Abbott RealTi*me* High Risk HPV

REF 02N09-092

G59196R06

B2NZ90

Read Highlighted Changes: Revised August 2022

Key to Symbols Used	
REF	Reference Number
LOT	Lot Number
IVD	In Vitro Diagnostic Medical Device
	Use By
CONTROL –	Negative Control
CONTROL +	Positive Control
AMPLIFICATION REAGENT PACK	Amplification Reagent Pack
	Upper Limit of Temperature
	Temperature Limit
	WARNING
Σ	Contains sufficient for <n> tests
	Consult instructions for use
	Manufacturer

See **REAGENTS** section for a full explanation of symbols used in reagent component naming.

NOTICE TO USER

If a serious incident occurs in relation to this device, the incident should be reported to the manufacturer and to the appropriate competent authority of the member state in which the user and/or the patient is established. To report to the manufacturer, see the contact information provided in the Customer service section or Technical assistance section of these instructions.

Customer Service

International: Call your Abbott Representative

This package insert must be read carefully prior to use. Package insert instructions must be followed accordingly. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

For laboratory professional use only.

NAME

Abbott RealTi*me* High Risk HPV

INTENDED USE

The Abbott RealTi*me* High Risk HPV is a qualitative in vitro test for the detection of DNA from 14 high risk human papillomavirus (HPV) genotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68 in clinical specimens. The assay specifically identifies HPV genotypes 16 and 18 while concurrently detecting the other high risk genotypes at clinically relevant infection levels.

The Abbott RealTi*me* High Risk HPV is indicated:

a) To screen patients with ASC-US (atypical squamous cells of undetermined significance) cervical cytology results to determine the need for referral to colposcopy. The results of this test are not intended to prevent women from proceeding to colposcopy.

b) To be used with cervical cytology to adjunctively screen to assess the presence or absence of high risk HPV genotypes.

c) To be used as a first-line primary screening test to identify women at increased risk for the development of cervical cancer or the presence of high-grade disease.

d) To assess the presence or absence of HPV genotypes 16 and 18 to identify women at increased risk for the development of cervical cancer or the presence of high-grade disease with or without cervical cytology.

The results from the Abbott RealTi*me* High Risk HPV, together with the physician's assessment of cytology history, other risk factors, and professional guidelines, may be used to guide patient management.

INTENDED USER

The intended users for the Abbott RealTi*me* High Risk HPV assay are laboratory and healthcare professionals.

SUMMARY AND EXPLANATION OF THE TEST

HPV is a small, non-enveloped, double-stranded DNA virus (approximately 8,000 base pairs) that replicates in the nucleus of squamous epithelial cells and induces hyperproliferative lesions.[1] HPV infections are among the most common sexually transmitted infections.[2] Most HPV infections have a benign clinical consequence and are cleared spontaneously.[3] However, persistent HPV infection may result in progression to cervical cancer.[4-7] More than one hundred different HPV genotypes have been identified, among which over forty infect mucosal and genital epithelia.[8] Genital HPV genotypes are generally classified into high risk (HR) and low risk (LR) groups based on their carcinogenic potential. HR HPV genotypes are associated with invasive cervical cancer or its immediate precursor (high-grade squamous intraepithelial lesion, cervical intraepithelial neoplasia or carcinoma *in situ*), whereas LR HPV genotypes induce benign lesion and are not associated with cervical cancer.[9-12] Approximately 70% of invasive cervical cancer cases worldwide are caused by HPV 16 and HPV 18.[13] Infection by HPV 16 or HPV 18 is associated with higher risk of disease progression compared to other HR HPV genotypes.[14] Compared with cervical screening methods identifying cytological abnormalities, molecular tests that specifically detect the presence of HR HPV DNA in cervical cells can potentially increase sensitivity and cost-effectiveness of cervical cancer screening programs.[15-20] Furthermore, HPV DNA tests can be effectively used in triaging patients with equivocal cytology, in post-therapeutic follow-up and in monitoring vaccine efficacy.[21-23]

The Abbott RealTi*me* HR HPV assay is a qualitative in vitro test that amplifies and detects HR HPV DNA in cervical cells collected in liquid media. The detection of 14 HR HPV genotypes (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) is achieved through a primer mix targeting a conserved region of HPV genomes and single-stranded DNA probes. The assay can differentiate between HPV 16, HPV 18 and non-HPV 16/18 genotypes (Other HR HPV).

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The Abbott RealTi*m*e HR HPV assay uses the Abbott *m*2000*sp* instrument or the manual sample preparation method for processing samples and the Abbott *m*2000*rt* instrument for amplification and detection. A primer mix consisting of 3 forward primers and 2 reverse primers targeting a conserved L1 region is used to amplify HPV targets. Signal for 14 HR HPV genotypes (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) is generated with the use of fluorescent labeled probes. Internal Control (IC) amplicons are generated with a primer set targeting an endogenous human beta globin sequence and are detected with the IC specific probe. The Abbott RealTi*m*e HR HPV assay detects the endogenous human beta globin sequence as sample validity control for cell adequacy, sample extraction and amplification efficiency. Probes for HPV 16, HPV 18, non-HPV 16/18 genotypes (Other HR HPV) and IC are labeled with different fluorophores allowing their signals to be distinguishable in a single reaction.

Sample Preparation

The purpose of sample preparation is to extract, concentrate, and purify the target DNA molecules for amplification.

The Abbott *m*Sample Preparation System$_{DNA}$ uses magnetic particle technology to capture nucleic acids and washes the particles to remove unbound sample components. The bound nucleic acids are eluted and are then ready for amplification.

NOTE: One Abbott *m*Sample Preparation System$_{DNA}$ kit is sufficient to complete 4 x 48 (192) HPV sample preparations.

The Abbott *m*2000*sp* automated instrument can be used to prepare samples for the Abbott RealTi*m*e HR HPV assay. The Abbott *m*2000*sp* provides automated sample eluate transfer and reaction assembly in the Abbott 96-Well Optical Reaction Plate.

Alternatively, samples can be prepared manually following the instructions in **Manual Sample Preparation Using the Abbott *m*Sample Preparation System$_{DNA}$ for RealTi*m*e High Risk HPV** (List No. 3N92). The manual sample preparation method requires manual transfer of the eluted samples to a Abbott 96-Well Optical Reaction Plate and manual reaction assembly before amplification.

Reagent Preparation and Reaction Plate Assembly

The Abbott *m*2000*sp* combines the Abbott RealTi*m*e HR HPV Amplification Reagent components (HPV Oligonucleotide Reagent, DNA Polymerase, and Activation Reagent). The Abbott *m*2000*sp* dispenses the resulting master mix to the Abbott 96-Well Optical Reaction Plate along with aliquots of the nucleic acid samples prepared by the Abbott *m*2000*sp*. The plate is ready, after manual application of the optical seal, for transfer to the Abbott *m*2000*rt*.

Amplification

During the amplification reaction on the automated Abbott *m*2000*rt*, the target DNA is amplified by DNA Polymerase in the presence of dNTPs and magnesium. The DNA Polymerase is a thermophilic enzyme that has been modified in its active site by a molecule that renders it inactive. When the enzyme is heated prior to the initiation of PCR, the inhibitory molecule is cleaved from the enzyme allowing it to regain its activity. In this way, the enzyme is only active at temperatures where specific DNA-DNA interactions occur. This greatly reduces non-specific PCR artifacts such as primer dimers. In the Abbott RealTi*m*e HR HPV assay, the DNA Polymerase is first activated at 92˚C for 10 minutes. During each subsequent round of thermal cycling, a high temperature is used to melt double-stranded DNA strands apart, followed by a low temperature where primers anneal to their respective targets and are extended to generate double-stranded DNA products. Exponential amplification of the products is achieved through repeated cycling between high and low temperatures, resulting in a billion-fold or greater amplification of target sequences. Amplification of both targets (HPV and IC) takes place simultaneously in the same reaction.

The target sequence for the Abbott RealTi*m*e HR HPV assay is in the conserved L1 region of the HPV genomes. A primer mix consisting of 3 forward primers and 2 reverse primers is designed to hybridize to the consensus regions among HPV genotypes of approximately 150 bases. The IC target sequence is a region of 136 bases in the endogenous human beta globin gene.

Detection

During the last 38 cycles of amplification, in an additional reading step, the temperature is lowered further to allow fluorescence detection of amplification products as the HPV and IC probes anneal to their targets (referred to as real-time fluorescence detection). The HPV and IC probes are single-stranded DNA oligonucleotides modified with a fluorescent moiety covalently linked to one end of the probe and a quenching moiety to the other end. In the absence of HPV or IC target sequences, the probes adopt a series of random conformations, some of which bring the quencher close enough to the excited fluorophore to absorb its energy before it can be fluorescently emitted. When a probe binds to its complementary sequence in the target, the fluorophore and the quencher are held apart, allowing fluorescent emission and detection by the Abbott *m*2000*rt*.

Signal for 14 HR HPV genotypes (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68) is generated with the use of fluorescent labeled probes. IC signal is generated with an IC specific probe. Probes for HPV 16, HPV 18, Other HR HPV and IC are labeled with different fluorophores allowing their distinct signals to be simultaneously detected and distinguishable in a single reaction. Signals for HPV 16, HPV 18, Other HR HPV, and IC are detected in VIC, NED, FAM, and Cy5 channels, respectively.

Assay Results

The Abbott RealTi*m*e HR HPV assay is a qualitative assay. Results are reported as detected or not detected. In addition, each detected signal (HPV 16, HPV 18, or Other HR HPV) is also listed in the reported result. Refer to the **RESULTS** section of the package insert for further details.

REAGENTS

The Abbott RealTi*m*e HR HPV assay consists of 2 kits:

- Abbott RealTi*m*e High Risk HPV Amplification Reagent Kit (List No. 02N09-092)
- Abbott RealTi*m*e High Risk HPV Control Kit (List No. 2N09-80)

Abbott RealTi*m*e High Risk HPV Amplification Reagent Kit (List No. 02N09-092)

AMPLIFICATION REAGENT PACK (4 packs, 24 tests/pack)

Each Reagent Pack contains:

- 1 Bottle (0.070 mL) DNA Polymerase (5.4 to 5.9 Units/µL) in a buffered solution with stabilizers.
- 1 Bottle (0.502 mL) HPV Oligonucleotide Reagent. < 0.1% synthetic oligonucleotides and < 1% dNTPs, in a buffered solution with a reference dye. Preservatives: sodium azide and 0.16% ProClin 950.
- 1 Bottle (0.778 mL) Activation Reagent. 38 mM magnesium chloride in a buffered solution. Preservatives: sodium azide and 0.15% ProClin 950.

  NOTE: The Abbott RealTi*m*e Reagent components (enzyme, oligonucleotide reagent, activation reagent) are intended for single-use only and unused reagents should be discarded.

Abbott RealTi*m*e High Risk HPV Control Kit (List No. 2N09-80)

Abbott RealTi*m*e High Risk HPV Negative Control

- **CONTROL −** (12 vials, 0.5 mL per vial)

  < 0.01% noninfectious DNA with Beta Globin sequence in a buffered solution with carrier DNA. Preservatives: sodium azide and 0.15% ProClin 950.

Abbott RealTi*m*e High Risk HPV Positive Control

- **CONTROL +** (12 vials, 0.5 mL per vial)

  < 0.01% noninfectious DNA with HPV and Beta Globin sequences in a buffered solution with carrier DNA. Preservatives: sodium azide and 0.15% ProClin 950.

  NOTE: The Negative and Positive Controls are intended for single-use only and unused reagents should be discarded.

WARNINGS AND PRECAUTIONS

- **IVD**
- For In Vitro Diagnostic Use
- In Vitro Test

Safety Precautions

Refer to the Abbott *m*2000*sp* (List No. 9K20) and Abbott *m*2000*rt* (List No. 9K25) Operations Manuals, Hazards Section, and **Manual Sample Preparation Using the Abbott *m*Sample Preparation System$_{DNA}$ for RealTi*m*e HR HPV** (List No. 3N92) for instructions on safety precautions.

- There are no human sourced materials in any of the Abbott RealTi*m*e HR HPV Amplification Reagents or Abbott RealTi*m*e HR HPV Controls.
- This product requires the handling of human specimens. It is recommended that all human sourced materials be considered potentially infectious and handled with appropriate biosafety practices. Wear disposable gloves while handling specimens and wash hands thoroughly afterwards. Use of protective eyewear is recommended.

The controls, HPV Oligonucleotide Reagent and Activation Reagent contain a methylisothiazolone (which is a component of ProClin).

The following warnings apply to the HPV Oligonucleotide Reagent, Activation Reagent and the controls.

Warning
Hazard-determining components of labeling:
2-Methyl-2H-isothiazol-3-one
Sodium Azide

H317	May cause an allergic skin reaction.
EUH032	Contact with acids liberates very toxic gas.
P261	Avoid breathing mist / vapours / spray.
P280	Wear protective gloves / protective clothing / eye protection / face protection.
P272	Contaminated work clothing should not be allowed out of the workplace.
P302+P352	IF ON SKIN: Wash with plenty of water.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
P501	Dispose of contents / container in accordance with local regulations.

Specimen Collection and Handling Precautions

- Cervical specimens collected in PreservCyt Solution (Hologic, Inc.) can be used with the Abbott RealTi*m*e HR HPV assay. The Rovers Cervex Brush® was used for specimen collection in validation studies. Users must follow the manufacturer's instructions for collecting and handling cervical specimens in PreservCyt Solution.
- Cervical specimens collected in SurePath Preservative Fluid (BD Life Sciences) can be used with the Abbott RealTi*m*e HR HPV assay. Either the sample from the original SurePath collection vial or the remaining cell pellet sample obtained after slide preparation with BD PrepStain Slide Processor (formerly TriPath Imaging PrepStain Slide Processor) can be used for testing. The Rovers Cervex Brush® was used for specimen collection in validation studies. Users must follow the manufacturer's instructions for collecting, handling and processing cervical specimens in SurePath Preservative Fluid.
- Cervical specimens collected with the Abbott Cervi-Collect Specimen Collection Kit can be used with the Abbott RealTi*m*e HR HPV assay. Users must follow the instructions in the Abbott Cervi-Collect Specimen Collection Kit Package Insert (List No. 4N73) for collecting and handling cervical specimens.

Laboratory Precautions

- During preparation of samples, compliance with good laboratory practices is essential to minimize the risk of cross-contamination between samples as well as the inadvertent introduction of nucleases into samples during and after the extraction procedure. Proper aseptic technique should always be used when working with DNA.
- Work area and instrument platforms must be considered potential sources of contamination.

  Change gloves after having contact with potential contaminants (such as DNases, specimens, eluates, and/or amplified product) before handling unopened reagents, negative control, positive control, or specimens. Refer to the Abbott *m*2000*sp,* and Abbott *m*2000*rt* Operations Manuals for instrument cleaning procedures.
- Wear appropriate personal protective equipment at all times.
- Use powder-free gloves.
- To reduce the risk of nucleic acid contamination due to aerosols formed during pipetting, pipettes with aerosol barrier tips must be used for all pipetting. The length of the tip should be sufficient to prevent contamination of the pipette barrel. While pipetting, care should be taken to avoid touching the pipette barrel to the inside of the sample tube or container. The use of extended aerosol barrier pipette tips is recommended.
- Change aerosol barrier pipette tips between ALL manual liquid transfers.
- Clean and disinfect spills of specimens and reagents as stated in the following manuals: the Abbott *m*2000*sp* Operations Manual, the Abbott *m*2000*rt* Operations Manual, and **Manual Sample Preparation Using the Abbott *m*Sample Preparation System$_{DNA}$ for RealTi*m*e High Risk HPV.**

Contamination Precautions

- Amplification reactions such as PCR are sensitive to accidental introduction of product from previous amplification reactions. Incorrect results could occur if either the clinical specimen or the reagents used become contaminated by accidental introduction of even a few molecules of amplification product. Measures to reduce the risk of contamination in the laboratory include physically separating the activities involved in performing PCR in compliance with good laboratory practices.
- The use of 3 dedicated areas within the laboratory is recommended for performing the Abbott RealTi*m*e HR HPV assay with the manual sample preparation using the Abbott *m*Sample Preparation System$_{DNA}$ and the Abbott *m*2000*rt*:
  - The Reagent Preparation Area is dedicated to combining the Abbott RealTi*m*e HR HPV Amplification Reagent components to create the amplification master mix and transferring aliquots of the master mix to the Abbott 96-Well Optical Reaction Plate. Laboratory coats, pipettes, and pipette tips used in the Reagent Preparation Area must remain in this area and not be moved to either the Sample Preparation Area or the Amplification Area. Do not bring target or amplification product into the Reagent Preparation Area.
  - The Sample Preparation Area is dedicated to processing samples (specimens, Abbott RealTi*m*e HR HPV Controls) and to adding processed samples and controls to the Abbott 96-Well Optical Reaction Plate. All reagents used in the Sample Preparation Area should remain in this dedicated area at all times. Laboratory coats, pipettes, pipette tips, and vortex mixers used in the Sample Preparation Area must remain in this area and not be moved to either the Reagent Preparation Area or the Amplification Area. Do not bring amplification product into the Sample Preparation Area.
  - The Amplification Area is dedicated to the amplification and detection of amplified product. Laboratory coats and equipment used in the Amplification Area must remain in this area and not be moved to either the Reagent Preparation Area or the Sample Preparation Area.
- Only 2 dedicated areas, Sample Preparation Area and Amplification Area, are recommended when the Abbott *m*2000*sp* and Abbott *m*2000*rt* are used.
- If the Abbott *m*2000*sp* run is aborted, dispose of all commodities and reagents according to the Abbott *m*2000*sp* Operations Manual. If the manual sample preparation procedure is incorrectly performed or is interrupted at any point so that the timing of the steps exceeds the recommended timing per the manual instructions, dispose of all commodities and reagents (if not being reused) according to the instructions in **Manual Sample Preparation Using the Abbott *m*Sample Preparation System$_{DNA}$ for RealTi*m*e High Risk HPV**.
- If the Abbott *m*2000*sp* master mix addition protocol is aborted after amplification reagents are added to the Abbott 96-Well Optical Reaction Plate, seal the Abbott 96-Well Optical Reaction Plate in a sealable plastic bag and dispose of according to the Abbott *m*2000*sp* Operations Manual, Hazards section, along with the gloves used to handle the plate. Do not import the test order onto the Abbott *m*2000*rt*. If manual preparation of the PCR reaction mix is aborted after amplification reagents are added to the Abbott 96-Well Optical Reaction Plate, seal the Abbott 96-Well Optical Reaction Plate in a sealable plastic bag and dispose of according to laboratory guidelines, along with the gloves used to handle the plate.
- For all completed, interrupted or aborted Abbott *m*2000*rt* runs, dispose of the Abbott 96-Well Optical Reaction Plate in a sealable plastic bag according to the Abbott *m*2000*rt* Operations Manual along with the gloves used to handle the plate.
- **Autoclaving the sealed reaction plate will not degrade the amplified product and may contribute to the release of the amplified product by opening the sealed plate. The laboratory area can become contaminated with amplified product if the waste materials are not carefully handled and contained.**
- Decontaminate and dispose of all specimens, reagents, and other potentially contaminated materials in accordance with local, state, and federal regulations.[24,25] All materials should be handled in a manner that minimizes the chance of potential contamination of the work area.

Contamination from External Deoxy-Uracil (dU)-Containing Amplified Product

- HPV amplification assays containing dU may cause contamination and inaccurate results in the Abbott RealTi*m*e HR HPV. When negative controls are persistently reactive or where contamination with dU-containing HPV amplified product is likely to have occurred, it is recommended that the laboratory uses a contamination control procedure. This procedure (List No. 2N09-66) is available through your Abbott representative.

REAGENT STORAGE AND HANDLING INSTRUCTIONS

NOTE: Care must be taken to separate the Abbott RealTi*m*e High Risk HPV Amplification Reagent Kit that is in use from direct contact with specimens and Abbott RealTi*m*e High Risk HPV Control Kit reagents.

Abbott RealTi*m*e High Risk HPV Amplification Reagent Kit (List No. 02N09-092)

- The Abbott RealTi*m*e High Risk HPV Amplification Reagent Pack must be stored at -25 to -15°C when not in use.
- Reagents are shipped on dry ice.

Abbott RealTi*m*e High Risk HPV Control Kit (List No. 2N09-80)

- The Abbott RealTi*m*e High Risk HPV Negative and Positive Controls must be stored at -10°C or colder.
- Reagents are shipped on dry ice.

INSTRUMENTS/METHODS

The Abbott RealTi*m*e HR HPV assay is performed with manual sample preparation method or on the Abbott *m*2000*sp* for sample extraction and the Abbott *m*2000*rt* for amplification and detection. Refer to **Manual Sample Preparation Using the Abbott *m*Sample Preparation System$_{DNA}$ for RealTi*m*e High Risk HPV,** the Abbott *m*2000*sp,* or the Abbott *m*2000*rt* Operations Manuals for detailed operating procedures.

The Abbott RealTi*m*e HR HPV application files must be installed on the Abbott *m*2000*rt* and/or Abbott *m*2000*sp* from the Abbott RealTi*m*e High Risk HPV Abbott *m*2000 System ROW Combined Application CD-ROM (List No. 4N05) prior to performing the assay. For detailed information on application file installation, refer to the Abbott *m*2000*sp* and the Abbott *m*2000*rt* Operations Manuals, Operating Instructions section.

SPECIMEN COLLECTION AND HANDLING INSTRUCTIONS

Specimen Collection

Specimens collected in PreservCyt Solution (Hologic, Inc.) or SurePath Preservative Fluid (TriPath Imaging, Inc.), or collected with Abbott Cervi-Collect Specimen Collection Kit (Abbott List No. 4N73) can be used with the Abbott RealTi*m*e HR HPV assay. For SurePath specimens, either the sample from the original SurePath collection vial or the remaining cell pellet sample obtained after cytological processing can be used. Users must follow the respective manufacturer's instructions for collecting cervical specimens in PreservCyt Solution or SurePath Preservative Fluid. Users must follow the instructions in the Abbott Cervi-Collect Specimen Collection Kit Package Insert (List No. 4N73) for collecting cervical specimens with the Abbott Cervi-Collect Specimen Collection Kit.

Specimen Transport and Storage

Cervical specimens collected in PreservCyt Solution can be transported at 15 to 30°C or 2 to 8°C and may be stored for up to 4 months at 15 to 30°C or up to 6 months at 2 to 8°C and −10°C or colder following collection.

Cervical specimens collected in SurePath Preservative Fluid (the sample from the original SurePath collection vial or the remaining cell pellet sample obtained after cytological processing) can be transported at 15 to 30°C or 2 to 8°C and may be stored for up to 2 months at 15 to 30°C or up to 6 months at 2 to 8°C and −10°C or colder following collection.

Cervical specimens collected with the Abbott Cervi-Collect Specimen Collection Kit can be transported at 2 to 30°C and may be stored for up to 14 days at 2 to 30°C or up to 90 days at −10°C or colder. Thaw specimens at 2 to 30°C. Specimens should not undergo more than 4 freeze/thaw cycles.

Time and temperature conditions for storage must be adhered to during transport. For domestic and international shipments, specimens should be packaged and labeled in compliance with applicable state, federal, and international regulations covering the transport of clinical, diagnostic, or biological specimens.

ASSAY PROCEDURE

This Abbott RealTi*m*e HR HPV package insert contains 2 assay protocols:

- Samples prepared for amplification using the manual sample preparation method following **ASSAY PROTOCOL A.**
- Samples prepared for amplification using the Abbott *m*2000*sp* instrument following **ASSAY PROTOCOL B.**

Materials Provided

- Abbott RealTi*m*e High Risk HPV Amplification Reagent Kit (List No. 02N09-092)

Materials Required But Not Provided

- Abbott RealTi*m*e High Risk HPV Control Kit (List No. 2N09-80)
- Abbott RealTi*m*e High Risk HPV *m*2000 System ROW Combined Application CD-ROM (List No. 4N05)
- **Materials for Manual Sample Preparation (Assay Protocol A)**

  Sample Preparation Area
  - Refer to the Materials and Equipment Required Section of **Manual Sample Preparation Using the Abbott *m*Sample Preparation System$_{DNA}$ for RealTi*m*e High Risk HPV** (List No. 3N92).
  - Abbott Optical Adhesive Covers (List No. 04J71-75)
  - Abbott Adhesive Cover Applicator (List No. 9K32-01)

  Reagent Preparation Area
  - Abbott 96-Well Optical Reaction Plate (List No. 04J71-70)
  - Abbott Splash-Free Support Base (List No. 09K31-01)
  - Calibrated precision pipettes capable of delivering 10 µL to 1000 µL
  - 20 µL to 1000 µL aerosol barrier pipette tips for precision pipettes
  - Single-use DNase-free tube or container
- **Materials for Abbott *m*2000*sp* (Assay Protocol B)**

  Sample Preparation Area
  - Abbott *m*2000*sp* instrument with Software Version 3.0 or higher
  - Abbott *m*Sample Preparation System$_{DNA}$ (List No. 06K12-24)

  NOTE: One kit is sufficient to complete 192 HPV sample preparations.
  - 5 mL Reaction Vessels (List No. 4J71-20)
  - Calibrated precision pipettes capable of delivering 10 µL to 1000 µL
  - 20 µL to 1000 µL aerosol barrier pipette tips for precision pipettes
  - Sample input tubes (refer to **ASSAY PROTOCOL B** section for details)
  - 1000 µL disposable tips (List No. 04J71-10)
  - 200 µL disposable tips (List No. 04J71-17)
  - Vortex mixer
  - USP grade 190 to 200 proof ethanol (95 to 100% ethanol). **Do not use ethanol that contains denaturants.**
  - Abbott Optical Adhesive Covers (List No. 04J71-75)
  - Abbott Adhesive Cover Applicator (List No. 9K32-01)
  - Abbott Splash-Free Support Base (List No. 09K31-01)
  - Master Mix Tube (List No. 04J71-80)
  - 200 mL Reagent Vessels (List No. 4J71-60)
  - Abbott 96-Deep-Well Plate (List No. 04J71-30)
  - Abbott 96-Well Optical Reaction Plate (List No. 04J71-70)
  - 13 mm Sample Racks
- **Materials for Abbott *m*2000*rt***
  - Abbott *m*2000*rt* instrument with Software Version 3.0 or higher
  - Abbott *m*2000*rt* Optical Calibration Kit (List No. 4J71-93)

Other Materials

- Biological safety cabinet approved for working with infectious materials
- Sealable plastic bags
- DNase-free water†
- Microcentrifuge Tubes†
- Cotton Tip Applicators (Puritan or equivalent)†

† **NOTE: These 3 items are used in the procedure for Monitoring the Laboratory for the Presence of Contamination. Refer to the QUALITY CONTROL PROCEDURES section of the package insert.**

Procedural Precautions

- Read the instructions in the package insert carefully before processing samples.
- Do not use kits or reagents beyond expiration date.
- Control kit lots and amplification reagent kit lots can be used interchangeably. Components contained within a kit are intended to be used together. For example, do not use the negative control from control kit lot X with the positive control from control kit lot Y.
- Amplification Reagent components (enzyme, oligonucleotide reagent and activation reagent) and Controls are for single-use only and should be discarded after use. Use new reagent vessels and new reaction vessels, for every new Abbott RealTi*m*e HR HPV assay run. At the end of each run, discard all these remaining reagents as stated in the Abbott *m*2000*sp* Operations Manual and **Manual Sample Preparation Using the Abbott *m*Sample Preparation System$_{DNA}$ for RealTi*m*e High Risk HPV**.
- The Abbott RealTi*m*e HR HPV Controls must be processed with the specimens to be tested. The use of the Abbott RealTi*m*e HR HPV Controls is integral to the performance of the Abbott RealTi*m*e HR HPV assay. Refer to the **QUALITY CONTROL PROCEDURES** section in the package insert for details.
- Use only USP grade 190 to 200 proof ethanol (95 to 100% ethanol) to prepare the *m*Wash 2$_{DNA}$ sample preparation reagent. **Do not use ethanol that contains denaturants.**
- Use aerosol barrier pipette tips or disposable pipettes only one time when pipetting. To prevent contamination to the pipette barrel while pipetting, care should be taken to avoid touching the pipette barrel to inside of the sample tube or container. The use of extended aerosol barrier pipette tips is recommended.
- Replace any empty or partially used 200 µL and 1000 µL disposable tips on the Abbott *m*2000*sp* with full trays before every run. Refer to the Abbott *m*2000*sp* Operations Manual, Operating Instructions section.
- Monitoring procedures for the presence of amplification product can be found in the **QUALITY CONTROL PROCEDURES** section in the package insert.
- To reduce the risk of nucleic acid contamination, clean and disinfect spills of specimens, reagents and controls by using a detergent solution followed by a tuberculocidal disinfectant such as 1.0% (v/v) sodium hypochlorite or other suitable disinfectant.

ASSAY PROTOCOL A: MANUAL SAMPLE PREPARATION METHOD AND ABBOTT *m*2000*rt* INSTRUMENT

Refer to the **WARNINGS AND PRECAUTIONS** section of the package insert before preparing samples.

1. Vortex each specimen for 15 to 20 seconds. Ensure that the contents of each vial are at the bottom after vortexing by tapping the vials on the bench to bring liquid to the bottom of the vial. Immediately transfer 400 µL of each specimen to a reaction tube.

   NOTE: Ensure that the volume of the cell pellet SurePath samples after cytological processing is approximately 2.8 mL. The sample volume must be adjusted to 6 mL using SurePath Preservative Fluid prior to vortexing and transferring.
2. Thaw control reagents at 15 to 30˚C or at 2 to 8˚C; see **QUALITY CONTROL PROCEDURES** section of the package insert.
   - Vortex each assay control for 15 to 20 seconds before use. Ensure that the contents of each vial are at the bottom after vortexing by tapping the vials on the bench to bring liquid to the bottom of the vial.
   - Once thawed, assay controls can be stored at 2 to 8˚C for up to 24 hours before use.
3. Thaw amplification reagents at 15 to 30˚C or at 2 to 8˚C and store at 2 to 8˚C until required for the amplification master mix procedure.
   - Once thawed, the amplification reagents can be stored at 2 to 8˚C for up to 24 hours if not used immediately.

   NOTE: A maximum of 96 reactions can be performed per run.

   <u>For up to 24 reactions use:</u> 1 tube of positive control, 1 tube of negative control, 1 amplification reagent pack, and 1 set of Abbott *m*Sample Preparation System$_{DNA}$ reagents.

   <u>For 25 to 48 reactions use:</u> 1 tube of positive control, 1 tube of negative control, 2 amplification reagent packs, and 1 set of Abbott *m*Sample Preparation System$_{DNA}$ reagents.

   <u>For 49 to 72 reactions use:</u> 1 tube of positive control, 1 tube of negative control, 3 amplification reagent packs, 1 bottle of *m*Microparticle$_{DNA}$ and *m*Lysis$_{DNA}$ Buffer, and 2 bottles of *m*Wash 1$_{DNA}$ Buffer, *m*Wash 2$_{DNA}$ Buffer and *m*Elution Buffer$_{DNA}$.

   <u>For 73 to 96 reactions use:</u> 1 tube of positive control, 1 tube of negative control, 4 amplification reagent packs, 1 bottle of *m*Microparticle$_{DNA}$ and *m*Lysis$_{DNA}$ Buffer, and 2 bottles of *m*Wash 1$_{DNA}$ Buffer, *m*Wash 2$_{DNA}$ Buffer and *m*Elution Buffer$_{DNA}$.

Sample Preparation Area

4. Refer to the Extraction Protocol section of **Manual Sample Preparation Using the Abbott *m*Sample Preparation System$_{DNA}$ for RealTi*m*e High Risk HPV** for sample preparation procedures.

   NOTE: Abbott *m*Sample Preparation System$_{DNA}$ reagents can be used up to 3 times within 14 days for a total of 48 samples when stored tightly capped at 15 to 30˚C. If reusing the Abbott *m*Sample Preparation System$_{DNA}$ reagents, mark the mWash 2$_{DNA}$ bottle to indicate that ethanol has already been added. Once prepared, do not add more ethanol to the mWash 2$_{DNA}$ bottle at any time. If reusing the Abbott *m*Sample Preparation System$_{DNA}$ reagents, after removing the caps from all the Abbott *m*Sample Preparation System$_{DNA}$ reagents, store the caps on a clean, absorbent surface for recapping after the run. NOTE: The assembly of the amplification master mix and sample eluates into the Abbott 96-Well Optical Reaction Plate (step 12) must be initiated within 1 hour after completion of Sample Preparation.

Amplification Area

5. Switch on and initialize the Abbott *m*2000*rt*. The Abbott *m*2000*rt* requires a 15-minute warm-up prior to starting a run. Refer to the Abbott *m*2000*rt* Operations Manual, Operating Instructions section.
6. Create the Abbott *m*2000*rt* test order. Refer to the Operating Instructions section of the Abbott *m*2000*rt* Operations Manual. From the Protocol screen, select the appropriate application file.

Reagent Preparation Area

NOTE: All reagent preparation must take place in the dedicated Reagent Preparation Area. Refer to the Contamination Precautions section of the package insert before preparing reagents. Change gloves before handling the amplification reagents.

7. Prepare the amplification master mix.
   - Each amplification reagent pack supports up to 24 reactions.
   - Prior to opening the amplification reagents, ensure that the contents of the amplification reagent pack are at the bottom by tapping the amplification reagent pack in an upright position on the bench to bring the liquid to the bottom of the vials.
   - Identify the amplification reagents as follows:
     - Activation Reagent (Reagent 1): clear bottle, teal cap
     - Oligonucleotide Reagent (Reagent 2): black bottle, white cap
     - DNA Polymerase (Reagent 3): clear bottle, white cap
   - Remove and discard caps.
   - Prepare the master mix by using a **PIPETTE DEDICATED FOR REAGENT USE ONLY** to add 278 µL of the HPV Activation Reagent (Reagent 1) and 402 µL of the HPV Oligonucleotide Reagent (Reagent 2) together in the DNA Polymerase bottle (Reagent 3). Mix the Enzyme vial containing the reaction mixture (master mix) by gently pipetting up and down 6 times. Avoid creating foam.
   - If performing 25 to 48 reactions, prepare the amplification master mix from 2 amplification reagent packs. If performing 49 to 72 reactions, prepare the amplification master mix from 3 amplification reagent packs. If performing 73 to 96 reactions, prepare the amplification master mix from 4 amplification reagent packs.

   NOTE: The Abbott *m*2000*rt* protocol (step 14) must be initiated within 1 hour of the addition of the activation reagent into the DNA Polymerase bottle (step 7).
8. Pipette the contents of the master mix from the enzyme bottle(s) into a single-use DNase-free tube. Mix by gently pipetting up and down 6 times. Avoid creating foam.
9. Prior to addition of master mix and sample, insert an Abbott 96-Well Optical Reaction Plate onto an Abbott Splash-Free Support Base to prevent contamination.
   - Contamination of the bottom of the Abbott 96-Well Optical Reaction Plate with fluorescent materials could potentially interfere with the HPV assay. The Abbott 96-Well Optical Reaction Plate should be held and transported with the Abbott Splash-Free Support Base to minimize contamination.

10. Using a **DEDICATED PIPETTE**, dispense 25 µL aliquots of the amplification master mix into each well of the Abbott 96-Well Optical Reaction Plate that will be used depending on the number of samples to be run, including controls. A calibrated repeat pipettor may be used. Visually verify that 25 µL has been dispensed into each well. **NOTE: Remaining activated master mix can be recapped and stored at −10°C or colder for up to 14 days and reused at a later time if the volume is sufficient. The activated master mix should not undergo more than 3 freeze/thaw cycles. The frozen master mix can be thawed at room temperature for up to 1 hour prior to the initiation of amplification and detection on the Abbott *m*2000*rt*.**
11. Transfer the Abbott 96-Well Optical Reaction Plate on the Abbott Splash-Free Support Base to the Sample Preparation Area.

Sample Preparation Area

12. In the Sample Preparation Area, transfer 25 µL of sample eluate to the Abbott 96-Well Optical Reaction Plate on the Abbott Splash-Free Support Base. **Use a separate pipette tip for each sample eluate transfer.** Visually verify that a total of 50 µL has been dispensed into each well.
13. Seal the Abbott 96-Well Optical Reaction Plate according to the instructions in the Abbott *m*2000*rt* Operations Manual.

Amplification Area

14. Place the Abbott 96-Well Optical Reaction Plate in the Abbott *m*2000*rt* and initiate the Abbott RealTi*m*e HR HPV protocol as described in the Abbott *m*2000*rt* Operations Manual, Operating Instructions section. At the completion of the run, assay results are reported on the Abbott *m*2000*rt*. Refer to the **RESULTS** section of the package insert for further details.
15. After the Abbott *m*2000*rt* has completed the amplification and detection protocol, remove the Abbott 96-Well Optical Reaction Plate and dispose of according to the instructions in the **Contamination Precautions** section of the package insert. Place the Abbott 96-Well Optical Reaction Plate in a sealable plastic bag and dispose of according to the Abbott *m*2000*rt* Operations Manual along with the gloves used to handle the plate.

Post Processing Procedures

1. Refer to the Clean Up section of **Manual Sample Preparation Using the Abbott *m*Sample Preparation System$_{DNA}$ for RealTi*m*e High Risk HPV**.
2. Clean the Abbott Splash-Free Support Base before next use, according to the Abbott *m*2000*rt* Operations Manual.

ASSAY PROTOCOL B: ABBOTT *m*2000*sp* AND ABBOTT *m*2000*rt* INSTRUMENTS

Refer to the **WARNINGS AND PRECAUTIONS** section of the package insert before preparing samples.

1. Vortex each specimen for 15 to 20 seconds. Ensure that the contents of each vial are at the bottom after vortexing by tapping the vials on the bench to bring liquid to the bottom of the vial. Immediately transfer the specimens to the sample input tubes.

   NOTE: Ensure that the volume of the cell pellet SurePath samples after cytological processing is approximately 2.8 mL. The sample volume must be adjusted to 6 mL using SurePath Preservative Fluid prior to vortexing and transferring.

   - For specimens collected in PreservCyt Solution or SurePath Preservative Fluid, to ensure that 400 µL of each specimen is transferred by the Abbott *m*2000*sp* to the reaction vessel:
     - transfer a minimum of 500 µL of each specimen if using Master Mix Tubes or Abbott Transport Tubes as sample input tubes.
     - transfer a minimum of 700 µL of each specimen if using 5 mL Reaction Vessels or any other 13 mm round bottom non-skirted tubes as sample input tubes.
   - For specimens collected with the Abbott Cervi-Collect Specimen Collection Kit, load the tubes without cap directly on the Abbott *m*2000*sp* (these specimens do not require a transfer).
2. Thaw control reagents at 15 to 30°C or at 2 to 8°C; see **QUALITY CONTROL PROCEDURES** section of the package insert.
   - Vortex each assay control for 15 to 20 seconds before use. Ensure that the contents of each vial are at the bottom after vortexing by tapping the vials on the bench to bring liquid to the bottom of the vial.
   - Once thawed, assay controls can be stored at 2 to 8°C for up to 24 hours before use.
3. Thaw amplification reagents at 15 to 30°C or at 2 to 8°C and store at 2 to 8°C until required for the amplification master mix procedure.
   - Once thawed, the amplification reagents can be stored at 2 to 8°C for up to 24 hours if not used immediately.

   NOTE: A maximum of 96 reactions can be performed per run.

   <u>For up to 24 reactions use:</u> 1 tube of positive control, 1 tube of negative control, 1 amplification reagent pack, and 1 set of Abbott *m*Sample Preparation System$_{DNA}$ reagents.

   <u>For 25 to 48 reactions use:</u> 1 tube of positive control, 1 tube of negative control, 2 amplification reagent packs, and 1 set of Abbott *m*Sample Preparation System$_{DNA}$ reagents.

   <u>For 49 to 72 reactions use:</u> 1 tube of positive control, 1 tube of negative control, 3 amplification reagent packs, 1 bottle of *m*Microparticle$_{DNA}$ and *m*Lysis$_{DNA}$ Buffer, and 2 bottles of *m*Wash 1$_{DNA}$ Buffer, *m*Wash 2$_{DNA}$ Buffer and *m*Elution Buffer$_{DNA}$.

   <u>For 73 to 96 reactions use:</u> 1 tube of positive control, 1 tube of negative control, 4 amplification reagent packs, 1 bottle of *m*Microparticle$_{DNA}$ and *m*Lysis$_{DNA}$ Buffer, and 2 bottles of *m*Wash 1$_{DNA}$ Buffer, *m*Wash 2$_{DNA}$ Buffer and *m*Elution Buffer$_{DNA}$.

   NOTE: Abbott *m*Sample Preparation System$_{DNA}$ is for single-use only and should be discarded after use. Use newly opened reagents for every new Abbott RealTi*m*e HR HPV assay run.
4. Place the controls and the patient specimens into the Abbott *m*2000*sp* sample rack.

   CAUTION: Use only 13 mm sample racks. Do NOT skip any positions in a sample rack. Load specimens and controls into the 13 mm sample racks in consecutive positions, starting with the first position in the first sample rack. Fill all positions in each sample rack without skipping any positions before loading specimens into the next sample rack.

   Insert specimen and control tubes into sample racks carefully to avoid splashing. If used, bar codes on tube labels must face right for scanning. Ensure that each tube is placed securely in the sample rack so that the bottom of the tube reaches the inside bottom of the rack.

   Load filled sample racks onto the Abbott *m*2000*sp* in consecutive sample rack positions, with the first rack farthest to the right on the worktable, and any additional rack progressively to the left of the first rack.
5. Open the Abbott *m*Sample Preparation System$_{DNA}$ reagent pack(s). Prepare the *m*Wash 2$_{DNA}$ by adding 70 mL of USP grade 190 to 200 proof ethanol (95 to 100% ethanol) to the *m*Wash 2$_{DNA}$ bottle as described in the Abbott *m*Sample Preparation System$_{DNA}$ product information. **Do not use ethanol that contains denaturants.** Gently invert each reagent bottle to ensure a homogenous solution and pour the contents into the appropriate reagent vessels per the Abbott *m*2000*sp* Operations Manual, Operating Instructions section. If crystals are observed in any of the reagent bottles upon opening, allow the reagent to equilibrate at room temperature until the crystals disappear. Do not use the reagents until the crystals have dissolved.

   NOTE: Before pouring the *m*Microparticles$_{DNA}$ into the 200 mL reagent vessels, vigorously mix or vortex until the *m*Microparticles$_{DNA}$ are fully resuspended.
6. Initiate the sample extraction protocol as described in the Abbott *m*2000*sp* Operations Manual, Operating Instructions section.
7. While the Abbott *m*2000*sp* is performing sample preparation, switch on and initialize the Abbott *m*2000*rt*. The Abbott *m*2000*rt* requires a 15-minute warm-up prior to starting a run. Refer to the Abbott *m*2000*rt* Operations Manual, Operating Instructions section.

   NOTE: Once sample preparation is completed, the master mix protocol should be started within 1 hour.
8. Load the amplification reagents and the master mix tube on the Abbott *m*2000*sp* worktable.
   - Prior to opening the amplification reagents, ensure that the contents of the amplification reagent pack(s) are at the bottom by tapping the amplification reagent pack(s) in an upright position on the bench to bring the liquid to the bottom of the vials.
   - Remove and discard vial caps.

   NOTE: Change gloves before handling the amplification reagents.
9. Initiate the Abbott *m*2000*sp* Master Mix Addition protocol as described in the Abbott *m*2000*sp* Operations Manual, Operating Instructions section.
10. After the Abbott *m*2000*sp* has completed the addition of samples and amplification reagents, seal the Abbott 96-Well Optical Reaction Plate according to the instructions in the Abbott *m*2000*sp* Operations Manual.

- Contamination of the bottom of the Abbott 96-Well Optical Reaction Plate with fluorescent materials could potentially interfere with the HPV assay. The Abbott 96-Well Optical Reaction Plate should be held and transported with the Abbott Splash-Free Support Base to minimize contamination.

NOTE: Within 1 hour of starting the master mix protocol, the sealed Abbott 96-Well Optical Reaction Plate should be transferred to the Abbott *m*2000*rt* to begin amplification/detection.

11. Place the Abbott 96-Well Optical Reaction Plate in the Abbott *m*2000*rt* and initiate the Abbott RealTi*m*e HR HPV assay protocol as described in the Abbott *m*2000*rt* Operations Manual, Operating Instructions section. At the completion of the run, assay results are reported on the Abbott *m*2000*rt*. Refer to the **RESULTS** section of the package insert for further details.
12. After the Abbott *m*2000*rt* has completed the amplification and detection protocol, remove the Abbott 96-Well Optical Reaction Plate and dispose of according to the instructions in the **Contamination Precautions** section of the package insert. Place the Abbott 96-Well Optical Reaction Plate in a sealable plastic bag and dispose of according to the Abbott *m*2000*rt* Operations Manual along with the gloves used to handle the plate.

Post Processing Procedures

1. At the end of each run, remove and discard all remaining reagents from the Abbott *m*2000*sp* worktable as stated in the Abbott *m*2000*sp* Operations Manual.
2. Decontaminate and dispose of all specimens, reagents, and other potentially contaminated materials in accordance with local, state, and federal regulations.
3. Clean the Abbott Splash-Free Support Base before next use, according to the Abbott *m*2000*rt* Operations Manual.

QUALITY CONTROL PROCEDURES

Abbott *m*2000*rt* Optical Calibration

Optical calibration of the Abbott *m*2000*rt* is required for the accurate measurement and discrimination of dye fluorescence during the Abbott RealTi*m*e HR HPV assay.

The following Abbott *m*2000*rt* Optical Calibration Plates are used to calibrate the Abbott *m*2000*rt* for the Abbott RealTi*m*e HR HPV assay:

- FAM Plate (Carboxyfluorescein)
- Cy5 Plate (Cyanine)
- NED Plate (ABI proprietary dye)
- ROX Plate (Carboxy-X-rhodamine)
- VIC Plate (Proprietary dye)

Refer to the Calibration Procedures section in the Abbott *m*2000*rt* Operations Manual for a detailed description of how to perform an Abbott *m*2000*rt* Optical Calibration.

Detection of Inhibition and/or Cell Inadequacy

The Abbott RealTi*m*e HR HPV assay detects the endogenous human beta globin sequence as Internal Control (IC) signal to evaluate cell adequacy, sample extraction and amplification efficiency. A flag or an error code is displayed when IC cycle number (CN) value of a sample or control exceeds the established range.

Negative and Positive Controls

A negative control and a positive control are required for every run to verify that the sample processing, the amplification, and the detection steps are performed correctly. The Abbott RealTi*m*e HR HPV controls need to be processed together with the samples prior to running the amplification portion of the assay.

The negative control is formulated with DNA containing IC sequence. The only signal detected for negative control should be the IC signal in the Cy5 channel. The positive control is formulated with DNA containing HPV 16, HPV 18, HPV 58 and IC sequences. All 4 signals (VIC signal for HPV 16, NED signal for HPV 18, FAM signal for HPV 58, and Cy5 signal for IC) should be detected in the positive control. A flag is displayed when a control result is out of range. If negative or positive controls are out of range, all of the samples and controls from that run must be reprocessed, beginning with sample preparation.

HR HPV must not be detected in the negative control. HR HPV detected in the negative control is indicative of contamination from other samples or amplified product introduced during sample preparation or during preparation of the Abbott 96-Well Optical Reaction Plate. To remove contamination, clean the Abbott *m*2000*sp* and the Abbott *m*2000*rt* according to the Abbott *m*2000*sp* and the Abbott *m*2000*rt* Operations Manuals. For manual sample preparation, clean the equipment according to the instructions in **Manual Sample Preparation Using the Abbott *m*Sample Preparation System$_{DNA}$ for RealTi*m*e High Risk HPV**. Following cleaning, repeat sample processing for controls and samples following the appropriate sample preparation protocol outlined in the package insert.

IC results for the negative control and positive control that are outside the validity limit indicate the occurrence of inhibition during sample preparation or during the amplification reaction steps of the assay. Repeat the processing for controls and samples following the appropriate sample preparation protocol outlined in the package insert.

Monitoring the Laboratory for the Presence of Contamination

It is recommended that the following procedure be done at least once a month to monitor laboratory surfaces and equipment for contamination. It is very important to test all areas that may have been exposed to processed samples and controls and/or amplification product. This includes routinely handled objects such as pipettes, Abbott *m*2000*sp,* and Abbott *m*2000*rt* function keys, bench surfaces and other equipment that may be present in the work areas.

1. Add 0.8 mL DNase-free water to a new Master Mix Tube.
2. Saturate the cotton tip of an applicator (Puritan or equivalent) in the DNase-free water from the Master Mix Tube.
3. Using the saturated cotton tip of the applicator, wipe the area to be monitored using a sweeping motion. Place the applicator into the Master Mix Tube.
4. Swirl the cotton tip in DNase-free water 10 times, then press the applicator along the inside of the tube so that the liquid drains back into the solution at the bottom of the Master Mix Tube. Discard the applicator.
5. Cap the Master Mix Tube and vortex.
6. Remove the caps from the Master Mix Tubes and test the sample according to the appropriate assay procedure section of the package insert.
7. Contamination is indicated by the detection of HR HPV in the swab samples.
   - If contamination is present, the instrument will report “HR HPV Detected” (disregard IC flag if present).
   - If there is no contamination, the instrument will report “Not Detected” or no result will be displayed (disregard error codes 4951 or 4952 if present).
8. If contamination is detected on the equipment, follow the cleaning and decontaminating guidelines given in that equipment’s operations manual. If HR HPV is detected on surfaces, clean the contaminated areas with 1.0% (v/v) sodium hypochlorite solution, followed by 70% ethanol or water.

   NOTE: Chlorine solutions may pit equipment and metal. Use sufficient amounts or repeated applications of 70% ethanol until chlorine residue is no longer visible.
9. Repeat testing of the contaminated area by following steps 1 through 6.
10. If the presence of contamination is detected again, repeat steps 8 and 9 until no HR HPV amplification is detected.

RESULTS

The Abbott RealTi*m*e HR HPV assay is a qualitative assay. A minimum of 1 negative control and 1 positive control are required with each run. The negative control serves to verify that HR HPV DNA contamination of the negative control did not occur during the sample preparation and set-up of the amplification reaction. If HR HPV signal is detected for the negative control, the -QC flag is displayed next to all sample results for the run. Samples with the -QC flag may have been similarly contaminated with analyte during processing. If the negative control is not processed, the -QC flag is indicated next to all sample results for that run.

The IC signal in samples serves to confirm that each sample had sufficient cell input for accurate HR HPV detection and was processed correctly and to indicate whether inhibitors of amplification are present. If the IC is out of range (ie, IC CN not generated or greater than or equal to a fixed cutoff cycle) and HR HPV is detected, the sample will have an interpretation of “HR HPV Detected”. An IC flag will be reported next to the result. If the IC is out of range and HR HPV is not detected, no result will be reported and an error code will be generated. The sample with the error code must be retested starting with sample preparation.

For more information about error codes and flags, refer to the Abbott *m*2000*rt* Operations Manual Version 3.0 and Operations Manual Addendum Version 3.0.

Results Reporting

Three HPV signals corresponding to HPV 16, HPV 18 and Other HR HPV are evaluated for each sample. Each signal is either determined as "Detected" if the CN is less than a fixed assay cutoff cycle or is determined as "Not Detected" if the CN is not generated or the CN is greater than or equal to the assay cutoff cycle. All the detected signals (HPV 16, HPV 18 or Other HR HPV) are reported in the sample result with the respective CN values (in parenthesis after the target result). Samples with any of the 3 HR HPV signals detected will have an interpretation of "HR HPV Detected". Samples with all 3 HR HPV signals not detected will have an interpretation of "Not Detected".

Assay results and interpretations will look similar to the following examples:

Sample ID	Results	Interpretation	Explanation
1	HPV 16 (20.76)	HR HPV Detected	HPV 16 is detected with a CN of 20.76 HPV 18 and Other HR HPV are not detected
2	HPV 18 (21.20)	HR HPV Detected	HPV 18 is detected with a CN of 21.20 HPV 16 and Other HR HPV are not detected
3	Other HR HPV (14.48)	HR HPV Detected	Other HR HPV is detected with a CN of 14.48 HPV 16 and HPV 18 are not detected
4	HPV 16 (22.20); Other HR HPV (17.21)	HR HPV Detected	HPV 16 and Other HR HPV are detected with CN of 22.20 and 17.21, respectively HPV 18 is not detected
5	HPV 18 (18.67); Other HR HPV (15.88)	HR HPV Detected	HPV 18 and Other HR HPV are detected with CN of 18.67 and 15.88, respectively HPV 16 is not detected
6	HPV 16 (24.51); HPV 18 (23.11)	HR HPV Detected	HPV 16 and HPV 18 are detected with CN of 24.51 and 23.11, respectively Other HR HPV is not detected
7	HPV 16 (21.35); HPV 18 (22.60); Other HR HPV (19.45)	HR HPV Detected	HPV 16 and HPV 18 and Other HR HPV are detected with CN of 21.35, 22.60, and 19.45, respectively
8	Not Detected	Not Detected	HR HPV is not detected

LIMITATIONS OF THE PROCEDURE

- For In Vitro Diagnostic Use Only.
- This method has been tested using clinically-collected PreservCyt and SurePath liquid pap and Abbott Cervi-Collect specimens. Performance with other specimen types has not been evaluated.
- Optimal performance of this test requires appropriate specimen collection, handling, and storage (refer to the **SPECIMEN COLLECTION AND HANDLING INSTRUCTIONS** section of the package insert).
- Use of the Abbott RealTi*m*e HR HPV assay is limited to personnel who have been trained on the use of the Abbott *m*2000*sp* or manual sample preparation method for sample extraction and Abbott *m*2000*rt* for amplification and detection.
- The instruments and assay procedures reduce the risk of contamination by amplification product. However, nucleic acid contamination from the controls, specimens, and amplification product must be controlled by good laboratory practice and careful adherence to the procedures specified in the package insert.
- A negative result does not preclude the possibility of infection because results are dependent on appropriate specimen collection. Test results may be affected by improper specimen collection, technical error, or specimen mix-up.
- As with any diagnostic test, results from the Abbott RealTi*m*e HR HPV assay should be interpreted in conjunction with other clinical and laboratory findings.

SPECIFIC PERFORMANCE CHARACTERISTICS

Genotype Inclusivity and Partial Genotyping

The ability of the Abbott RealTi*m*e HR HPV assay to detect 14 HR HPV genotypes (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) and to distinguish HPV 16 and HPV 18 from the other 12 HR HPV genotypes was evaluated. Fifty-one samples containing HPV DNA targets from each of the 14 genotypes individually and in combinations were tested as listed in Table 1. Results from 51 samples that included 14 samples with single genotype, 25 samples with 2 genotypes and 12 samples with 3 genotypes were reported accurately; the presence or absence of HPV 16 and HPV 18 DNA was accurately determined in each case.

Table 1: Genotype Detection and Partial Genotyping Capability

Sample No.	HPV Genotype	Reported Result
1	HPV 16	HPV 16
2	HPV 18	HPV 18
3	HPV 31	Other HR HPV
4	HPV 33	Other HR HPV
5	HPV 35	Other HR HPV
6	HPV 39	Other HR HPV
7	HPV 45	Other HR HPV
8	HPV 51	Other HR HPV
9	HPV 52	Other HR HPV
10	HPV 56	Other HR HPV
11	HPV 58	Other HR HPV
12	HPV 59	Other HR HPV
13	HPV 66	Other HR HPV
14	HPV 68	Other HR HPV
15	HPV 16 and HPV 18	HPV 16; HPV 18
16	HPV 16 and HPV 31	HPV 16; Other HR HPV
17	HPV 16 and HPV 33	HPV 16; Other HR HPV
18	HPV 16 and HPV 35	HPV 16; Other HR HPV
19	HPV 16 and HPV 39	HPV 16; Other HR HPV
20	HPV 16 and HPV 45	HPV 16; Other HR HPV
21	HPV 16 and HPV 51	HPV 16; Other HR HPV
22	HPV 16 and HPV 52	HPV 16; Other HR HPV
23	HPV 16 and HPV 56	HPV 16; Other HR HPV
24	HPV 16 and HPV 58	HPV 16; Other HR HPV
25	HPV 16 and HPV 59	HPV 16; Other HR HPV
26	HPV 16 and HPV 66	HPV 16; Other HR HPV
27	HPV 16 and HPV 68	HPV 16; Other HR HPV
28	HPV 18 and HPV 31	HPV 18; Other HR HPV
29	HPV 18 and HPV 33	HPV 18; Other HR HPV
30	HPV 18 and HPV 35	HPV 18; Other HR HPV
31	HPV 18 and HPV 39	HPV 18; Other HR HPV
32	HPV 18 and HPV 45	HPV 18; Other HR HPV
33	HPV 18 and HPV 51	HPV 18; Other HR HPV
34	HPV 18 and HPV 52	HPV 18; Other HR HPV
35	HPV 18 and HPV 56	HPV 18; Other HR HPV
36	HPV 18 and HPV 58	HPV 18; Other HR HPV
37	HPV 18 and HPV 59	HPV 18; Other HR HPV
38	HPV 18 and HPV 66	HPV 18; Other HR HPV
39	HPV 18 and HPV 68	HPV 18; Other HR HPV
40	HPV 16 and HPV 18 and HPV 31	HPV 16; HPV 18; Other HR HPV
41	HPV 16 and HPV 18 and HPV 33	HPV 16; HPV 18; Other HR HPV
42	HPV 16 and HPV 18 and HPV 35	HPV 16; HPV 18; Other HR HPV
43	HPV 16 and HPV 18 and HPV 39	HPV 16; HPV 18; Other HR HPV
44	HPV16 and HPV18 and HPV 45	HPV 16; HPV 18; Other HR HPV
45	HPV 16 and HPV 18 and HPV 51	HPV 16; HPV 18; Other HR HPV
46	HPV 16 and HPV 18 and HPV 52	HPV 16; HPV 18; Other HR HPV

Sample No.	HPV Genotype	Reported Result
47	HPV 16 and HPV 18 and HPV 56	HPV 16; HPV 18; Other HR HPV
48	HPV 16 and HPV 18 and HPV 58	HPV 16; HPV 18; Other HR HPV
49	HPV 16 and HPV 18 and HPV 59	HPV 16; HPV 18; Other HR HPV
50	HPV 16 and HPV 18 and HPV 66	HPV 16; HPV 18; Other HR HPV
51	HPV 16 and HPV 18 and HPV 68	HPV 16; HPV 18; Other HR HPV

Clinical Sensitivity and Specificity in Referral Population: Disease Detection

A total of 512 PreservCyt liquid pap specimens from a referral population were tested with the Abbott RealTi*m*e HR HPV assay and the hc2 High-Risk HPV DNA Test (HC2). The clinical sensitivity and specificity for detection of disease were determined for both assays. The presence of disease was defined by a histology result of Cervical Intraepithelial Neoplasia (CIN) 2 or greater. For subjects lacking a histology evaluation, disease status was defined by a liquid based cytology (LBC) result of high grade squamous intraepithelial lesion (HSIL) or greater at enrollment in colposcopy clinics. Disease prevalence in this population was 24.6%. Of 126 disease positive subjects, 121 were detected by the Abbott RealTi*m*e HR HPV assay and 119 were detected by HC2. Of 386 disease negative specimens, 154 were not detected by the Abbott RealTi*m*e HR HPV assay and 147 were not detected by HC2. The sensitivity of the Abbott RealTi*m*e HR HPV assay for detection of disease was 96.0% and of HC2 was 94.4%. The specificity of the Abbott RealTi*m*e HR HPV assay in this referral population was 39.9% and of HC2 was 38.1% (Table 2).

Table 2: Clinical Performance for Detection of Disease in Referral Population

Test	Sensitivity (95% CI)	Specificity (95% CI)	Positive Predictive Value	Negative Predictive Value
Abbott RealTi*m*e HR HPV	96.0% (91.0-98.7%)	39.9% (35.0-45.0%)	34.3%	96.9%
HC2	94.4% (88.9-97.7%)	38.1% (33.2-43.1%)	33.2%	95.5%

A total of 128 subjects from this population had a cytology result of ASC-US. In this ASC-US population, the clinical sensitivity was 100% for both the Abbott RealTi*m*e HR HPV assay and HC2. The clinical specificity of the Abbott RealTi*m*e HR HPV assay was 46.2% and of HC2 was 45.2%.

Clinical Sensitivity and Specificity in Referral Population: High Risk HPV Detection

The sensitivity and specificity of the Abbott RealTi*m*e HR HPV assay for detection of HR HPV were evaluated by testing 517 PreservCyt liquid pap specimens collected from a referral population. The high risk HPV status of cervical specimens was determined by the concordance between the Abbott RealTi*m*e HR HPV assay and HC2 tests and by further analysis of the specimens with discordant results using LINEAR ARRAY HPV Genotyping Test (Linear Array). A total of 337 specimens were detected by both assays and 136 specimens were not detected by either assay. The results of 44 discordant specimens were resolved by Linear Array. Of the 363 HR HPV positive specimens, 354 were detected by the Abbott RealTi*m*e HR HPV assay and 346 were detected by HC2. Of the 154 HR HPV negative specimens, 153 were not detected by the Abbott RealTi*m*e HR HPV assay and 137 were not detected by HC2. The sensitivity of the Abbott RealTi*m*e HR HPV assay for detection of HR HPV was 97.5% and of HC2 assay was 95.3%. The specificity of the Abbott RealTi*m*e HR HPV assay was 99.4% and of HC2 assay was 89.0% (Table 3).

Table 3: Sensitivity and Specificity for Detection of HR HPV

Test	Sensitivity (95% CI)	Specificity (95% CI)
Abbott RealTi*m*e HR HPV	97.5% (95.3-98.9%)	99.4% (96.4-100%)
HC2	95.3% (92.6-97.2%)	89.0% (82.9-93.4%)

Clinical Specificity in General Screening Population with Normal Cytology (Age ≥ 30 years)

A total of 362 cytologically normal PreservCyt liquid pap specimens collected in a general screening population from women 30 years of age or older were tested with the Abbott RealTi*m*e HR HPV assay and HC2. The clinical specificity was determined for both assays. The Abbott RealTi*m*e HR HPV assay detected 4.1% of the specimens and HC2 detected 3.0% of the specimens. In this population, the clinical specificity of the Abbott RealTi*m*e HR HPV assay and HC2 were 95.9% and 97.0% respectively.

Table 4: Clinical Specificity in General Screening Population with Normal Cytology (Age ≥ 30 years)

Test	Number detected/ tested	Detection Rate	Specificity (95% CI)
Abbott RealTi*m*e HR HPV	15/362	4.1%	95.9% (93.3-97.7%)
HC2	11/362	3.0%	97.0% (94.6-98.5%)

Clinical Sensitivity and Specificity from Additional Studies on Referral Populations: Disease Detection

The clinical sensitivity and specificity for detection of disease among referral populations were determined for Abbott RealTi*m*e HR HPV assay in 4 studies[26-29] in comparison with HC2. All specimens were collected in PreservCyt Solution. The results from peer-reviewed literature are summarized in Table 5.

Table 5: Clinical Performance for Detection of Disease in Referral Populations

Study	Number Disease Positive[a]	Number Disease Negative[a]	Sensitivity (95% CI)		Specificity (95% CI)	
			Abbott RealTi*m*e HR HPV	HC2	Abbott RealTi*m*e HR HPV	HC2
1[26]	229	473	97.8% (95.0-99.3%)	95.6% (92.1-97.9%)	32.8% (28.6-37.2%)	35.7% (31.4-40.2%)
2[27]	39	76	90.0% (85.0-95.0%)	95.0% (91.0-99.0%)	50.0% (41.0-59.0%)	50.0% (41.0-59.0%)
3[28]	359	740	93.3% (90.1-95.6%)	96.3% (93.8-98.0%)	27.3% (24.1-30.7%)	19.5% (16.7-22.6%)
4[29]	156	163	92.4% (87.0-96.0%)	91.7% (86.3-95.5%)	61.7% (53.8-69.2%)	58.6% (50.6-66.3%)

[a] Disease positive specimens were generally defined as having a histology result of CIN2 or greater. Disease negative specimens were generally defined as having a histology result of less than CIN2.

Clinical Sensitivity and Specificity from Additional Studies on ASC-US Populations: Disease Detection

The clinical sensitivity and specificity for detection of disease among patients with ASC-US or equivalent cytology results were determined for Abbott RealTi*m*e HR HPV assay in 2 studies[26,30] in comparison with HC2. All specimens were collected in PreservCyt Solution. The results from peer-reviewed literature are summarized in Table 6.

Table 6: Clinical Performance for Detection of Disease in ASC-US Populations

Study	Number Disease Positive	Number Disease Negative	Sensitivity (95% CI)		Specificity (95% CI)	
			Abbott RealTi*m*e HR HPV	HC2	Abbott RealTi*m*e HR HPV	HC2
1[26]	52	141	96.2 % (86.8-99.5%)	94.2% (84.1-98.8%)	33.3% (25.6-41.8%)	39.0% (30.9-47.6%)
2[a,30]	37	240	97.3%[b]	97.4%[b]	39.6%[b]	33.6%[b]

[a] Study subjects included in this data set had a cytology result of borderline dyskaryosis, which correlates with atypical squamous cells.[31]

[b] The 95% CI range is not reported by the publication.[30]

Clinical Sensitivity and Specificity in Screening Populations: Disease Detection

The clinical sensitivity and specificity for detection of disease among screening populations were determined for Abbott RealTi*m*e HR HPV assay in 3 studies[32-34] in comparison with benchmark tests. All specimens were collected in PreservCyt Solution. The results from peer-reviewed literature are summarized in Table 7.

Table 7: Clinical Performance for Detection of Disease in Screening Populations (Age ≥ 30 years)

Study	Number Disease Positive	Number Disease Negative	Sensitivity (95% CI)		Specificity (95% CI)	
			Abbott RealTi*me* HR HPV	Benchmark Test[a]	Abbott RealTi*me* HR HPV	Benchmark Test[a]
1[32]	38	3,091	100% (86.5-100%)	97.4% (86.2-99.9%)	93.3% (92.4-94.2%)	91.8% (90.8-92.7%)
2[33]	68	858	95.6% (87.2-98.6%)	98.5% (90.3-99.8%)	92.0% (90.0-93.5%)	91.8% (89.9-93.4%)
3[34]	16	4,629[b]	100% (79.4-100%)	100% (79.4-100%)	90.3% (89.4-91.1%)	88.8% (87.9-89.7%)

[a] Benchmark test for Studies 1 and 3 was HC2. Benchmark test for Study 2 was GP5+/6+ PCR.

[b] Based on the specimens tested with Abbott RealTi*me* HR HPV.

Accuracy in Identification of HPV 16 and/or HPV 18 in Women with Cervical Disease

The performance of the Abbott RealTi*me* HR HPV in identification of HPV 16 and/or HPV 18 in cervical disease (CIN2 or greater) is evaluated based on the results from a referral population.[26] Out of 229 specimens with cervical disease, 210 had a valid Abbott RealTi*me* HR HPV result with an interpretation of "HR HPV Detected" and a valid Linear Array result that reported one or more of the high risk HPV genotypes targeted by Abbott RealTi*me* HR HPV. The overall agreement for detection of HPV 16 and/or HPV 18 between the Abbott RealTi*me* HR HPV and Linear Array tests was 100% (210/210).

Table 8: Genotyping Accuracy for HPV 16 and/or HPV 18

		Abbott RealTi*me* HR HPV	
		HPV 16 and/or HPV 18 Detected[a]	Other HR HPV Detected[b]
Linear Array	HPV 16 and/or HPV 18 Reported[c]	153	0
	Non-HPV 16/18 High Risk Genotype(s) Reported[d]	0	57

[a] These specimens were detected for HPV 16 and/or HPV 18 signal(s) with or without Other HR HPV signal detected.

[b] These specimens were not detected for HPV 16 or HPV 18 signal and detected for Other HR HPV signal.

[c] These specimens were reported with HPV 16 and/or HPV 18 genotype(s) with or without non-HPV 16/18 high risk HPV genotype(s) reported.

[d] These specimens were reported with 1 or more of the non-HPV 16/18 high risk HPV genotypes that are targeted by Abbott RealTi*me* HR HPV. HPV 16 or HPV 18 was not reported.

Estimate of Relative Disease Risk Associated with Different Genotype Results

The relative risks of having cervical disease (CIN2 or greater) were estimated for HPV 16 and/or HPV 18 Detected vs. Other HR HPV Detected results based on data obtained in a referral population,[26] an ASC-US Population,[26] and a screening population (women 30 years of age or older).[32]

Table 9: Relative Risk of Cervical Disease Associated with Different Genotype Results (HPV 16 and/or HPV 18 Detected vs Other HR HPV Detected)

Study	Relative Risk	95% CI
Referral Population	2.1	(1.7, 2.7)
ASC-US Population	2.6	(1.5, 4.6)
Screening Population (Age ≥ 30 years)	2.5	(1.4, 4.4)

Analytical Sensitivity for High Risk HPV Genotypes

Analytical sensitivity of the Abbott RealTi*me* HR HPV assay was determined by testing HPV DNA from each of 14 HR HPV genotypes in the presence of human cellular DNA in PreservCyt Solution. Four hundred microliters of sample is used per assay. For each genotype, a minimum of 4 levels, with 9 replicates at each level were tested. Testing was performed with 3 lots of amplification reagents on 3 Abbott *m*2000 RealTi*me* Systems.

Probit analysis determined that with a probability of greater than 95%, HPV 16, 18, 35, 39, 45, 51, 59, 66, and 68 can be detected at 500 copies per assay, HPV 31, 33, 52, and 56 can be detected at 2,000 copies per assay and HPV 58 at 5,000 copies per assay.

Analytical Specificity (Cross-reactivity)

A panel of bacteria, viruses and fungi were evaluated for potential cross-reactivity in the Abbott RealTi*me* HR HPV assay (Table 10). The panel included 15 Low Risk HPV genotypes and other organisms that can be found in the female anogenital tract. Human cellular DNA was also evaluated for potential cross-reactivity. Each potential cross-reactant was spiked into HPV negative samples at concentrations (per 0.4 mL sample input) shown in Table 10. Purified nucleic acids were used except where noted. Cross-reactivity was not observed with any of the organisms tested.

Table 10: Cross-reactivity Panel

Organisms	Concentration	Organisms	Concentration
Bacteroides fragilis	10^7 genomic copies	HPV 6	10^7 genomic copies
Candida albicans[a]	10^7 CFU	HPV 11	10^7 genomic copies
Chlamydia trachomatis[a]	10^7 EBs	HPV 13	10^7 genomic copies
Corynebacterium genitalium	10^7 genomic copies	HPV 26	10^7 genomic copies
Enterobacter cloacae	10^7 genomic copies	HPV 30	10^7 genomic copies
Enterococcus faecalis	10^7 genomic copies	HPV 32	10^7 genomic copies
Escherichia coli	10^7 genomic copies	HPV 40	10^7 genomic copies
Gardnerella vaginalis	10^7 genomic copies	HPV 42	10^7 genomic copies
Haemophilis ducreyi	10^7 genomic copies	HPV 43	10^7 genomic copies
Lactobacilllus acidophilus	10^7 genomic copies	HPV 44	10^7 genomic copies
Mycoplasma genitalium	10^7 genomic copies	HPV 53	10^7 genomic copies
Mycoplasma hominis	10^7 genomic copies	HPV 54	10^7 genomic copies
Neisseria gonorrhoeae	10^7 genomic copies	HPV 55	10^7 genomic copies
Neisseria meningitides	10^7 genomic copies	HPV 57	10^7 genomic copies
Proteus mirabilis	10^7 genomic copies	HPV 61	10^7 genomic copies
Staphylococcus aureus	10^7 genomic copies	HSV-I	10^7 genomic copies
Staphylococcus epidermidis	10^7 genomic copies	HSV-II	10^7 genomic copies
Streptococcus pneumoniae	10^7 genomic copies	HBV	10^7 genomic copies
Trichomonas vaginalis	10^6 genomic copies	HCV[b]	10^6 viral RNA copies
Ureaplasma urealyticum	10^7 genomic copies	HIV-1	10^6 viral RNA copies
Human Cellular DNA	10^7 genomic copies		

[a] Cultured microorganisms.

[b] Clinical specimen

Repeatability and Reproducibility

The repeatability and reproducibility of the Abbott RealTi*m*e HR HPV assay was evaluated by testing a panel of 20 well-characterized clinical specimen pools (10 HR HPV positive and 10 HR HPV negative). The 20 panel members were tested by 2 operators. Each operator, using a unique combination of reagent lot and instrument pair, tested 2 replicates of each panel member per day for 4 days for a total of 8 replicates. Percent (%) Agreement results, based on comparison of the Abbott RealTi*m*e HR HPV results to expected results, for each panel member individually and for overall negative and positive panels are shown in Table 11. For positive samples, results for each HPV signal (HPV 16, HPV 18, and Other HR HPV) were accurately reported for all replicates. The overall agreement for 319 results compared with expected results was 100%. The agreement for 159 comparisons between the 2 operators using 2 different reagent lots and 2 instruments was 100%.

Table 11: Reproducibility

Panel No.	Expected Result	N	% Detected	% Agreement
1	Not Detected	16	0	100
2	Not Detected	16	0	100
3	Not Detected	16	0	100
4	Not Detected	16	0	100
5	Not Detected	16	0	100
6	Not Detected	16	0	100
7	Not Detected	16	0	100
8	Not Detected	16	0	100
9	Not Detected	16	0	100
10	Not Detected	16	0	100
11	HR HPV Detected (Other HR HPV)	16	100	100
12	HR HPV Detected (HPV 16; HPV 18)	16	100	100
13	HR HPV Detected (HPV 16)	16	100	100
14	HR HPV Detected (HPV 16; Other HR HPV)	16	100	100
15	HR HPV Detected (Other HR HPV)	16	100	100
16	HR HPV Detected (Other HR HPV)	16	100	100
17	HR HPV Detected (Other HR HPV)	15[a]	100	100
18	HR HPV Detected (Other HR HPV)	16	100	100
19	HR HPV Detected (Other HR HPV)	16	100	100
20	HR HPV Detected (Other HR HPV)	16	100	100
Negative Samples (panels 1-10)		160	0	100
Positive Samples (panels 11-20)		159	100	100

[a] Invalid reaction was excluded from the analysis.

Reproducibility Between Manual and Abbott *m*2000*sp* Sample Preparation Methods

Two different sample processing options are available for the Abbott RealTi*m*e HR HPV assay: manual and Abbott *m*2000*sp*. The reproducibility between Abbott *m*2000*sp* and manual sample preparation methods was determined by testing separate aliquots of the same cervical specimens using these different sample preparation methods. For each comparison, 42 Abbott Cervi-Collect Specimens and 110 PreservCyt liquid pap specimens were tested. Agreement between Abbott m2000sp and manual sample preparation methods (Table 12) was 95% and 100%, respectively.

Table 12: Agreement Between Abbott *m*2000*sp* and Manual Sample Preparation

		Manual Sample Preparation	
		Detected	Not Detected
Abbott Cervi-Collect Specimen			
Abbott *m*2000*sp*	Detected	37	0
	Not Detected	2	3
PreservCyt Specimen			
Abbott *m*2000*sp*	Detected	55	0
	Not Detected	0	55

Potentially Interfering Substances

The potential for interference in the Abbott RealTi*m*e HR HPV assay was assessed with substances that may be present in cervical specimens. HR HPV negative samples and HR HPV positive samples were tested in the presence or absence of each of the substances listed in Table 13. Blood and mucus were spiked into PreservCyt solution at a concentration of 5%, all other substances at a concentration of 0.5%. Interference was not observed with any of the substances tested.

Table 13: Potentially Interfering Substances Tested

Blood
Mucus
CLOTRIMAZOLE Vaginal Cream (2%)
Delfen Vaginal Contraceptive Foam
Gynecort 1% Hydrocortisone Anti-itch Creme
K-Y Jelly
Lubrin
MetroGel-Vaginal
Miconazole Nitrate Vaginal Suppositories USP
Monistat-1 Day or Night Treatment
Norforms Deodorant Suppositories
Terazol-3 Vaginal Cream
Vagi-gard Povidone Iodine Medicated Douche
Vagisil Anti-Itch Creme
Vagisil Intimate Lubricant
Yeast Gard Homeopathic Vaginal Suppositories
Zovirax Cream (Acyclovir) 5%

Performance for Detection of High Risk HPV with Specimens Collected Using Abbott Cervi-Collect Specimen Collection Kit

Specimens collected with the Abbott Cervi-Collect Specimen Collection Kit were tested with the Abbott RealTi*m*e HR HPV assay. Specimens collected in PreservCyt Solution from the same subjects were tested with the Abbott RealTi*m*e HR HPV assay and with HC2. A total of 153 paired specimens that had sufficient volume for all 3 tests were included in the analysis. The high risk HPV status of cervical specimens was determined by the concordance of the Abbott RealTi*m*e HR HPV and HC2 results, and by further analysis of the specimens with discordant results using Linear Array. Among the 70 HR HPV positive specimens, the detection rates were 92.9%, 98.6% and 84.3% for Abbott RealTi*m*e HR HPV using Cervi-Collect specimens, Abbott RealTi*m*e HR HPV using PreservCyt liquid pap specimens and HC2, respectively (Table 14). Among the 83 HR HPV negative specimens, the detection rates were 3.6%, 2.4% and 3.6% for Abbott RealTi*m*e HR HPV using Cervi-Collect specimens, Abbott RealTi*m*e HR HPV using PreservCyt liquid pap specimens and HC2, respectively (Table 14).

Table 14: HR HPV Detection

Test	HR HPV Positive (N=70)		HR HPV Negative (N=83)	
	Number detected	% Detected (95% CI)	Number detected	% Detected (95% CI)
Abbott RealTi*m*e HR HPV with Cervi-Collect	65	92.9 (84.1-97.6)	3	3.6 (0.8-10.2)
Abbott RealTi*m*e HR HPV with PreservCyt Liquid Pap	69	98.6 (92.3-100)	2	2.4 (0.3-8.4)
HC2 with PreservCyt Liquid Pap	59	84.3 (73.6-91.9)	3	3.6 (0.8-10.2)

The agreement in Abbott RealTi*m*e HR HPV results with specimens collected in Cervi-Collect versus specimens collected in PreservCyt Solution from the same patients was 94.4% (Table 15).

Table 15: Agreement between Cervi-Collect and PreservCyt Liquid Pap Specimens

		Abbott RealTi*m*e HR HPV Cervi-Collect	
		Detected	Not Detected
Abbott RealTi*m*e HR HPV PreservCyt Liquid Pap	**Detected**	69	6
	Not Detected	3	83

Agreement = 94.4% (152/161)

Performance for Detection of High Risk HPV with Specimens Collected in SurePath Preservative Fluid

To assess the performance of the Abbott RealTi*m*e HR HPV assay with specimens collected in SurePath Preservative Fluid, a total of 265 specimens collected in SurePath Preservative Fluid were tested with both the Abbott RealTi*m*e HR HPV assay and the HC2 test. Both the sample from the original SurePath collection vial and the remaining cell pellet sample obtained after cytological processing were tested with the Abbott RealTi*m*e HR HPV assay. The cell pellet sample was tested with HC2 per manufacturer's instructions. The high risk HPV status of cervical specimens was determined by the concordance of the Abbott RealTi*m*e HR HPV and HC2 results, and by further analysis of the specimens with discordant results using Linear Array. Of the 265 samples tested, there were 2 samples that returned invalid Linear Array results. Therefore, the comparison between the Abbott RealTi*m*e and HC2 assays was reduced to a total of 263 samples. Among the 138 HR HPV positive specimens, the detection rates were 98.6%, 97.1% and 99.3% for Abbott RealTi*m*e HR HPV using the sample from the original collection vial, Abbott RealTi*m*e HR HPV using the cell pellet sample and HC2, respectively (Table 16). Among the 125 HR HPV negative specimens, the detection rates were 0.0%, 0.0% and 13.6% for Abbott RealTi*m*e HR HPV using the sample from the original collection vial, Abbott RealTi*m*e HR HPV using the cell pellet sample and HC2, respectively (Table 16).

Table 16: HR HPV Detection

Test	HR HPV Positive (N=138)		HR HPV Negative (N=125)	
	Number detected	% Detected (95% CI)	Number detected	% Detected (95% CI)
Abbott RealTi*m*e HR HPV with SurePath samples from Original Collection Vial	136	98.6 (94.9-99.8)	0	0 (0.0-2.9)
Abbott RealTi*m*e HR HPV with SurePath samples from Cell Pellet	134	97.1 (92.7-99.2)	0	0 (0.0-2.9)
HC2 with SurePath samples from Cell Pellet	137	99.3 (96.0-100)	17	13.6 (8.1-20.9)

The agreement in Abbott RealTi*m*e HR HPV results (n=265) with the SurePath sample from the original collection vial versus the cell pellet sample was 99.2% (Table 17).

Table 17: Agreement between SurePath Samples from Original Collection Vial and Cell Pellet

		Abbott RealTi*m*e HR HPV Cell Pellet	
		Detected	Not Detected
Abbott RealTi*m*e HR HPV Original Collection Vial	**Detected**	134	2
	Not Detected	0	129

Agreement = 99.2% (263/265)

Since this comparison examines Abbott testing results only, Linear Array results were not used; therefore, a total of 265 samples were used in the Analysis in Table 17.

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TECHNICAL ASSISTANCE

For technical assistance, call Abbott Technical Services at 1-800-553-7042 (within the US) or +49-6122-580 (outside the US), or visit the Abbott website at www.molecular.abbott.

SUMMARY OF SAFETY AND PERFORMANCE STATEMENT

A summary of safety and performance (SSP) for this device is available at https://ec.europa.eu/tools/eudamed. This is the SSP location after the launch of European Database on Medical Devices. Search for device using UDI-DI provided on the outer packaging of the device.

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Abbott

NOTA PARA EL USUARIO

Si se produjera un incidente grave relacionado con este producto, el incidente debe comunicarse al fabricante y a las autoridades competentes del estado miembro en el que se encuentre el usuario o el paciente. Para ponerse en contacto con el fabricante, consulte la información de contacto indicada en el apartado de Asistencia técnica de estas instrucciones de uso.

Para uso exclusivo por profesionales del laboratorio.

FINALIDAD DE USO

Para uso en diagnóstico *in vitro*. Abbott Real*Time* High Risk HPV Controls (controles) se utilizan para establecer la validez del procesamiento del ensayo Abbott Real*Time* High Risk HPV para la detección del DNA del papilomavirus humano (VPH) de alto riesgo en muestras clínicas.

USUARIO PREVISTO

Los usuarios previstos para el ensayo Abbott Real*Time* High Risk HPV son técnicos de laboratorio y profesionales sanitarios.

CONTENIDO

1. **CONTROL −** **Abbott Real*Time* High Risk HPV Negative Control (control negativo) (n° de ref.: 2N09Z) (12 frascos, 0,5 ml cada uno).** < 0,01% de DNA no infeccioso con secuencia de beta-globina en solución tamponada con DNA portador. Conservantes: azida sódica y ProClin 950 al 0,15%.
2. **CONTROL +** **Abbott Real*Time* High Risk HPV Positive Control (control positivo) (n° de ref.: 2N09A) (12 frascos, 0,5 ml cada uno).** < 0,01% de DNA no infeccioso con secuencias de beta-globina y VPH en solución tamponada con DNA portador. Conservantes: azida sódica y ProClin 950 al 0,15%.

- Abbott Real*Time* High Risk HPV Control Kit (equipo de controles) sólo puede utilizarse con el ensayo Abbott Real*Time* High Risk HPV (nº de ref.: 2N09).

ESTANDARIZACIÓN

La estandarización se lleva a cabo fabricando cada plásmido a una concentración predeterminada.

Para estos plásmidos linearizados dianas, los materiales de origen cualificado son plásmidos purificados procedentes de un proveedor certificado:

- Plásmidos para el control positivo para VPH:
  - Plásmido de DNA para VPH 16
  - Plásmido de DNA para VPH 18
  - Plásmido de DNA para VPH 58
  - Plásmido de DNA para beta globina
- Plásmidos para el control negativo para VPH:
  - Plásmido de DNA para el control interno para VPH

PRECAUCIONES

- **IVD**
- No utilizar una vez transcurrida la fecha de caducidad.

Los componentes de Abbott Real*Time* High Risk HPV Control Kit (equipo de controles, nº de ref.: 2N09-80) contienen lo siguiente:

- 2-metil-2H-isotiazol-3-ona
- Azida sódica

Se aplican las siguientes advertencias:

Advertencia

EUH032	En contacto con ácidos libera gases muy tóxicos.
H317	Puede provocar una reacción alérgica en la piel.
P261	Evitar respirar la niebla/los vapores/el aerosol.
P280	Llevar guantes/prendas/gafas de protección.
P272	Las prendas de trabajo contaminadas no podrán sacarse del lugar de trabajo.
P302+P352	EN CASO DE CONTACTO CON LA PIEL: lavar con agua abundante.
P333+P313	En caso de irritación o erupción cutánea: consultar a un médico.
P362+P364	Quitar las prendas contaminadas y lavarlas antes de volver a usarlas.
P501	Eliminar el contenido/el recipiente conforme a las normativas locales.

−10°C

CONDICIONES PARA EL TRANSPORTE

Transportar con nieve carbónica.

ASISTENCIA TÉCNICA

Si requiere asistencia técnica, póngase en contacto con el Centro de Asistencia Técnica de Abbott (telf.: 1-800-553-7042 si llama desde EE. UU. y telf: +49-6122-580 si llama desde fuera de EE. UU.) o consulte la página web de Abbott en www.molecular.abbott.

ProClin está a nombre de su propietario.

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Diciembre de 2021

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NOTA PER L'UTENTE

Qualora si verifichi un incidente grave associato all'utilizzo del presente dispositivo, tale incidente deve essere segnalato al fabbricante e all'autorità competente appropriata dello Stato membro in cui si trova l'utente e/o il paziente. Per le comunicazioni al fabbricante fare riferimento alle informazioni di contatto indicate nella sezione dedicata al servizio clienti oppure all'assistenza tecnica delle presenti istruzioni.

Esclusivamente per uso professionale in laboratorio.

FINALITÀ D'USO

Per uso diagnostico *in vitro*. Gli Abbott Real*Time* High Risk HPV Controls vengono utilizzati per stabilire la validità della seduta analitica del dosaggio Abbott Real*Time* High Risk HPV nella rilevazione del DNA di papillomavirus umano (HPV) ad alto rischio in campioni clinici.

UTENTI PREVISTI

Il dosaggio Abbott Real*Time* High Risk HPV è destinato all'uso da parte di addetti di laboratorio e personale sanitario qualificato.

CONTENUTO

1. **CONTROL −** **Abbott Real*Time* High Risk HPV Negative Control (n. di listino 2N09Z) (12 flaconi, 0,5 ml per flacone).** DNA non infettivo <0,01% con sequenza di beta globina in una soluzione tamponata con DNA carrier. Conservanti: sodio azoturo e ProClin 950 allo 0,15%.
2. **CONTROL +** **Abbott Real*Time* High Risk HPV Positive Control (n. di listino 2N09A) (12 flaconi, 0,5 ml per flacone).** DNA non infettivo <0,01% con sequenze di HPV e di beta globina in una soluzione tamponata con DNA carrier. Conservanti: sodio azoturo e ProClin 950 allo 0,15%.

- Abbott Real*Time* High Risk HPV Control Kit deve essere utilizzato solamente con il dosaggio Abbott Real*Time* High Risk HPV (n. di listino 2N09).

STANDARDIZZAZIONE

La standardizzazione si ottiene producendo ciascun plasmide a una concentrazione predeterminata.

Per questi target plasmidici linearizzati, i materiali di partenza qualificati sono plasmidi purificati ricevuti da uno o più fornitori certificati:

- Plasmidi del controllo positivo HPV:
  - DNA plasmidico dell'HPV 16
  - DNA plasmidico dell'HPV 18
  - DNA plasmidico dell'HPV 58
  - DNA plasmidico di beta globina
- Plasmidi del controllo negativo HPV:
  - DNA plasmidico del controllo interno HPV

PRECAUZIONI

- **IVD**
- Non usare oltre la data di scadenza.

I componenti di Abbott Real*Time* High Risk HPV Control Kit (n. di listino 2N09-80) contengono i seguenti componenti:

- 2-metil-2H-isotiazol-3-one
- sodio azoturo

Si applicano le seguenti avvertenze:

Attenzione

EUH032	A contatto con acidi libera gas molto tossici.
H317	Può provocare una reazione allergica della pelle.
P261	Evitare di respirare la nebbia/i vapori/aerosol.
P280	Indossare guanti/indumenti protettivi/Proteggere gli occhi.
P272	Gli indumenti da lavoro contaminati non devono essere portati fuori dal luogo di lavoro.
P302+P352	IN CASO DI CONTATTO CON LA PELLE: lavare abbondantemente con acqua.
P333+P313	In caso di irritazione o eruzione della pelle, consultare un medico.
P362+P364	Togliere gli indumenti contaminati e lavarli prima di indossarli nuovamente.
P501	Smaltire il contenuto/recipiente in conformità alla regolamentazione locale.

−10°C

CONDIZIONI DI SPEDIZIONE

Spedire in ghiaccio secco.

ASSISTENZA TECNICA

Per ricevere assistenza tecnica i clienti negli Stati Uniti possono contattare Abbott Technical Services al numero 1-800-553-7042. Al di fuori degli Stati Uniti contattare il numero +49-6122-580 o visitare il sito web Abbott www.molecular.abbott.

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Abbott GmbH
Max-Planck-Ring 2
65205 Wiesbaden, Germany

Dicembre 2021

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AVISO AO UTILIZADOR

Qualquer incidente grave associado a este dispositivo deve ser comunicado ao fabricante e às entidades competentes do estado-membro onde o utilizador e/ou o doente tem estabelecimento permanente. Para comunicações ao fabricante, consultar os dados para contacto na secção Assistência Técnica destas instruções.

Para uso exclusivo por profissionais de laboratório.

FINALIDADE DE USO

Para utilização em diagnóstico *in vitro*. Os controlos Abbott Real*Time* High Risk HPV são utilizados para estabelecer a validade do ensaio Abbott Real*Time* High Risk HPV quando utilizado para a deteção de ADN do papilomavírus humano de alto risco (HPV) em amostras clínicas.

UTILIZADOR PREVISTO

O ensaio Abbott Real*Time* High Risk HPV destina-se a ser utilizado por profissionais de saúde e técnicos de laboratório.

CONTEÚDO

1. **CONTROL −** **Abbott Real*Time* High Risk HPV Negative Control (Nº de Lista 2N09Z) (12 frascos, 0,5 ml por frasco).** <0,01% de ADN não infecioso com sequência de betaglobina numa solução tamponada com ADN transportador. Conservantes: azida sódica e 0,15% de ProClin 950.
2. **CONTROL +** **Abbott Real*Time* High Risk HPV Positive Control (Nº de Lista 2N09A) (12 frascos, 0,5 ml por frasco).** <0,01% de ADN não infecioso com sequências de HPV e de betaglobina numa solução tamponada com ADN transportador. Conservantes: azida sódica e 0,15% de ProClin 950.

- O Abbott Real*Time* High Risk HPV Control Kit só pode ser utilizado com o ensaio Abbott Real*Time* High Risk HPV (Nº de Lista 2N09).

PADRONIZAÇÃO

A padronização é feita através do fabrico de uma concentração predeterminada de cada plasmídeo.

Para estes plasmídeos linearizados alvo, os materiais de origem qualificados são plasmídeos purificados provenientes de um fornecedor ou fornecedores certificados:

- Plasmídeos para controlo positivo do HPV:
  - Plasmídeo de ADN do HPV 16
  - Plasmídeo de ADN do HPV 18
  - Plasmídeo de ADN do HPV 58
  - Plasmídeo de ADN de betaglobina
- Plasmídeos para controlo negativo do HPV:
  - Plasmídeo de ADN para controlo interno do HPV

PRECAUÇÕES

- **IVD**
- Não utilizar após o final do prazo de validade.

Os componentes do Abbott Real*Time* High Risk HPV Control Kit (Nº de lista 2N09-80) contêm os seguintes componentes:

- 2-metil-2H-isotiazol-3-ona
- Azida sódica

Aplicam-se os seguintes avisos:

Atenção

EUH032	Em contacto com ácidos liberta gases muito tóxicos.
H317	Pode provocar uma reação alérgica cutânea.
P261	Evitar respirar as névoas/vapores/aerossóis.
P280	Usar luvas de proteção/vestuário de proteção/proteção ocular.
P272	A roupa de trabalho contaminada não pode sair do local de trabalho.
P302+P352	SE ENTRAR EM CONTACTO COM A PELE: lavar abundantemente com água.
P333+P313	Em caso de irritação ou erupção cutânea: consulte um médico.
P362+P364	Retirar a roupa contaminada e lavá-la antes de a voltar a usar.
P501	Eliminar o conteúdo/recipiente em conformidade com os regulamentos locais.

−10°C

CONDIÇÕES DE TRANSPORTE

Transportar em gelo seco.

ASSISTÊNCIA TÉCNICA

Para assistência técnica, contactar os serviços técnicos Abbott através do número de telefone 800 849 228 ou visitar o sítio do Abbott em www.molecular.abbott.

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Dezembro 2021

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Abbott Real*Time* High Risk HPV

REF 2N09-80

G59198R05

C2N099

CE 0123

Read Highlighted Changes: Revised December 2021.
Bitte Änderungen beachten: Überarbeitet im Dezember 2021.
Faire attention aux modifications: Révision de décembre 2021.
Consulte las modificaciones marcadas: Revisado en diciembre de 2021.
Fare attenzione alle modifiche: Revisione di dicembre 2021.
Consultar as alterações assinaladas: Revisto em dezembro de 2021.

Controls

Key to symbols used
Erläuterung der verwendeten Symbole / Légende des symboles utilisés / Clave de los símbolos utilizados / Legenda dei simboli utilizzati / Legenda dos símbolos utilizados

REF	Reference Number / Bestellnummer / Référence / Número de referencia / Numero di listino / Número de referência
IVD	*In Vitro* Diagnostic Medical Device / In-vitro-Diagnostikum / Dispositif médical de diagnostic *in vitro* / Producto sanitario para diagnóstico *in vitro* / Dispositivo medico-diagnostico *in vitro* / Dispositivo médico para diagnóstico *in vitro*
	Consult instructions for use / Gebrauchsanweisung beachten / Consulter les instructions d'utilisation / Consulte las instrucciones de uso / Consultare le istruzioni per l'uso / Consultar as instruções de utilização
	Upper limit of temperature / Temperaturobergrenze / Conserver jusqu'à / Límite superior de temperatura / Limite di temperatura superiore / Limite superior de temperatura
LOT	Lot Number / Chargenbezeichnung / Numéro de lot / Número de lote / Numero di lotto / Número de lote
CONTROL −	Negative Control / Negative Kontrolle / Contrôle négatif / Control negativo / Controllo negativo / Controlo negativo
CONTROL +	Positive Control / Positive Kontrolle / Contrôle positif / Control positivo / Controllo positivo / Controlo positivo
	Warning / Achtung / Mise en garde / Advertencia / Attenzione / Atenção
	Manufacturer / Hersteller / Fabricant / Fabricante / Fabbricante / Fabricante

Abbott

NOTICE TO USER

If a serious incident occurs in relation to this device, the incident should be reported to the manufacturer and to the appropriate competent authority of the member state in which the user and/or the patient is established. To report to the manufacturer, see the contact information provided in the Customer service section or Technical assistance section of these instructions.

For laboratory professional use only.

INTENDED USE

For In Vitro Diagnostic Use. The Abbott RealTi*m*e High Risk HPV Controls are used to establish run validity of the Abbott RealTi*m*e High Risk HPV assay when used for the detection of high risk human papillomavirus (HPV) DNA in clinical specimens.

INTENDED USER

The intended users for the Abbott RealTi*m*e High Risk HPV assay are laboratory and healthcare professionals.

CONTENTS

1. **CONTROL –** **Abbott RealTi*m*e High Risk HPV Negative Control (List No. 2N09Z)**
   (12 vials, 0.5 mL per vial). <0.01% noninfectious DNA with Beta Globin sequence in a buffered solution with carrier DNA. Preservatives: sodium azide and 0.15% ProClin 950.
2. **CONTROL +** **Abbott RealTi*m*e High Risk HPV Positive Control (List No. 2N09A)**
   (12 vials, 0.5 mL per vial). <0.01% noninfectious DNA with HPV and Beta Globin sequences in a buffered solution with carrier DNA. Preservatives: sodium azide and 0.15% ProClin 950.

- The Abbott RealTi*m*e High Risk HPV Control Kit must only be used with the Abbott RealTi*m*e High Risk HPV assay (List No. 2N09).

STANDARDIZATION

Standardization is achieved by manufacturing to a pre-determined concentration of each plasmid.

For these linearized plasmid targets, the qualified starting materials are purified plasmids that are received from a certified vendor or vendors:

- HPV Positive Control plasmids:
  - HPV 16 DNA Plasmid
  - HPV 18 DNA Plasmid
  - HPV 58 DNA Plasmid
  - Beta Globin DNA Plasmid
- HPV Negative Control plasmids:
  - HPV Internal Control DNA Plasmid

PRECAUTIONS

- **IVD**
- Do not use beyond expiration date.

Components of the Abbott RealTi*m*e High Risk HPV Control Kit (List No. 2N09-80) contain the following components:

- 2-Methyl-2H-isothiazol-3-one
- Sodium azide

The following warnings apply:

Warning

EUH032	Contact with acids liberates very toxic gas.
H317	May cause an allergic skin reaction.
P261	Avoid breathing mist / vapours / spray.
P280	Wear protective gloves / protective clothing / eye protection.
P272	Contaminated work clothing should not be allowed out of the workplace.
P302+P352	IF ON SKIN: Wash with plenty of water.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
P501	Dispose of contents / container in accordance with local regulations.

SHIPPING CONDITIONS

Ship on dry ice.

TECHNICAL ASSISTANCE

For technical assistance, call Abbott Technical Services at 1-800-553-7042 (within the US) or +49-6122-580 (outside the US), or visit the Abbott website at www.molecular.abbott.

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December 2021

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HINWEIS FÜR DEN BENUTZER

Bei schwerwiegenden Vorfällen im Zusammenhang mit diesem Produkt sollte der Vorfall dem Hersteller und der zuständigen Behörde des Landes, in dem der Benutzer und/oder Patient wohnhaft sind, gemeldet werden. Kontaktinformationen zum Hersteller enthält der Abschnitt „Kundendienst" in dieser Packungsbeilage.

Nur für die professionelle Anwendung im Labor.

VERWENDUNGSZWECK

Zur Verwendung als In-vitro-Diagnostikum. Die Abbott RealTi*m*e High Risk HPV Controls dienen zur Sicherstellung der Testgültigkeit des Abbott RealTi*m*e High Risk HPV Assays beim Nachweis von DNA des humanen Hochrisiko-Papillomavirus (HPV) in Patientenproben.

VORGESEHENE BENUTZER

Die vorgesehenen Benutzer des Abbott RealTi*m*e High Risk HPV Assays sind Fachpersonal in Laboren und medizinischen Einrichtungen.

INHALT

1. **CONTROL –** **Abbott RealTi*m*e High Risk HPV Negative Control (Best.-Nr. 2N09Z)**
   (12 Fläschchen, je 0,5 ml). <0,01 % nicht infektiöse DNA mit Beta-Globin-Sequenz in einer gepufferten Lösung mit Träger-DNA. Konservierungsmittel: Natriumazid und 0,15 % ProClin 950.
2. **CONTROL +** **Abbott RealTi*m*e High Risk HPV Positive Control (Best.-Nr. 2N09A)**
   (12 Fläschchen, je 0,5 ml). <0,01 % nicht infektiöse DNA mit HPV und Beta-Globin-Sequenzen in einer gepufferten Lösung mit Träger-DNA. Konservierungsmittel: Natriumazid und 0,15 % ProClin 950.

- Der Abbott RealTi*m*e High Risk HPV Control Kit darf nur mit dem Abbott RealTi*m*e High Risk HPV Assay (Best.-Nr. 2N09) verwendet werden.

STANDARDISIERUNG

Die Standardisierung wird erreicht, indem jedes Plasmid in einer zuvor festgelegten Konzentration hergestellt wird.

Die qualifizierten Ausgangsmaterialien für diese linearisierten Plasmid-Ziele sind gereinigte Plasmide, die von einem oder mehreren zertifizierten Anbietern bezogen werden:

- Plasmide für HPV Positive Kontrolle:
  - HPV 16 DNA-Plasmid
  - HPV 18 DNA-Plasmid
  - HPV 58 DNA-Plasmid
  - Beta-Globin-DNA-Plasmid
- Plasmide für HPV Negative Kontrolle:
  - HPV Interne Kontrolle DNA-Plasmid

VORSICHTSMASSNAHMEN

- **IVD**
- Nicht über das Verfallsdatum hinaus verwenden.

Komponenten des Abbott RealTi*m*e High Risk HPV Control Kit (Best.-Nr. 2N09-80) enthalten die folgenden Bestandteile:

- 2-Methyl-2H-isothiazol-3-on
- Natriumazid

Es gelten die folgenden Gefahrenhinweise:

Achtung

EUH032	Entwickelt bei Berührung mit Säure sehr giftige Gase.
H317	Kann allergische Hautreaktionen verursachen.
P261	Einatmen von Nebel / Dampf / Aerosol vermeiden.
P280	Schutzhandschuhe / Schutzkleidung / Augenschutz tragen.
P272	Kontaminierte Arbeitskleidung nicht außerhalb des Arbeitsplatzes tragen.
P302+P352	BEI BERÜHRUNG MIT DER HAUT: Mit viel Wasser waschen.
P333+P313	Bei Hautreizung oder -ausschlag: Ärztlichen Rat einholen / ärztliche Hilfe hinzuziehen.
P362+P364	Kontaminierte Kleidung ausziehen und vor erneutem Tragen waschen.
P501	Inhalt / Behälter gemäß den geltenden gesetzlichen Vorschriften entsorgen.

TRANSPORTBEDINGUNGEN

Auf Trockeneis versenden.

KUNDENDIENST

Bei Fragen wenden Sie sich bitte an Ihren Abbott Kundendienst unter 1-800-553-7042 (innerhalb der USA) oder +49-6122-580 (außerhalb der USA) oder besuchen Sie die Internetseite von Abbott unter www.molecular.abbott.

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Dezember 2021

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AVIS AUX UTILISATEURS

Si un incident grave se produit avec cet appareil, signaler l'incident au fabricant ainsi qu'aux autorités nationales compétentes du pays dans lequel l'utilisateur et/ou le patient se trouvent. Afin de contacter le fabricant, se reporter aux coordonnées indiquées dans la partie Service Clients ou Assistance technique de cette notice.

Réservé à un usage professionnel en laboratoire.

DOMAINE D'APPLICATION

Pour diagnostic *in vitro*. Les Abbott RealTi*m*e High Risk HPV Controls sont utilisés pour établir la validité du test Abbott RealTi*m*e High Risk HPV lors de la détection de l'ADN du papillomavirus humain (HPV) à haut risque dans les échantillons cliniques.

UTILISATEURS CONCERNES

Le test Abbott RealTi*m*e High Risk HPV est destiné au personnel de laboratoire et aux professionnels de santé.

COMPOSITION

1. **CONTROL –** **Abbott RealTi*m*e High Risk HPV Negative Control (Réf. 2N09Z)**
   (12 flacons de 0,5 ml chacun). < 0,01 % d'ADN non infectieux avec une séquence bêta-globine dans une solution tampon contenant de l'ADN entraîneur. Conservateurs : azide de sodium et ProClin 950 à 0,15 %.
2. **CONTROL +** **Abbott RealTi*m*e High Risk HPV Positive Control (Réf. 2N09A)**
   (12 flacons de 0,5 ml chacun). < 0,01 % d'ADN non infectieux avec de l'HPV et des séquences bêta-globine dans une solution tampon contenant de l'ADN entraîneur. Conservateurs : azide de sodium et ProClin 950 à 0,15 %.

- L'Abbott RealTi*m*e High Risk HPV Control Kit ne doit être utilisé qu'avec le test Abbott RealTi*m*e High Risk HPV (Réf. 2N09).

STANDARDISATION

La standardisation est obtenue par la fabrication à une concentration prédéterminée de chaque plasmide.

Pour ces cibles de plasmides linéarisés, les substances de départ qualifiées sont des plasmides purifiés obtenus auprès d'un ou de fournisseur(s) certifié(s) :

- Plasmides du contrôle positif HPV :
  - ADN plasmidique de l'HPV 16
  - ADN plasmidique de l'HPV 18
  - ADN plasmidique de l'HPV 58
  - ADN plasmidique bêta-globine
- Plasmides du contrôle négatif HPV :
  - ADN plasmidique de l'HPV de contrôle interne

PRECAUTIONS

- **IVD**
- Ne pas utiliser au-delà de la date de péremption.

L'Abbott RealTi*m*e High Risk HPV Control Kit (Réf. 2N09-80) contient les composants suivants :

- 2-méthyl-2H-isothiazole-3-one
- Azide de sodium

Les mises en garde suivantes s'appliquent :

Mise en garde

EUH032	Au contact d'un acide, dégage un gaz très toxique.
H317	Peut provoquer une allergie cutanée.
P261	Eviter de respirer les brouillards / vapeurs / aérosols.
P280	Porter des gants de protection / des vêtements de protection / un équipement de protection des yeux.
P272	Les vêtements de travail contaminés ne devraient pas sortir du lieu de travail.
P302+P352	EN CAS DE CONTACT AVEC LA PEAU : Laver abondamment à l'eau.
P333+P313	En cas d'irritation ou d'éruption cutanée : Consulter un médecin.
P362+P364	Enlever les vêtements contaminés et les laver avant réutilisation.
P501	Eliminer le contenu / récipient conformément aux réglementations locales.

CONDITIONS D'EXPEDITION

Expédier sur de la carboglace.

ASSISTANCE TECHNIQUE

Pour obtenir une assistance technique, appeler le Service Clients Abbott au 1-800-553-7042 (aux Etats-Unis) ou au +49-6122-580 (en dehors des Etats-Unis), ou consulter le site Internet d'Abbott à l'adresse suivante : www.molecular.abbott.

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Décembre 2021

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