U.S. FOOD & DRUG ADMINISTRATION

Welcome To Today's Webinar

Thanks for joining us!
We'll get started in a few minutes

Today's Topic:
Labeling Requirements for In Vitro Diagnostic Products (IVD), Including LDTs, Under 21 CFR 809.10(b)

September 24, 2024

Labeling for In Vitro Diagnostic Products (IVDs), Including Laboratory Developed Tests (LDTs), Under 21 CFR 809.10(b)

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Office of Health Technology 7: Office of In Vitro Diagnostic Devices
Office of Product Evaluation and Quality

Center for Devices and Radiological Health
U.S. Food and Drug Administration

Phaseout Policy for IVDs offered as LDTs: Stage 2

Requirements NOT Covered in Other Stages of the Phaseout Policy, Including:

Labeling for In Vitro Diagnostic Products
21 CFR Parts 801, 809

Compliance expected by May 6, 2026, for most IVDs offered as LDTs

[Laboratory Developed Tests | FDA]

Learning Objectives

- Understand labeling requirements for in vitro diagnostic products (IVDs) under 21 CFR 809.10(b)
- Understand compliance with labeling requirements for test systems that are IVDs offered as LDTs

Labeling

Labeling is defined under section 201 of the Federal Food, Drug, and Cosmetic Act

"all labels and other written, printed, or graphic matter upon any article or any of its containers or wrappers, or accompanying such article."

21 CFR Part 801
MEDICAL DEVICES LABELING

21 CFR Part 809
IN VITRO DIAGNOSTIC PRODUCTS FOR HUMAN USE

21 CFR Section 809.10
Labeling for in vitro diagnostic products

809.10(b)
Labeling accompanying an IVD

What is labeling accompanying an IVD and why is it important?

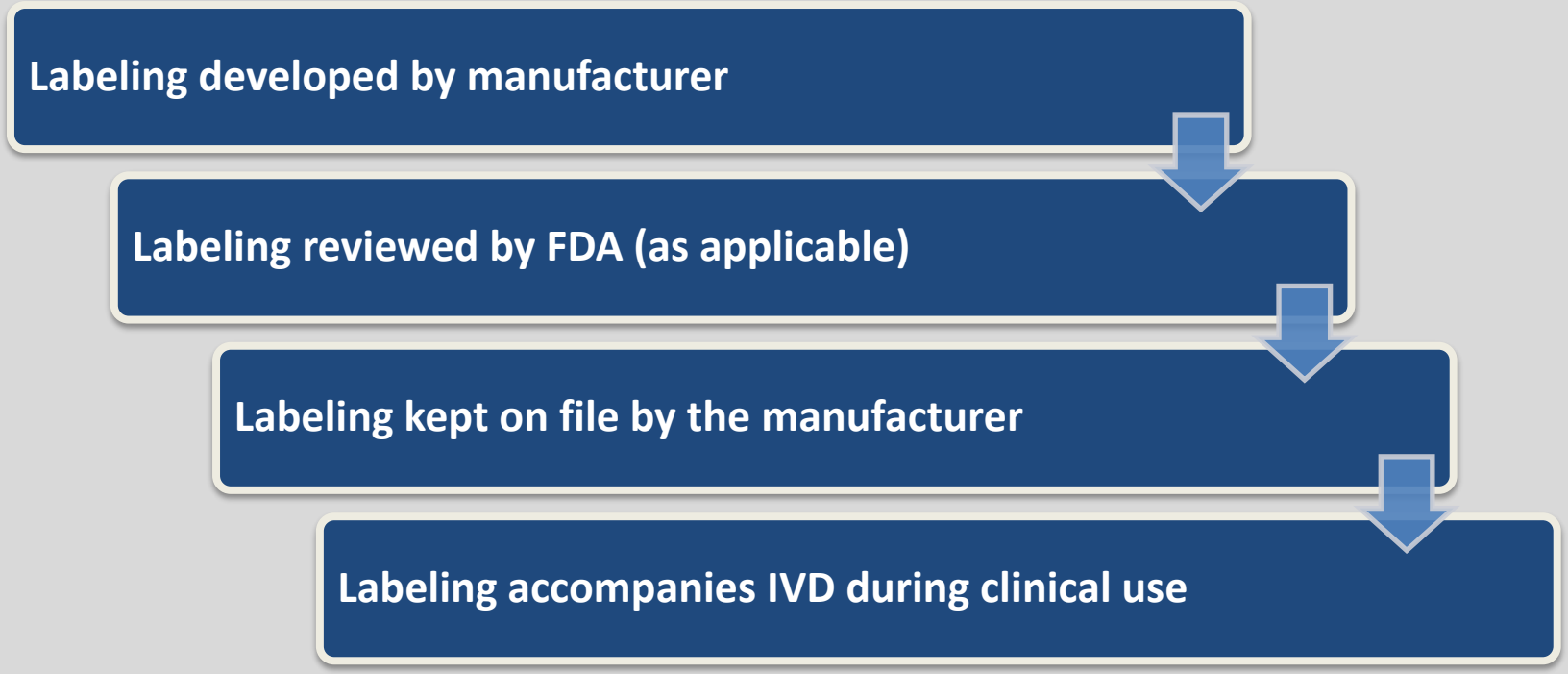
Labeling accompanying an IVD may include one or more of the following:

- **Package Insert**
- **Test Protocol**
- **Reagent and instrument specification documents**
- **Test Menu**
- **Test Report Template**

Labeling provides users, HCPs, and patients information on the IVD including its use, limitations, and performance.

Labeling must prominently display all required information and be truthful and non-misleading. An IVD without such labeling would be **misbranded**.

Labeling Process for IVDs



FDA Expectations for Submission of Labeling for IVDs offered as LDTs

Provide labeling as part of premarket review submission

- IVDs offered as LDTs that are not exempt from premarket review

No submission of labeling to FDA

- IVDs exempt from premarket review
- Modified version of another manufacturer's FDA-authorized test within scope described in preamble to LDT Final Rule
- LDT, non-molecular antisera for rare RBC antigens when there is no alternative IVD

FDA intends to request submission of labeling at the time of device listing

- IVD offered as LDT, first marketed before May 6, 2024, not modified beyond scope described in preamble to LDT Final Rule
- LDT, unmet need within an integrated healthcare system
- LDT, approved by NYS CLEP

*This information is intended to provide a high-level overview of when labeling is submitted to FDA for IVDs offered as LDTs. This table does not address all IVDs (e.g., tests for 564 declarations). Please refer to the preamble to the rule for additional details and policies.

Labeling Requirements Under 809.10(b)

21 CFR 809.10(b)

- (1) Name of Product
- (2) Intended Use
- (3) Summary and Explanation of Test
- (4) Principles of the Procedure
- (5) Reagents
- (6) Instruments
- (7) Specimen Collection/Preparation
- (8) Procedure
- (9) Results
- (10) Limitations
- (11) Expected Values
- (12) Specific Performance Characteristics
- (13) Bibliography
- (14) Name/Place of Business
- (15) Date of Issuance of Labeling

Examples of how to comply with labeling requirements under 809.10(b) for test systems, including LDTs

Labeling can be presented in different formats.

For LDTs, the required information might be contained in more than one document, such as the test protocol, test report template, and test menu.

Name and Intended Use

Example: FoundationFocus™ CDX$_{BRCA}$

809.10(b)(1)

The proprietary name and established name (common or usual name), if any

809.10(b)(2)

The intended use or uses of the product and the type of procedure, e.g., qualitative or quantitative

FoundationFocus CDx*BRCA*
Technical Information

Foundation Medicine, Inc.
150 Second Street, Cambridge, MA 02141
Phone: 617.418.2200

1. Intended Use

The FoundationFocus™ CDx*BRCA* is a next generation sequencing based *in vitro* diagnostic device for qualitative detection of *BRCA1* and *BRCA2* alterations in formalin-fixed paraffin-embedded (FFPE) ovarian tumor tissue. The FoundationFocus CDx*BRCA* assay detects sequence alterations in *BRCA1* and *BRCA2* (*BRCA1/2*) genes. Results of the assay are used as an aid in identifying ovarian cancer patients for whom treatment with Rubraca™ (rucaparib) is being considered. If a patient is positive for any of the deleterious alterations specified in the *BRCA1/2* classification, the patient may be eligible for treatment with Rubraca. This assay is to be performed at Foundation Medicine, Inc., a single laboratory site located at 150 Second Street, Cambridge, MA 02141.

Summary and Explanation

809.10(b)(3)

Include a short history of the methodology, with pertinent references and a balanced statement of the special merits and limitations of this method or product. If the product labeling refers to any other procedure, appropriate literature citations shall be included and the labeling shall explain the nature of any differences from the original and their effect on the results.

Example: ARUP Laboratories AAV5 DetectCDx

Summary and explanation of the test:

The AAV5 DetectCDx™ uses a bridging immunoassay to detect antibodies to AAV5 in human sodium [illegible] plasma specimens. The AAV5 DetectCDx™ uses a combination of concurrently conducted screening and confirmatory steps to reliably detect antibodies specific for AAV5 capsid. Patients evaluated with the AAV5 DetectCDx™ who are anti-AAV5 antibody negative (result of Not Detected) are eligible for treatment with valoctocogene roxaparvovec-rvox (ROCTAVIAN) under the supervision of a physician. Patients evaluated with the AAV5 DetectCDx™ who are anti-AAV5 antibody positive (result of Detected) are not eligible for treatment with ROCTAVIAN.

Valoctocogene roxaparvovec-rvox (ROCTAVIAN), or AAV5-hFVIII-SQ drug product, is a gene therapy treatment for severe hemophilia A, an X-linked recessive bleeding disorder that affects approximately 1 in 5,000 males. Hemophilia A is caused by deficiency in the activity of coagulation factor VIII (FVIII), an essential cofactor in the intrinsic coagulation cascade. This disorder can be inherited or acquired, leading to insufficient quantities of FVIII or a dysfunctional FVIII.

ROCTAVIAN is an adeno-associated virus serotype 5 (AAV5)-based gene therapy vector that expresses the SQ form of human FVIII (hFVIII-SQ) under the control of a liver-specific promoter. The AAV5 viral capsid mediates binding and uptake into cells, as well as trafficking to the cell nucleus. The vector genome contains a transgene expression cassette inserted between the AAV DNA terminal sequences (referred to as ITRs). After unpackaging of the vector genome in the cell nucleus, recombination between the ITRs generates double-stranded, circular vector genomes that persist mainly as un-integrated episomes. The transgene codes for an active form of FVIII that is used in the coagulation process. ROCTAVIAN is delivered by single intravenous dose and was designed to achieve stable expression of active FVIII in the plasma, synthesized from vector-transduced liver tissue.

Since pre-existing anti-AAV5 antibodies may neutralize ROCTAVIAN, only patients who demonstrate no detectable anti-AAV5 antibodies as determined by the AAV5 DetectCDx will be eligible for treatment with ROCTAVIAN. The presence of neutralizing activity against AAV capsids in non-human primates (NHPs) can inhibit liver transduction and expression of the transgene product (Jiang, 2006, Blood); (Wang, 2011, Hum Gene Ther), while immune-deficient mice reconstituted with purified human immunoglobulins demonstrated a titer-dependent reduction in transgene expression when dosed with AAV vectors (Scallan

Statement of the special merits of the test.

Summarizes and explains the clinical context for test

Summarizes and explains the history of the method and analyte being measured by the test, with references

Statement of the limitations of the test

Warnings and precautions:

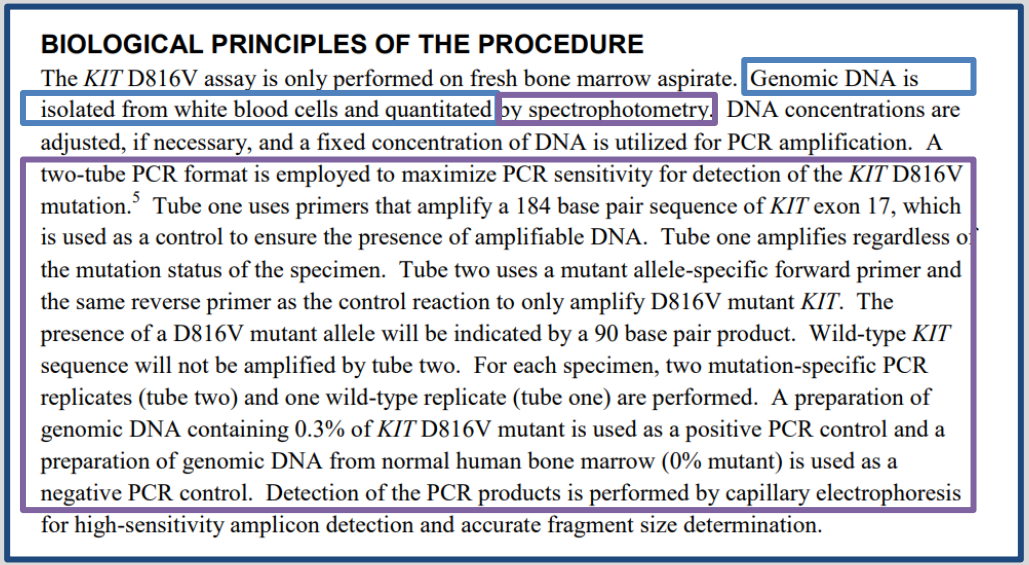
- When drawing blood for the AAV5 DetectCDx™ assay, universal pre[illegible]tions for bloodborne pathogens should be observed.
- Patients with rheumatoid factor levels greater than 476 IU/mL will interfere with the ability for the AAV5 DetectCDx™ to accurately detect anti-AAV5 antibodies.
- Patient samples with triglyceride levels greater than 500 mg/dL will interfere with the ability of the AAV5 DetectCDx™ to accurately detect anti-AAV5 antibodies.

Principles of the Procedure

809.10(b)(4)

- The chemical, physical, physiological, or biological principles of the procedure.
- Explain concisely, with chemical reactions and techniques involved, if applicable

Example: *KIT* D816V Mutation Detection by PCR for Gleevec Eligibility in Aggressive Systemic Mastocytosis



BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The *KIT* D816V assay is only performed on fresh bone marrow aspirate. Genomic DNA is isolated from white blood cells and quantitated by spectrophotometry. DNA concentrations are adjusted, if necessary, and a fixed concentration of DNA is utilized for PCR amplification. A two-tube PCR format is employed to maximize PCR sensitivity for detection of the *KIT* D816V mutation.[5] Tube one uses primers that amplify a 184 base pair sequence of *KIT* exon 17, which is used as a control to ensure the presence of amplifiable DNA. Tube one amplifies regardless of the mutation status of the specimen. Tube two uses a mutant allele-specific forward primer and the same reverse primer as the control reaction to only amplify D816V mutant *KIT*. The presence of a D816V mutant allele will be indicated by a 90 base pair product. Wild-type *KIT* sequence will not be amplified by tube two. For each specimen, two mutation-specific PCR replicates (tube two) and one wild-type replicate (tube one) are performed. A preparation of genomic DNA containing 0.3% of *KIT* D816V mutant is used as a positive PCR control and a preparation of genomic DNA from normal human bone marrow (0% mutant) is used as a negative PCR control. Detection of the PCR products is performed by capillary electrophoresis for high-sensitivity amplicon detection and accurate fragment size determination.

Specimen Collection and Preparation

809.10(b)(7)

Specimen collection and preparation for analysis, including a description of:

(i) Special precautions regarding specimen collection including special preparation of the patient as it bears on the validity of the test.

(ii) Additives, preservatives, etc., necessary to maintain the integrity of the specimen.

(iii) Known interfering substances.

(iv) Recommended storage, handling or shipping instructions for the protection and maintenance of stability of the specimen.

Example: FoundationFocus™ CDX_{BRCA}

Sample Collection and Test Ordering

To order the FoundationFocus CDx_{BRCA} assay, the Test Requisition Form (TRF) included in the test kit must be fully completed and signed by the ordering physician or other authorized medical professional. Please refer to Specimen Preparation Instructions and mailing instructions include in the test kit.

Specimen Collection and Preparation

Example: FoundationFocus™ CDx$_{BRCA}$

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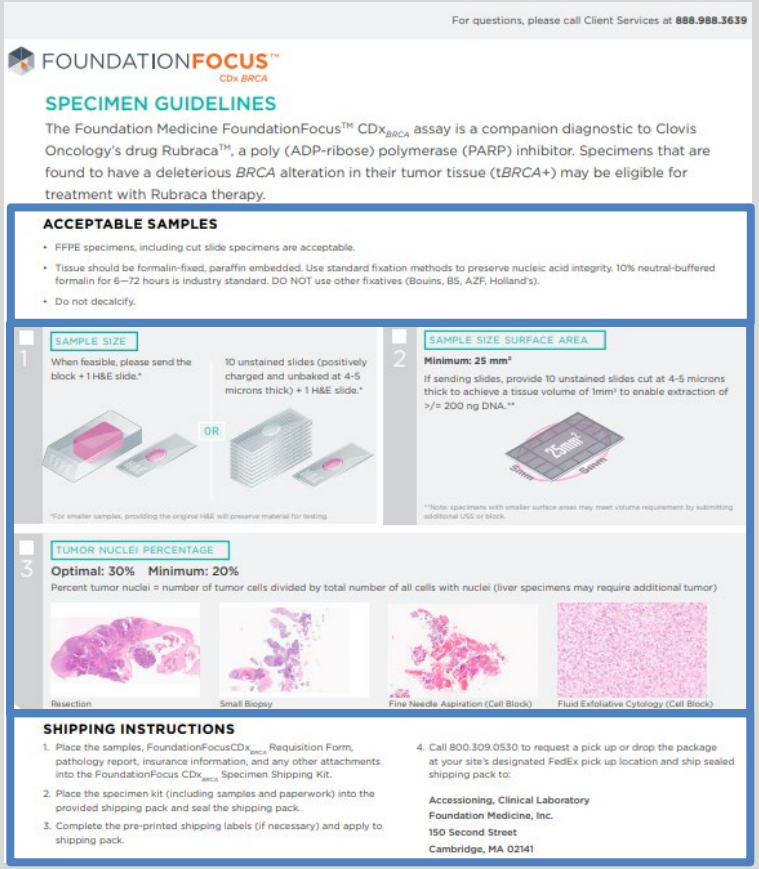

For questions, please call Client Services at **888.988.3639**

FOUNDATIONFOCUS™ CDx BRCA

SPECIMEN GUIDELINES

The Foundation Medicine FoundationFocus™ CDx$_{BRCA}$ assay is a companion diagnostic to Clovis Oncology's drug Rubraca™, a poly (ADP-ribose) polymerase (PARP) inhibitor. Specimens that are found to have a deleterious *BRCA* alteration in their tumor tissue (t*BRCA*+) may be eligible for treatment with Rubraca therapy.

ACCEPTABLE SAMPLES

- FFPE specimens, including cut slide specimens are acceptable.
- Tissue should be formalin-fixed, paraffin embedded. Use standard fixation methods to preserve nucleic acid integrity. 10% neutral-buffered formalin for 6–72 hours is industry standard. DO NOT use other fixatives (Bouins, B5, AZF, Holland's).
- Do not decalcify.

1 SAMPLE SIZE

When feasible, please send the block + 1 H&E slide.*

10 unstained slides (positively charged and unbaked at 4-5 microns thick) + 1 H&E slide.*

OR

*For smaller samples, providing the original H&E will preserve material for testing.

2 SAMPLE SIZE SURFACE AREA

Minimum: 25 mm²

If sending slides, provide 10 unstained slides cut at 4-5 microns thick to achieve a tissue volume of 1mm³ to enable extraction of >/= 200 ng DNA.**

25mm²

5mm 5mm

**Note: specimens with smaller surface areas may meet volume requirement by submitting additional USS or block.

3 TUMOR NUCLEI PERCENTAGE

Optimal: 30% Minimum: 20%

Percent tumor nuclei = number of tumor cells divided by total number of all cells with nuclei (liver specimens may require additional tumor)

Resection | Small Biopsy | Fine Needle Aspiration (Cell Block) | Fluid Exfoliative Cytology (Cell Block)

SHIPPING INSTRUCTIONS

1. Place the samples, FoundationFocusCDx$_{BRCA}$ Requisition Form, pathology report, insurance information, and any other attachments into the FoundationFocus CDx$_{BRCA}$ Specimen Shipping Kit.
2. Place the specimen kit (including samples and paperwork) into the provided shipping pack and seal the shipping pack.
3. Complete the pre-printed shipping labels (if necessary) and apply to shipping pack.
4. Call 800.309.0530 to request a pick up or drop the package at your site's designated FedEx pick up location and ship sealed shipping pack to:

Accessioning, Clinical Laboratory
Foundation Medicine, Inc.
150 Second Street
Cambridge, MA 02141

Specimen Collection and Preparation

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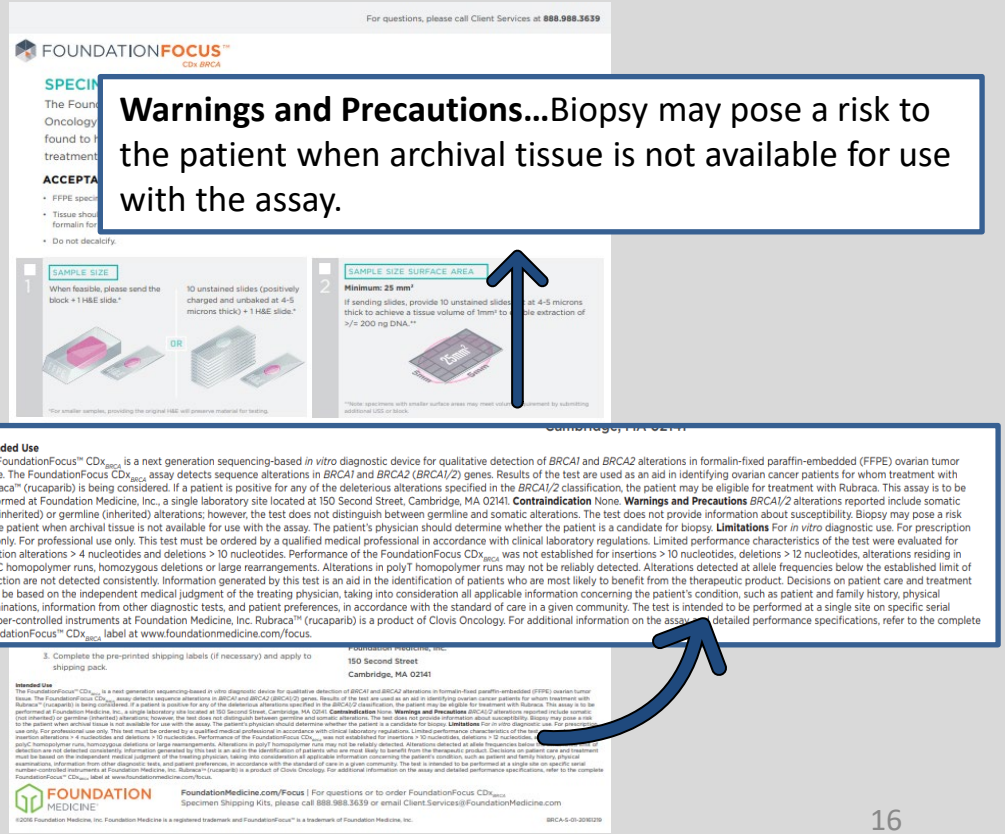

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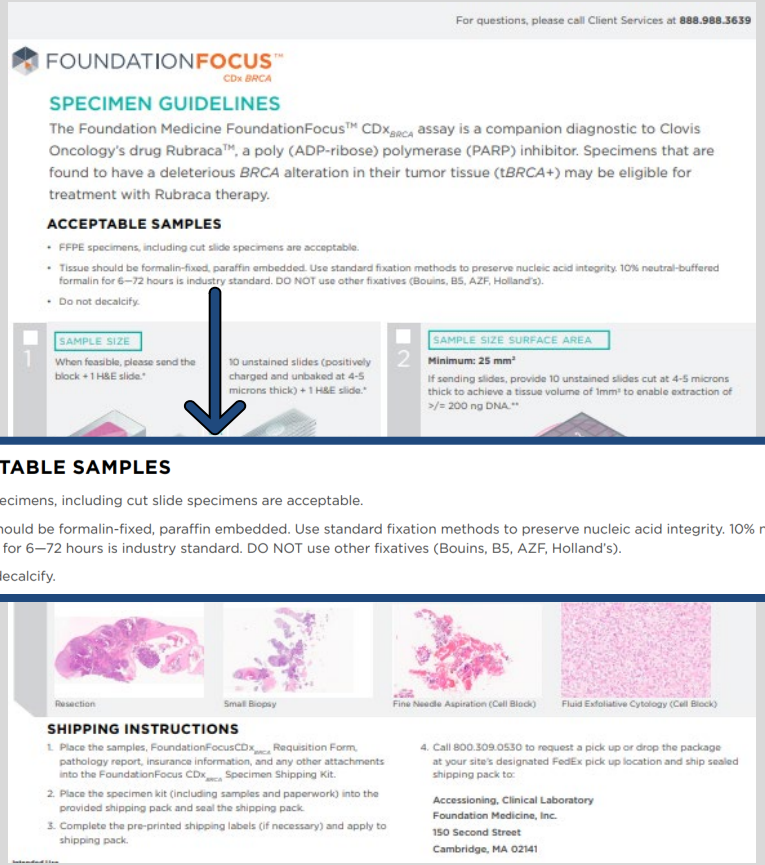

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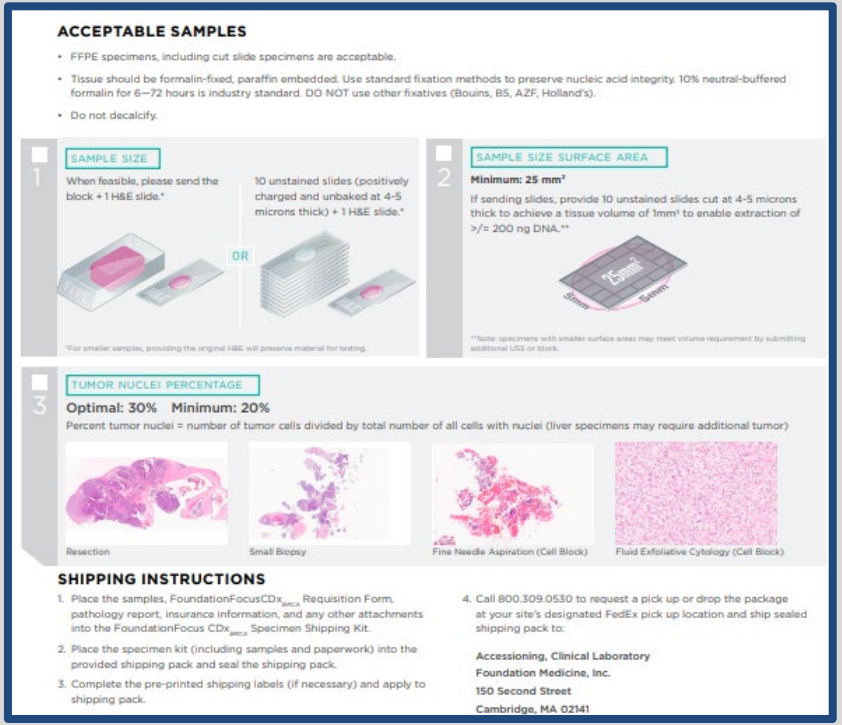

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Specimen Collection and Preparation

Example:

[ARUP Laboratories AAV5 DetectCDx]

Collection Instructions

- Collect the patient's whole blood in a 3.2% sodium citrate tube.
- Samples that exceed 7.3% sodium citrate cannot be evaluated and may require patient redraw.
- NOTE: When drawing blood for the AAV5 DetectCDx test, universal precautions for bloodborne pathogens should be observed.
- Centrifuge the specimen and separate the plasma within 72 hours of collection. Refer to your manufacturer's manual for recommended centrifuge speed and duration.
- Transfer 1 mL (minimum: 0.5 mL) of plasma into a polypropylene pour-off (transport) tube. Sample stability for the AAV5 DetectCDx™ has not been evaluated in tube types other than the ARUP Transport Tube (polypropylene).
- Failure to provide sufficient volume may result in the need for patient redraw.
- Label the transport tube with the patient's first and last name, date of birth, and sex.
- Freeze plasma specimen at -10°C or below.
- Ship frozen plasma specimens to ARUP as soon as possible on dry ice and use overnight delivery to ensure next day arrival at ARUP. NOTE: Plasma specimens must be frozen before they are shipped to ARUP Laboratories.
- Plasma samples can be stored frozen (-10 to -70°C) for up to 12 months. Minimize number of freeze/thaw events, not to exceed 6 events.

Example: [Alinity m HR HPV AMP]

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Collection

Users must follow the respective manufacturer's instructions for collecting cervical specimens in ThinPrep PreservCyt Solution (Hologic Inc.) or SurePath Preservative Fluid (BD).

Specimen Type

Specimens collected using an endocervical brush/spatula and placed in ThinPrep PreservCyt Solution or using a cervical broom-like collection device and placed in SurePath Preservative Fluid can be used with the Alinity m HR HPV assay. For ThinPrep and SurePath specimens, the aliquot that is removed either prior to or after cytological processing from the collection vial can be used. The aliquot can be transferred to Alinity m Transport Tube (List No. 09N49-010 or 09N49-011) or Alinity m Labeled Tube with Pierceable Cap (List No. 09N65-050) and capped with Alinity m Pierceable Cap provided separately (List No. 09N49-012) or together with the tube (List No. 09N49-010 or 09N49-011) for storage.

Alinity m HR HPV assay performance with other collection devices or specimen types has not been evaluated.

The instrument does not provide the capability to verify specimen types. It is the responsibility of the operator to use the correct specimen types in the assay.

Specimen Storage

Collection Medium	Temperature	Maximum Storage Time[a]
ThinPrep PreservCyt Solution	15°C to 30°C	6 Months
	2°C to 8°C	6 Months
	−25°C to −15°C	6 Months
SurePath Preservative Fluid	15°C to 30°C	14 Days
	2°C to 8°C	3 Months
	−25°C to −15°C	3 Months

[a] From date of collection.

Specimen Shipping

Ship specimens according to the recommended storage temperature and time listed in the **Specimen Storage** section. Package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical, diagnostic, or biological specimens.

Preparation for Analysis

ThinPrep specimens and SurePath specimens need to be transferred to an Alinity m Transport Tube (List No. 09N49-010 or 09N49-011) or Alinity m Labeled Tube with Pierceable Cap (List No. 09N65-050) for processing on the Alinity m System. Vortex each specimen for 15 to 20 seconds. Ensure that the contents in the ThinPrep or SurePath vial are on the bottom by tapping the vial on the bench.

Immediately transfer a volume of each specimen based on aliquot source to a transport tube prior to loading on the Alinity m System.

Specimen Type	Aliquot Source	Transport Tube Specimen Volume[c]
ThinPrep	Pre-Cytology Specimen[a]	0.55 mL – 2.0 mL
	Post-Cytology Specimen	
	Specimen Not Intended for Cytology	
SurePath	Pre-Cytology Specimen[b]	0.5 mL (single aliquot)
	Post-Cytology Specimen	0.5 mL – 2.0 mL
	Specimen Not Intended for Cytology	

[a] No more than a single aliquot may be removed from the ThinPrep specimen prior to cytology processing. Refer to manufacturer's instructions for use.

[b] No more than a single aliquot (no more than 0.5 mL) can be removed from the SurePath specimen prior to cytology processing. Refer to manufacturer's instructions for use.

[c] Transport tube specimen volume includes 0.4 mL instrument aspiration volume and dead volume.

The transport tubes may be capped with an Alinity m Pierceable Cap (List No. 09N49-012). When handling specimens in transport tubes, do not touch the top of pierceable caps to avoid contamination. All specimen tubes must be labeled with specimen ID barcodes, or must be identified with a specimen ID and rack and position.

Note: Do not use specimens which appear bloody or have a dark brown color.

Procedure

809.10(b)(8)

Procedure: A step-by-step outline of recommended procedures from reception of the specimen to obtaining results. List any points that may be useful in improving precision and accuracy.

809.10(b)(8)(i) A list of all materials provided, e.g., reagents, instruments and equipment, with instructions for their use.

809.10(b)(8)(ii) A list of all materials required but not provided. Include such details as sizes, numbers, types, and quality.

809.10(b)(8)(iii) A description of the amounts of reagents necessary, times required for specific steps, proper temperatures, wavelengths, etc.

809.10(b)(8)(iv) A statement describing the stability of the final reaction material to be measured and the time within which it shall be measured to assure accurate results.

809.10(b)(8)(v) Details of calibration: Identify reference material. Describe preparation of reference sample(s), use of blanks, preparation of the standard curve, etc. The description of the range of calibration should include the highest and the lowest values measurable by the procedure.

809.10(b)(8)(vi) Details of kinds of quality control procedures and materials required. If there is need for both positive and negative controls, this should be stated. State what are considered satisfactory limits of performance.

For LDTs, this information is typically contained in more than one document. Most commonly, high-level information on the procedure is included as a summary in a "primary" labeling document while more detailed procedures are described in the test protocol

Procedure

Example: [ARUP Laboratories AAV5 DetectCDx]

Principles of the test procedure:

The AAV5 DetectCDx™ is to be performed only at ARUP Laboratories, a single laboratory site located at 500 Chipeta Way, Salt Lake City, UT 84108.

A MULTI-ARRAY® 96-well plate is coated with unlabeled AAV5-CMV-GFP capsid, washed, blocked with assay diluent containing casein, and washed again. The patient plasma specimen is diluted and then added in duplicate to specific wells of the plate. If anti-AAV5 antibodies are present in the specimen, they will bind to the unlabeled AAV5-CMV-GFP capsid coating the wells. After incubation with patient specimen, the plate is washed, and SULFO-TAG AAV5-CMV-GFP capsid is added to each well. Anti-AAV5 antibodies bind to SULFO-TAG capsid (also referred to as ruthenylated capsid), which participates in an electrochemiluminescence (ECL) reaction. After incubation and washing, tripropylamine (TPA) substrate is added to each well. The plate is read on a research use only (RUO) ECL-based plate reader. Each well of the plate is electrically stimulated and the resultant ECL signal is measured.

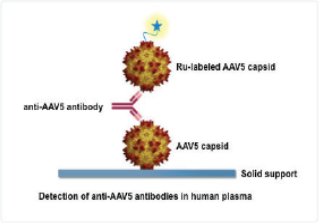


Figure 1. Anti-AAV5 antibody forms a bridge between AAV5 capsid coating the immunoassay plate and ruthenylated AAV5 capsid. The Ru-label participates in the generation of an electrochemiluminescent signal that indicates the presence of anti-AAV5 antibodies.

Each 96-well plate includes a cut point control (CC), negative control (NEG), a low antibody positive control (LPC), and a high antibody positive control (HPC). For run acceptance, the NEG, CC, HPC, and LPC must meet the pre-established criteria for the between-well coefficient of variation (CV) for replicate wells. The HPC and LPC must screen and confirm positive, and the HPC, LPC, and NEG signals must fall within the established acceptance range.

Results for the screening step are expressed as a Screen Index (SI). The SI is calculated by dividing the normalized screening result by the screening cut point. Results for the confirmatory step are expressed as a Confirm Index (CI). The confirm index (CI) is obtained by calculating the ratio of mean signals obtained for the confirmatory and screening assays and dividing this by the confirmatory cut point. The CI is not considered if anti-AAV5 antibodies are not detected in the screening step. Results are based on the values obtained for the SI and CI (see Figure 2):

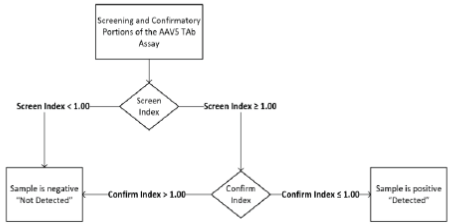


Figure 2. Summary of resulting and reporting for the two-step AAV5 DetectCDx™

Specimens with SI < 1.00, or SI ≥ 1.00 with a CI > 1.00, are reported as Not Detected for anti-AAV5 antibodies.

Specimens with SI ≥ 1.00 and CI ≤ 1.00 are reported as Detected for anti-AAV5 antibodies.

Reagents:

The primary reagents for the AAV5 DetectCDx™ include:

AAV5 DetectCDx™ Reagents and Storage Conditions

Reagent	Storage Conditions	Component(s)
AAV5 Coated Plate Set	Refrigerated (2 to 8 °C)	• MULTI-ARRAY® 96-well plate • AAV5 Confirmatory Reagent • AAV5 Detection Reagent
AAV5 Control Set	Frozen (-70 °C)	• Low positive control • High positive control • Cut point control • Negative control
Read Buffer T (1X)	Room temperature (20 to 25 °C)	Read Buffer T (1X)

Additional reagents used in the AAV5 DetectCDx:

- TBS Buffer (1X) with 1% casein
- 1X DPBS
- Tween 20 (proteomics grade), 1.0% (v/v)
- ProClin 300, 0.05% (v/v)

Instruments: The MULTI-ARRAY® 96-well plate used in the AAV5 DetectCDx™ is read on a MESO QuickPlex SQ 120 instrument, as identified by a specific serial number.

General laboratory instruments and materials that are also used in the AAV5 DetectCDx™ include:

- Refrigerator capable of 2 to 8 °C
- Freezers capable for -10 °C or colder and -70 °C or colder
- Single-channel pipette set
- Multi-channel pipettes
- Vortex mixer
- Minicentrifuge capable of 400 RPM
- Microplate shaker
- Microplate washer
- Microplate adhesive film
- PCR aluminum sealing film
- 0.2 mL and 1.2 mL 8-well strip tubes with cap

Procedure

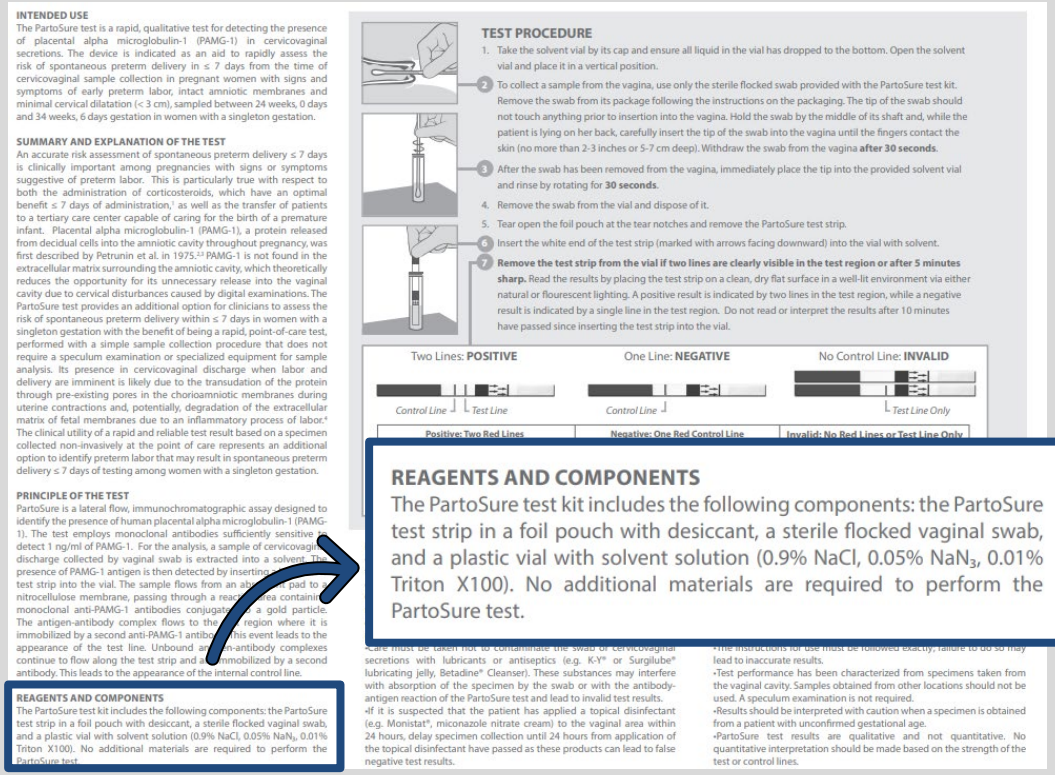
809.10(b)(8)(i)

A list of all materials provided, e.g., reagents, instruments and equipment, with instructions for their use.

809.10(b)(8)(ii)

A list of all materials required but not provided. Include such details as sizes, numbers, types, and quality.

Example: PartoSure Test



INTENDED USE

The PartoSure test is a rapid, qualitative test for detecting the presence of placental alpha microglobulin-1 (PAMG-1) in cervicovaginal secretions. The device is indicated as an aid to rapidly assess the risk of spontaneous preterm delivery in ≤ 7 days from the time of cervicovaginal sample collection in pregnant women with signs and symptoms of early preterm labor, intact amniotic membranes and minimal cervical dilatation (< 3 cm), sampled between 24 weeks, 0 days and 34 weeks, 6 days gestation in women with a singleton gestation.

SUMMARY AND EXPLANATION OF THE TEST

An accurate risk assessment of spontaneous preterm delivery ≤ 7 days is clinically important among pregnancies with signs or symptoms suggestive of preterm labor. This is particularly true with respect to both the administration of corticosteroids, which have an optimal benefit ≤ 7 days of administration,[1] as well as the transfer of patients to a tertiary care center capable of caring for the birth of a premature infant. Placental alpha microglobulin-1 (PAMG-1), a protein released from decidual cells into the amniotic cavity throughout pregnancy, was first described by Petrunin et al. in 1975.[2,3] PAMG-1 is not found in the extracellular matrix surrounding the amniotic cavity, which theoretically reduces the opportunity for its unnecessary release into the vaginal cavity due to cervical disturbances caused by digital examinations. The PartoSure test provides an additional option for clinicians to assess the risk of spontaneous preterm delivery within ≤ 7 days in women with a singleton gestation with the benefit of being a rapid, point-of-care test, performed with a simple sample collection procedure that does not require a speculum examination or specialized equipment for sample analysis. Its presence in cervicovaginal discharge when labor and delivery are imminent is likely due to the transudation of the protein through pre-existing pores in the chorioamniotic membranes during uterine contractions and, potentially, degradation of the extracellular matrix of fetal membranes due to an inflammatory process of labor.[4] The clinical utility of a rapid and reliable test result based on a specimen collected non-invasively at the point of care represents an additional option to identify preterm labor that may result in spontaneous preterm delivery ≤ 7 days of testing among women with a singleton gestation.

PRINCIPLE OF THE TEST

PartoSure is a lateral flow, immunochromatographic assay designed to identify the presence of human placental alpha microglobulin-1 (PAMG-1). The test employs monoclonal antibodies sufficiently sensitive to detect 1 ng/ml of PAMG-1. For the analysis, a sample of cervicovaginal discharge collected by vaginal swab is extracted into a solvent. The presence of PAMG-1 antigen is then detected by inserting the test strip into the vial. The sample flows from an absorbent pad to a nitrocellulose membrane, passing through a reagent area containing monoclonal anti-PAMG-1 antibodies conjugated to a gold particle. The antigen-antibody complex flows to the test region where it is immobilized by a second anti-PAMG-1 antibody. This event leads to the appearance of the test line. Unbound antigen-antibody complexes continue to flow along the test strip and are immobilized by a second antibody. This leads to the appearance of the internal control line.

REAGENTS AND COMPONENTS

The PartoSure test kit includes the following components: the PartoSure test strip in a foil pouch with desiccant, a sterile flocked vaginal swab, and a plastic vial with solvent solution (0.9% NaCl, 0.05% NaN_3, 0.01% Triton X100). No additional materials are required to perform the PartoSure test.

TEST PROCEDURE

1. Take the solvent vial by its cap and ensure all liquid in the vial has dropped to the bottom. Open the solvent vial and place it in a vertical position.
2. To collect a sample from the vagina, use only the sterile flocked swab provided with the PartoSure test kit. Remove the swab from its package following the instructions on the packaging. The tip of the swab should not touch anything prior to insertion into the vagina. Hold the swab by the middle of its shaft and, while the patient is lying on her back, carefully insert the tip of the swab into the vagina until the fingers contact the skin (no more than 2-3 inches or 5-7 cm deep). Withdraw the swab from the vagina **after 30 seconds**.
3. After the swab has been removed from the vagina, immediately place the tip into the provided solvent vial and rinse by rotating for **30 seconds**.
4. Remove the swab from the vial and dispose of it.
5. Tear open the foil pouch at the tear notches and remove the PartoSure test strip.
6. Insert the white end of the test strip (marked with arrows facing downward) into the vial with solvent.
7. **Remove the test strip from the vial if two lines are clearly visible in the test region or after 5 minutes sharp.** Read the results by placing the test strip on a clean, dry flat surface in a well-lit environment via either natural or flourescent lighting. A positive result is indicated by two lines in the test region, while a negative result is indicated by a single line in the test region. Do not read or interpret the results after 10 minutes have passed since inserting the test strip into the vial.

Two Lines: **POSITIVE** — Control Line, Test Line

One Line: **NEGATIVE** — Control Line

No Control Line: **INVALID** — Test Line Only

Positive: Two Red Lines	Negative: One Red Control Line	Invalid: No Red Lines or Test Line Only

REAGENTS AND COMPONENTS

The PartoSure test kit includes the following components: the PartoSure test strip in a foil pouch with desiccant, a sterile flocked vaginal swab, and a plastic vial with solvent solution (0.9% NaCl, 0.05% NaN_3, 0.01% Triton X100). No additional materials are required to perform the PartoSure test.

Care must be taken not to contaminate the swab or cervicovaginal secretions with lubricants or antiseptics (e.g. K-Y® or Surgilube® lubricating jelly, Betadine® Cleanser). These substances may interfere with absorption of the specimen by the swab or with the antibody-antigen reaction of the PartoSure test and lead to invalid test results.

•If it is suspected that the patient has applied a topical disinfectant (e.g. Monistat®, miconazole nitrate cream) to the vaginal area within 24 hours, delay specimen collection until 24 hours from application of the topical disinfectant have passed as these products can lead to false negative test results.

•The instructions for use must be followed exactly; failure to do so may lead to inaccurate results.

•Test performance has been characterized from specimens taken from the vaginal cavity. Samples obtained from other locations should not be used. A speculum examination is not required.

•Results should be interpreted with caution when a specimen is obtained from a patient with unconfirmed gestational age.

•PartoSure test results are qualitative and not quantitative. No quantitative interpretation should be made based on the strength of the test or control lines.

Procedure

809.10(b)(8)(i)

A list of all materials provided, e.g., reagents, instruments and equipment, with instructions for their use.

809.10(b)(8)(ii)

A list of all materials required but not provided. Include such details as sizes, numbers, types, and quality.

Example: ADVIA Centaur Anti-HBe2 assay

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
10720831	1 ReadyPack primary reagent pack containing ADVIA Centaur aHBe2 Lite Reagent, Solid Phase, and Ancillary Well Reagent	50
	ADVIA Centaur aHBe2 Master Curve card	
	1 vial ADVIA Centaur aHBe2 CAL low calibrator CAL L	
	1 vial ADVIA Centaur aHBe2 CAL high calibrator CAL H	
	ADVIA Centaur aHBe2 CAL calibrator assigned value card and barcode labels	

Materials Required but Not Provided

The following materials are required to perform this assay, but are not provided:

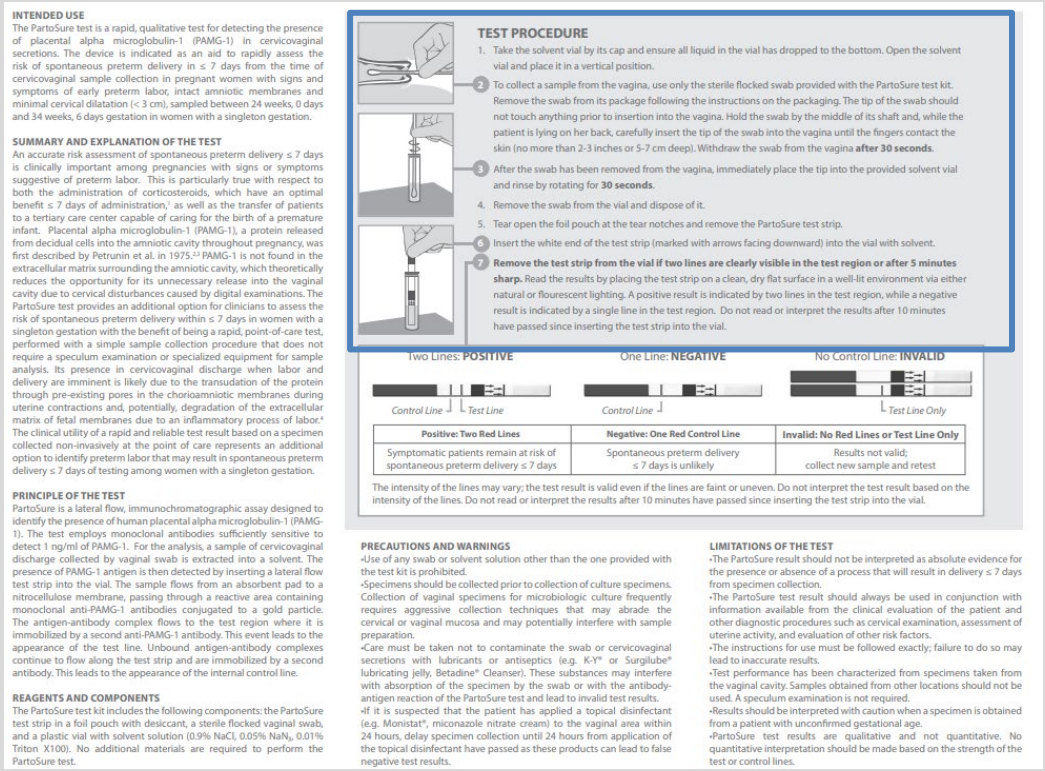
Item		Description		
REF	10720832	ADVIA Centaur aHBe2 QC (quality control)	2 x 10.0 mL negative control, level 1	CONTROL - 1
			2 x 10.0 mL positive control, level 2	CONTROL + 2
		Quality control lot-specific value sheet and barcode labels		
REF	01137199	ADVIA Centaur Wash 1 WASH 1	2 x 1500 mL/pack	
REF	03773025	ADVIA Centaur Wash 1 WASH 1	2 x 2500 mL/pack	

Procedure

Example: PartoSure Test

809.10(b)(8)(iii)

A description of the amounts of reagents necessary, times required for specific steps, proper temperatures, wavelengths, etc.



INTENDED USE

The PartoSure test is a rapid, qualitative test for detecting the presence of placental alpha microglobulin-1 (PAMG-1) in cervicovaginal secretions. The device is indicated as an aid to rapidly assess the risk of spontaneous preterm delivery in ≤ 7 days from the time of cervicovaginal sample collection in pregnant women with signs and symptoms of early preterm labor, intact amniotic membranes and minimal cervical dilatation (< 3 cm), sampled between 24 weeks, 0 days and 34 weeks, 6 days gestation in women with a singleton gestation.

SUMMARY AND EXPLANATION OF THE TEST

An accurate risk assessment of spontaneous preterm delivery ≤ 7 days is clinically important among pregnancies with signs or symptoms suggestive of preterm labor. This is particularly true with respect to both the administration of corticosteroids, which have an optimal benefit ≤ 7 days of administration,[1] as well as the transfer of patients to a tertiary care center capable of caring for the birth of a premature infant. Placental alpha microglobulin-1 (PAMG-1), a protein released from decidual cells into the amniotic cavity throughout pregnancy, was first described by Petrunin et al. in 1975.[2,3] PAMG-1 is not found in the extracellular matrix surrounding the amniotic cavity, which theoretically reduces the opportunity for its unnecessary release into the vaginal cavity due to cervical disturbances caused by digital examinations. The PartoSure test provides an additional option for clinicians to assess the risk of spontaneous preterm delivery within ≤ 7 days in women with a singleton gestation with the benefit of being a rapid, point-of-care test, performed with a simple sample collection procedure that does not require a speculum examination or specialized equipment for sample analysis. Its presence in cervicovaginal discharge when labor and delivery are imminent is likely due to the transudation of the protein through pre-existing pores in the chorioamniotic membranes during uterine contractions and, potentially, degradation of the extracellular matrix of fetal membranes due to an inflammatory process of labor.[4] The clinical utility of a rapid and reliable test result based on a specimen collected non-invasively at the point of care represents an additional option to identify preterm labor that may result in spontaneous preterm delivery ≤ 7 days of testing among women with a singleton gestation.

PRINCIPLE OF THE TEST

PartoSure is a lateral flow, immunochromatographic assay designed to identify the presence of human placental alpha microglobulin-1 (PAMG-1). The test employs monoclonal antibodies sufficiently sensitive to detect 1 ng/ml of PAMG-1. For the analysis, a sample of cervicovaginal discharge collected by vaginal swab is extracted into a solvent. The presence of PAMG-1 antigen is then detected by inserting a lateral flow test strip into the vial. The sample flows from an absorbent pad to a nitrocellulose membrane, passing through a reactive area containing monoclonal anti-PAMG-1 antibodies conjugated to a gold particle. The antigen-antibody complex flows to the test region where it is immobilized by a second anti-PAMG-1 antibody. This event leads to the appearance of the test line. Unbound antigen-antibody complexes continue to flow along the test strip and are immobilized by a second antibody. This leads to the appearance of the internal control line.

REAGENTS AND COMPONENTS

The PartoSure test kit includes the following components: the PartoSure test strip in a foil pouch with desiccant, a sterile flocked vaginal swab, and a plastic vial with solvent solution (0.9% NaCl, 0.05% NaN_3, 0.01% Triton X100). No additional materials are required to perform the PartoSure test.

TEST PROCEDURE

1. Take the solvent vial by its cap and ensure all liquid in the vial has dropped to the bottom. Open the solvent vial and place it in a vertical position.
2. To collect a sample from the vagina, use only the sterile flocked swab provided with the PartoSure test kit. Remove the swab from its package following the instructions on the packaging. The tip of the swab should not touch anything prior to insertion into the vagina. Hold the swab by the middle of its shaft and, while the patient is lying on her back, carefully insert the tip of the swab into the vagina until the fingers contact the skin (no more than 2-3 inches or 5-7 cm deep). Withdraw the swab from the vagina **after 30 seconds**.
3. After the swab has been removed from the vagina, immediately place the tip into the provided solvent vial and rinse by rotating for **30 seconds**.
4. Remove the swab from the vial and dispose of it.
5. Tear open the foil pouch at the tear notches and remove the PartoSure test strip.
6. Insert the white end of the test strip (marked with arrows facing downward) into the vial with solvent.
7. **Remove the test strip from the vial if two lines are clearly visible in the test region or after 5 minutes sharp.** Read the results by placing the test strip on a clean, dry flat surface in a well-lit environment via either natural or flourescent lighting. A positive result is indicated by two lines in the test region, while a negative result is indicated by a single line in the test region. Do not read or interpret the results after 10 minutes have passed since inserting the test strip into the vial.

Two Lines: **POSITIVE** — Control Line, Test Line

One Line: **NEGATIVE** — Control Line

No Control Line: **INVALID** — Test Line Only

Positive: Two Red Lines	Negative: One Red Control Line	Invalid: No Red Lines or Test Line Only
Symptomatic patients remain at risk of spontaneous preterm delivery ≤ 7 days	Spontaneous preterm delivery ≤ 7 days is unlikely	Results not valid; collect new sample and retest

The intensity of the lines may vary; the test result is valid even if the lines are faint or uneven. Do not interpret the test result based on the intensity of the lines. Do not read or interpret the results after 10 minutes have passed since inserting the test strip into the vial.

PRECAUTIONS AND WARNINGS

- Use of any swab or solvent solution other than the one provided with the test kit is prohibited.
- Specimens should be collected prior to collection of culture specimens. Collection of vaginal specimens for microbiologic culture frequently requires aggressive collection techniques that may abrade the cervical or vaginal mucosa and may potentially interfere with sample preparation.
- Care must be taken not to contaminate the swab or cervicovaginal secretions with lubricants or antiseptics (e.g. K-Y® or Surgilube® lubricating jelly, Betadine® Cleanser). These substances may interfere with absorption of the specimen by the swab or with the antibody-antigen reaction of the PartoSure test and lead to invalid test results.
- If it is suspected that the patient has applied a topical disinfectant (e.g. Monistat®, miconazole nitrate cream) to the vaginal area within 24 hours, delay specimen collection until 24 hours from application of the topical disinfectant have passed as these products can lead to false negative test results.

LIMITATIONS OF THE TEST

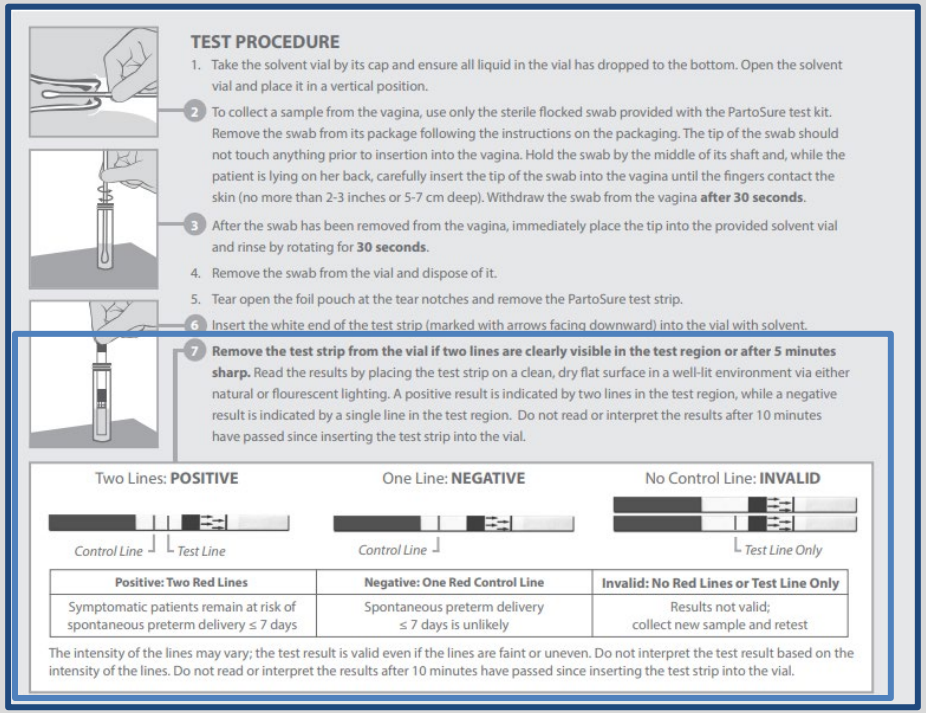
- The PartoSure result should not be interpreted as absolute evidence for the presence or absence of a process that will result in delivery ≤ 7 days from specimen collection.
- The PartoSure test result should always be used in conjunction with information available from the clinical evaluation of the patient and other diagnostic procedures such as cervical examination, assessment of uterine activity, and evaluation of other risk factors.
- The instructions for use must be followed exactly; failure to do so may lead to inaccurate results.
- Test performance has been characterized from specimens taken from the vaginal cavity. Samples obtained from other locations should not be used. A speculum examination is not required.
- Results should be interpreted with caution when a specimen is obtained from a patient with unconfirmed gestational age.
- PartoSure test results are qualitative and not quantitative. No quantitative interpretation should be made based on the strength of the test or control lines.

Procedure

809.10(b)(8)(iv)

A statement describing the stability of the final reaction material to be measured and the time within which it shall be measured to assure accurate results.

Example: PartoSure Test



TEST PROCEDURE

1. Take the solvent vial by its cap and ensure all liquid in the vial has dropped to the bottom. Open the solvent vial and place it in a vertical position.
2. To collect a sample from the vagina, use only the sterile flocked swab provided with the PartoSure test kit. Remove the swab from its package following the instructions on the packaging. The tip of the swab should not touch anything prior to insertion into the vagina. Hold the swab by the middle of its shaft and, while the patient is lying on her back, carefully insert the tip of the swab into the vagina until the fingers contact the skin (no more than 2-3 inches or 5-7 cm deep). Withdraw the swab from the vagina **after 30 seconds**.
3. After the swab has been removed from the vagina, immediately place the tip into the provided solvent vial and rinse by rotating for **30 seconds**.
4. Remove the swab from the vial and dispose of it.
5. Tear open the foil pouch at the tear notches and remove the PartoSure test strip.
6. Insert the white end of the test strip (marked with arrows facing downward) into the vial with solvent.
7. **Remove the test strip from the vial if two lines are clearly visible in the test region or after 5 minutes sharp.** Read the results by placing the test strip on a clean, dry flat surface in a well-lit environment via either natural or flourescent lighting. A positive result is indicated by two lines in the test region, while a negative result is indicated by a single line in the test region. Do not read or interpret the results after 10 minutes have passed since inserting the test strip into the vial.

Two Lines: **POSITIVE** — *Control Line*, *Test Line*

One Line: **NEGATIVE** — *Control Line*

No Control Line: **INVALID** — *Test Line Only*

Positive: Two Red Lines	Negative: One Red Control Line	Invalid: No Red Lines or Test Line Only
Symptomatic patients remain at risk of spontaneous preterm delivery ≤ 7 days	Spontaneous preterm delivery ≤ 7 days is unlikely	Results not valid; collect new sample and retest

The intensity of the lines may vary; the test result is valid even if the lines are faint or uneven. Do not interpret the test result based on the intensity of the lines. Do not read or interpret the results after 10 minutes have passed since inserting the test strip into the vial.

Procedure

809.10(b)(8)(v)

Details of calibration: Identify reference material. Describe preparation of reference sample(s), use of blanks, preparation of the standard curve, etc. The description of the range of calibration should include the highest and the lowest values measurable by the procedure.

Example: PartoSure Test

Not applicable, there is no calibration for this visually read test

Example: Abbott RealTime IDH1

Abbott *m*2000*rt* Optical Calibration

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. Optical calibration of the Abbott *m*2000*rt* instrument is required for the accurate measurement and discrimination of dye fluorescence during the Abbott RealTi*m*e IDH1 assay.

The following Abbott *m*2000*rt* Optical Calibration Plates are used to calibrate the Abbott *m*2000*rt* instrument for the Abbott RealTi*m*e IDH1 assay:

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

Procedure

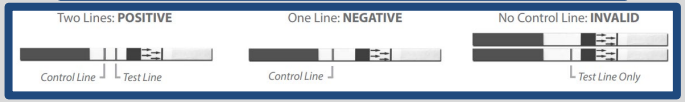
809.10(b)(8)(vi)

Details of kinds of quality control procedures and materials required. If there is need for both positive and negative controls, this should be stated. State what are considered satisfactory limits of performance.

Example: PartoSure Test

QUALITY CONTROL

The PartoSure test strip contains an internal procedural control mechanism that ensures analytical functionality. The appearance of one or two lines in the results region of the test strip verifies the integrity of the test procedure and components.



Example: ADVIA Centaur Anti-HBe2 Assay

Performing Quality Control

For quality control of the ADVIA Centaur aHBe2 assay, use ADVIA Centaur aHBe2 Quality Control at least once during each day that samples are analyzed. Use the quality control material in accordance with the quality control instructions for use.

For the assigned values, refer to the lot-specific value sheet provided. A satisfactory level of performance is achieved when the analyte values obtained are within the expected control interval for the system, or within your interval, as determined by an appropriate internal laboratory quality control scheme. Follow your laboratory's quality control procedures if the results obtained do not fall within the acceptable limits. For information about entering quality control definitions, refer to the system online help.

Follow government regulations or accreditation requirements for quality control frequency. Individual laboratory quality control programs and procedures may require more frequent quality control testing.

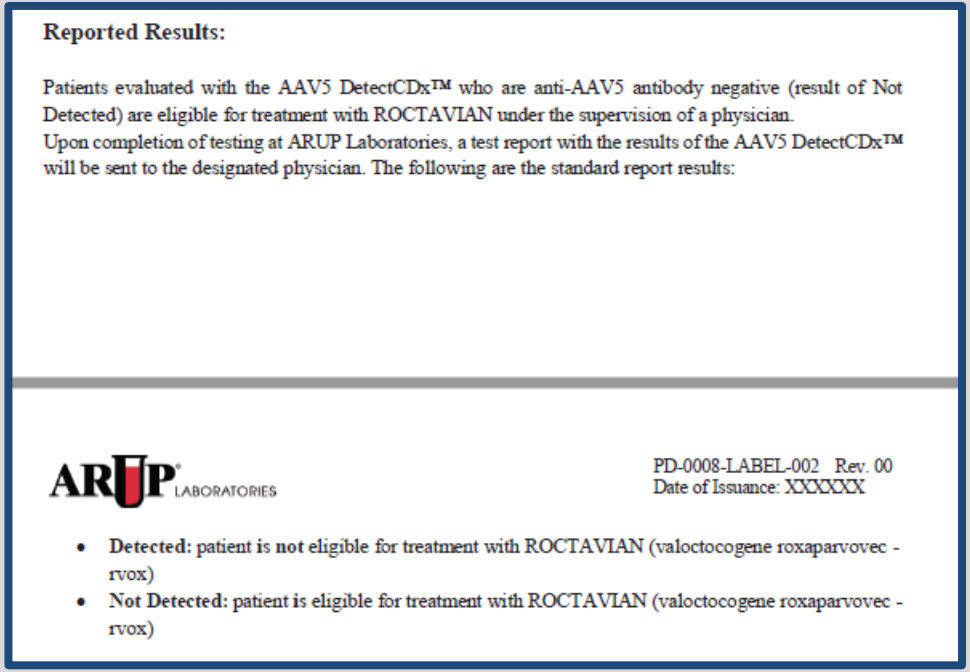
Results

809.10(b)(9)

Results:

- Explain the procedure for calculating the value of the unknown.
- Give an explanation for each component of the formula used for the calculation of the unknown.
- Include a sample calculation, step-by-step, explaining the answer.
- The values shall be expressed to the appropriate number of significant figures.
- **If the test provides other than quantitative results, provide an adequate description of expected results**

Example: ARUP Laboratories AAV5 DetectCDx



Reported Results:

Patients evaluated with the AAV5 DetectCDx™ who are anti-AAV5 antibody negative (result of Not Detected) are eligible for treatment with ROCTAVIAN under the supervision of a physician.
Upon completion of testing at ARUP Laboratories, a test report with the results of the AAV5 DetectCDx™ will be sent to the designated physician. The following are the standard report results:

ARUP LABORATORIES

PD-0008-LABEL-002 Rev. 00
Date of Issuance: XXXXXX

- **Detected:** patient is **not** eligible for treatment with ROCTAVIAN (valoctocogene roxaparvovec - rvox)
- **Not Detected:** patient is eligible for treatment with ROCTAVIAN (valoctocogene roxaparvovec - rvox)

Limitation of the Procedure

809.10(b)(10)

Limitation of the procedure:
Include a statement of limitations of the procedure.

State known extrinsic factors or interfering substances affecting results.

If further testing, either more specific or more sensitive, is indicated in all cases where certain results are obtained, the need for the additional test shall be stated.

Example: FoundationOne Liquid CDx

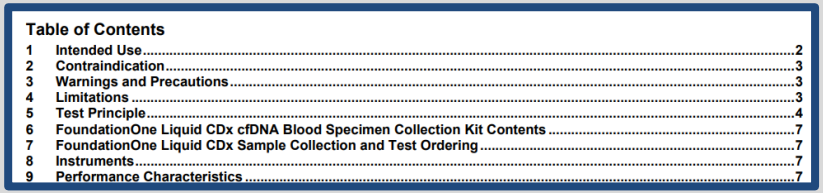
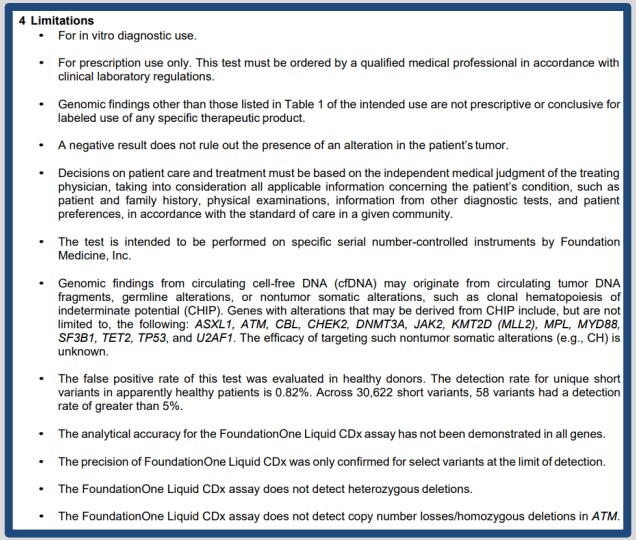


Table of Contents



4 Limitations

- For in vitro diagnostic use.
- For prescription use only. This test must be ordered by a qualified medical professional in accordance with clinical laboratory regulations.
- Genomic findings other than those listed in Table 1 of the intended use are not prescriptive or conclusive for labeled use of any specific therapeutic product.
- A negative result does not rule out the presence of an alteration in the patient's tumor.
- Decisions on patient care and treatment must be based on the independent medical judgment of the treating physician, taking into consideration all applicable information concerning the patient's condition, such as patient and family history, physical examinations, information from other diagnostic tests, and patient preferences, in accordance with the standard of care in a given community.
- The test is intended to be performed on specific serial number-controlled instruments by Foundation Medicine, Inc.
- Genomic findings from circulating cell-free DNA (cfDNA) may originate from circulating tumor DNA fragments, germline alterations, or nontumor somatic alterations, such as clonal hematopoiesis of indeterminate potential (CHIP). Genes with alterations that may be derived from CHIP include, but are not limited to, the following: *ASXL1, ATM, CBL, CHEK2, DNMT3A, JAK2, KMT2D (MLL2), MPL, MYD88, SF3B1, TET2, TP53*, and *U2AF1*. The efficacy of targeting such nontumor somatic alterations (e.g., CH) is unknown.
- The false positive rate of this test was evaluated in healthy donors. The detection rate for unique short variants in apparently healthy patients is 0.82%. Across 30,622 short variants, 58 variants had a detection rate of greater than 5%.
- The analytical accuracy for the FoundationOne Liquid CDx assay has not been demonstrated in all genes.
- The precision of FoundationOne Liquid CDx was only confirmed for select variants at the limit of detection.
- The FoundationOne Liquid CDx assay does not detect heterozygous deletions.
- The FoundationOne Liquid CDx assay does not detect copy number losses/homozygous deletions in *ATM*.

Expected Values

809.10(b)(11)

Expected values: State the range(s) of expected values as obtained with the product from studies of various populations. Indicate how the range(s) was established and identify the population(s) on which it was established

Example: ADVIA Centaur Anti-HBe2 Assay

Expected Values

The study was designed to test samples from patients with general signs and symptoms of hepatitis or a high risk of HBV infection, including pregnant women. The analysis included 1697 samples in the following categories: acute, chronic, early recovery, recovery, immune natural infection, recovered, HBV vaccine response, not previously infected with HBV, and unclassified.

The study population was 28.0% Caucasian, 67.8% Black, 2.1% Asian, and 2.1% from unknown or other race. The patients were nearly equally divided by sex (55.7% female, 44.3% male). The mean age was 45 years. Patients in the study population were from the following geographic regions: Florida (32.9%), California (24.2%), Maryland (22.6%), Tennessee (6.8%), Georgia (4.9%), Nevada (3.9%), Massachusetts (3.7%), and other locations (1.0%).

The ADVIA Centaur aHBe2 results for the prospective population for all sites combined by age group and gender are summarized in the following table:

Distribution of Study Population by Age Group and Gender (All Testing Sites)

Age Range (Years)	Gender	Reactive N[a]	Reactive %[b]	Nonreactive N	Nonreactive %	Total Number Tested
17–20	Male	0	–	0	–	0
	Female	0	0.0	19	100.0	19
	Overall	0	0.0	19	100.0	19
21–30	Male	0	0.0	85	100.0	85
	Female	3	1.2	254	98.8	257
	Overall	3	0.9	339	99.1	342
31–40	Male	4	4.2	91	95.8	95
	Female	8	4.1	188	95.9	196
	Overall	12	4.1	279	95.9	291
41–50	Male	16	11.0	130	89.0	146
	Female	21	13.2	138	86.8	159
	Overall	37	12.1	268	87.9	305

Example: ARUP Laboratories AAV5 DetectCDx

Expected Values

Patient Population Demographics:

A number of patient population demographic variables were analyzed for their potential association with AAV5 DetectCDx assay results (Detected vs Not Detected).

Percent of Detected AAV5 DetectCDx Results Stratified by Race and Ethnicity		
Race	*N*	*Percent Detected*
White	618	27.8% (172/618)
Asian	159	28.3% (45/159)
Black or African American	110	34.5% (38/110)
Native Hawaiian or other Pacific Islander	2	0.0% (0/2)
Not Provided or Multiple	138	40.6% (56/138)
Combined	1,027	30.3% (311/1,027)
Ethnicity		
Hispanic or Latino	27	29.6% (8/27)
Not Hispanic or Latino	965	29.8% (288/965)
Not provided	35	42.9% (15/35)
Combined	1,027	30.3% (311/1,027)

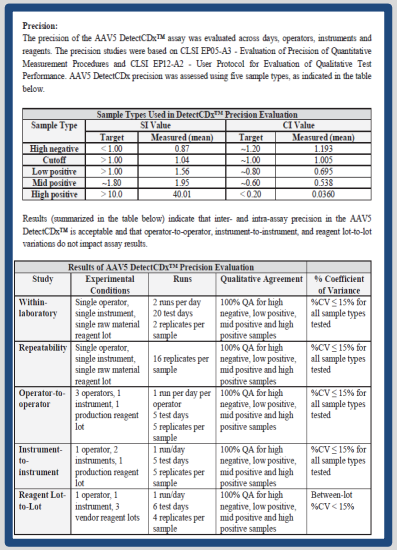
Higher seropositivity (percent of results Detected) was observed for the "Black or African American" group (34.5% Detected).

Performance Characteristics

809.10(b)(12)

Specific performance characteristics: Include, as appropriate, information describing such things as accuracy, precision, specificity, and sensitivity. These shall be related to a generally accepted method using biological specimens from normal and abnormal populations. Include a statement summarizing the data upon which the specific performance characteristics are based.

Example: ARUP Laboratories AAV5 DetectCDx



Precision:
The precision of the AAV5 DetectCDx™ assay was evaluated across days, operators, instruments and reagents. The precision studies were based on CLSI EP05-A3 - Evaluation of Precision of Quantitative Measurement Procedures and CLSI EP12-A2 - User Protocol for Evaluation of Qualitative Test Performance. AAV5 DetectCDx precision was assessed using five sample types, as indicated in the table below.

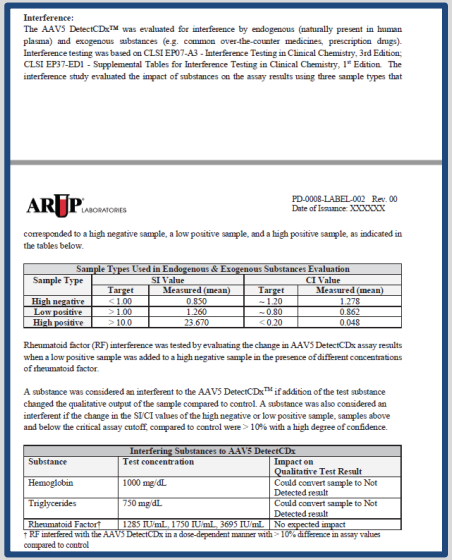
Sample Types Used in DetectCDx™ Precision Evaluation

Sample Type	SI Value		CI Value	
	Target	Measured (mean)	Target	Measured (mean)
High negative	< 1.00	0.87	~1.20	1.193
Cutoff	> 1.00	1.04	~1.00	1.005
Low positive	> 1.00	1.56	~0.80	0.695
Mid positive	~1.80	1.95	~0.60	0.338
High positive	> 10.0	40.01	< 0.20	0.0360

Results (summarized in the table below) indicate that inter- and intra-assay precision in the AAV5 DetectCDx™ is acceptable and that operator-to-operator, instrument-to-instrument, and reagent lot-to-lot variations do not impact assay results.

Results of AAV5 DetectCDx™ Precision Evaluation

Study	Experimental Conditions	Runs	Qualitative Agreement	% Coefficient of Variance
Within-laboratory	Single operator, single instrument, single run material reagent lot	2 runs per day 20 test days 2 replicates per sample	100% QA for high negative, low positive, mid positive and high positive samples	%CV ≤ 15% for all sample types tested
Repeatability	Single operator, single instrument, single run material reagent lot	16 replicates per sample	100% QA for high negative, low positive, mid positive and high positive samples	%CV ≤ 15% for all sample types tested
Operator-to-operator	3 operators, 1 instrument, 1 production reagent lot	1 run per day per operator 5 test days 5 replicates per sample	100% QA for high negative, low positive, mid positive and high positive samples	%CV ≤ 15% for all sample types tested
Instrument-to-instrument	1 operator, 2 instruments, 1 production reagent lot	1 run/day 5 test days 5 replicates per sample	100% QA for high negative, low positive, mid positive and high positive samples	%CV ≤ 15% for all sample types tested
Reagent Lot-to-Lot	1 operator, 1 instrument, 3 vendor reagent lots	1 run/day 6 test days 4 replicates per sample	100% QA for high negative, low positive, mid positive and high positive samples	Between-lot %CV < 15%



Interference:
The AAV5 DetectCDx™ was evaluated for interference by endogenous (naturally present in human plasma) and exogenous substances (e.g. common over-the-counter medicines, prescription drugs). Interference testing was based on CLSI EP07-A3 - Interference Testing in Clinical Chemistry, 3rd Edition; CLSI EP37-ED1 - Supplemental Tables for Interference Testing in Clinical Chemistry, 1st Edition. The interference study evaluated the impact of substances on the assay results using three sample types that

ARUP LABORATORIES

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Date of Issuance: XXXXXX

corresponded to a high negative sample, a low positive sample, and a high positive sample, as indicated in the tables below.

Sample Types Used in Endogenous & Exogenous Substances Evaluation

Sample Type	SI Value		CI Value	
	Target	Measured (mean)	Target	Measured (mean)
High negative	< 1.00	0.850	~ 1.20	1.278
Low positive	> 1.00	1.260	~ 0.80	0.862
High positive	> 10.0	23.670	< 0.20	0.048

Rheumatoid factor (RF) interference was tested by evaluating the change in AAV5 DetectCDx assay results when a low positive sample was added to a high negative sample in the presence of different concentrations of rheumatoid factor.

A substance was considered an interferent to the AAV5 DetectCDx™ if addition of the test substance changed the qualitative output of the sample compared to control. A substance was also considered an interferent if the change in the SI/CI values of the high negative or low positive sample, samples above and below the critical assay cutoff, compared to control were > 10% with a high degree of confidence.

Interfering Substances to AAV5 DetectCDx

Substance	Test concentration	Impact on Qualitative Test Result
Hemoglobin	1000 mg/dL	Could convert sample to Not Detected result
Triglycerides	750 mg/dL	Could convert sample to Not Detected result
Rheumatoid Factor†	1285 IU/mL, 1750 IU/mL, 3695 IU/mL	No expected impact

† RF interfered with the AAV5 DetectCDx in a dose-dependent manner with > 10% difference in assay values compared to control

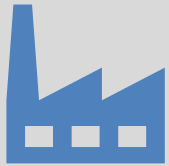
Cross-reactivity with other antibodies:
Cross-reactivity in the AAV5 DetectCDx™ assay to antibodies other than anti-AAV5 antibodies is unknown. A positive assay result can occur due to detection of antibodies other than anti-AAV5 antibodies.

Prozone effect:
The AAV5 DetectCDx™ was evaluated to determine whether elevated concentrations of anti-AAV5 antibody produce a prozone (hook) effect. The study samples utilized distinct plasma samples from three (3) non-hemophilia A donors that represent the highest AAV5 titer positive samples that were previously identified in historical studies conducted at ARUP Laboratories. Individual two-fold dilution series were created by diluting the high titer positive AAV5 plasma samples into the anti-AAV5 negative plasma sample for eight (8) dilution steps to cover the range from high positive to negative Screen Index and Confirm Index values.

The results from this test indicate that a prozone effect was not observed for samples with starting SI values of ~90. Human specimens with SI values greater than 90 were not evaluated in this study and may exhibit a prozone effect.

Carryover:
The possibility of carryover and well-to-well cross-talk was evaluated for the AAV5 DetectCDx™ assay. The study sample set indicated in the table below was used to create an alternating pattern of negative and high positive samples.

809.10(b)(13) Bibliography: Include pertinent references keyed to the text.



809.10(b)(14) Name and place of business of manufacturer, packer, or distributor.

809.10(b)(15) Date of issuance of the last revision of the labeling identified as such.

Reagents and Instruments

809.10(b)(5) Reagents

Reagents:

(i) A declaration of the established name… quantity, proportion or concentration of each reactive ingredient… statement … characterizing catalytic or nonreactive ingredients...

(ii) A statement of warnings or precautions… a statement “For In Vitro Diagnostic Use” and any other limiting statements...

(iii) Adequate instructions for reconstitution, mixing, dilution, etc.

(iv) Appropriate storage instructions adequate to protect the stability of the product...

(v) A statement of any purification or treatment required for use.

(vi) Physical, biological, or chemical indications of instability or deterioration.

809.10(b)(6) Instruments

Instruments:

(i) Use or function.

(ii) Installation procedures and special requirements.

(iii) Principles of operation.

(iv) Performance characteristics and specifications.

(v) Operating instructions.

(vi) Calibration procedures including materials and/or equipment to be used.

(vii) Operational precautions and limitations.

(viii) Hazards.

(ix) Service and maintenance information.

Reagents and Instruments Labeled for Clinical Diagnostic Use

Test systems that are developed for use with reagents and instruments labeled for clinical diagnostic use (i.e., not labeled for research or investigational use) that have package inserts that comply with the requirements under 809.10(b)(5) and 809.10(b)(6), respectively, and where the reagents and instruments are being used in accordance with their labeled intended use, often reference the compliant labeling rather than repeating information in the test system labeling.

Such reagents and instruments are typically listed in the test system labeling as the materials that are "required but not provided," as required under 809.10(b)(8)(ii).

Reagents and Instruments NOT Labeled for Clinical Diagnostic Use

Test systems that are developed using reagent(s) or instrument(s) that are NOT appropriately labeled for clinical diagnostic use (i.e., intended for research use only) or where the reagents and instruments are being used in the test system in a manner that is not in accordance with their labeled intended use, must include information in the test system labeling to meet the requirements under 809.10(b)(5) and 809.10(b)(6).

The manufacturer of the test system is responsible for qualifying, under its own quality system, such reagents and instruments for use in a test system.

Reagents and Instruments

Example: ARUP Laboratories AAV5 DetectCDx

Reagents:

The primary reagents for the AAV5 DetectCDx™ include:

AAV5 DetectCDx™ Reagents and Storage Conditions

Reagent	Storage Conditions	Component(s)
AAV5 Coated Plate Set	Refrigerated (2 to 8 °C)	• MULTI-ARRAY® 96-well plate • AAV5 Confirmatory Reagent • AAV5 Detection Reagent
AAV5 Control Set	Frozen (-70 °C)	• Low positive control • High positive control • Cut point control • Negative control
Read Buffer T (1X)	Room temperature (20 to 25 °C)	Read Buffer T (1X)

Additional reagents used in the AAV5 DetectCDx:

- TBS Buffer (1X) with 1% casein
- 1X DPBS
- Tween 20 (proteomics grade), 1.0% (v/v)
- ProClin 300, 0.05% (v/v)

Instruments: The MULTI-ARRAY® 96-well plate used in the AAV5 DetectCDx™ is read on a MESO QuickPlex SQ 120 instrument, as identified by a specific serial number.

Example: Abbott RealTime IDH1

Slides 37-47

Reagents

809.10(b)(5)(i)

- Declaration of the established name (common or usual name)
- Quantity, proportion, or concentration of each reactive ingredient. For biological material, the source and a measure of its activity
  - Stated in the system generally used and recognized by the intended user (e.g., metric, international units)

- Statement indicating the presence of and characterizing any catalytic or nonreactive ingredients, e.g., buffers, preservatives, stabilizers

Example: Abbott RealTime IDH1

REAGENTS

Abbott RealTime IDH1 Amplification Reagent Kit (List No. 08N90-090)

1. OLIGONUCLEOTIDE REAGENT 1 **Abbott RealTime IDH1 Oligonucleotide Reagent 1 (List No. 8N90A) (1 vial, 0.905 mL)**
<0.1% synthetic oligonucleotides and <1% dNTP, in a buffered solution with a reference dye. Preservatives: sodium azide and 0.15% ProClin® 950.

2. OLIGONUCLEOTIDE REAGENT 2 **Abbott RealTime IDH1 Oligonucleotide Reagent 2 (List No. 8N90B) (1 vial, 0.905 mL)**
<0.1% synthetic oligonucleotides and <1% dNTP, in a buffered solution with a reference dye. Preservatives: sodium azide and 0.15% ProClin 950.

3. DNA POLYMERASE **Abbott RealTime IDH1 DNA Polymerase (List No. 8N90E) (2 vials, 0.051 mL per vial)**
DNA Polymerase (5.4 to 5.9 Units/µL) in a buffered solution with stabilizers.

4. ACTIVATION REAGENT **Abbott RealTime IDH1 Activation Reagent (List No. 8N90M) (1 vial, 0.930mL)**
50 mM magnesium chloride in a buffered solution. Preservatives: sodium azide and 0.15% ProClin 950.

Reagents

809.10(b)(5)(ii)

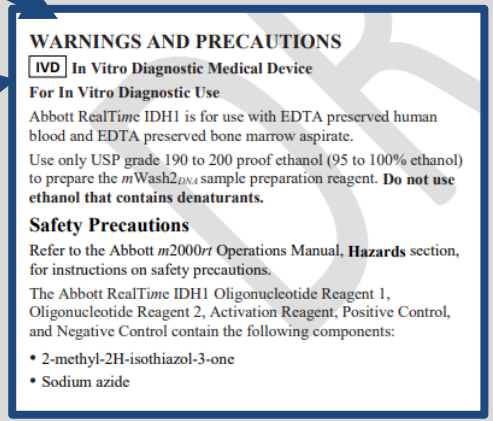
Statement of warnings or precautions for users as established in the regulations contained in 16 CFR part 1500 (Hazardous Substances) and any other warnings appropriate to the hazard presented by the product

Statement "For In Vitro Diagnostic Use"

Any other limiting statements appropriate to the intended use

The limiting statement appropriate to the intended use of a prescription in vitro diagnostic product shall bear the symbol statement “Rx only” or “℞ only” or the statement “Caution: Federal law restricts this device to sale by or on the order of a ___”, the blank to be filled with the word “physician”, “dentist”, “veterinarian”, or with the descriptive designation of any other practitioner licensed by the law of the State in which the practitioner practices to use or order the use of the device.

Example: Abbott RealTime IDH1



WARNINGS AND PRECAUTIONS

IVD **In Vitro Diagnostic Medical Device**

For In Vitro Diagnostic Use

Abbott RealTi*m*e IDH1 is for use with EDTA preserved human blood and EDTA preserved bone marrow aspirate.

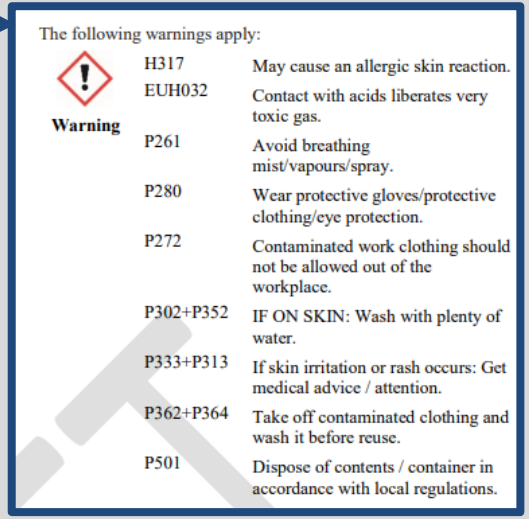
Use only USP grade 190 to 200 proof ethanol (95 to 100% ethanol) to prepare the *m*Wash2$_{DNA}$ sample preparation reagent. **Do not use ethanol that contains denaturants.**

Safety Precautions

Refer to the Abbott *m*2000*rt* Operations Manual, **Hazards** section, for instructions on safety precautions.

The Abbott RealTi*m*e IDH1 Oligonucleotide Reagent 1, Oligonucleotide Reagent 2, Activation Reagent, Positive Control, and Negative Control contain the following components:

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



The following warnings apply:

Warning

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.
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.

Reagents

809.10(b)(5)(ii)

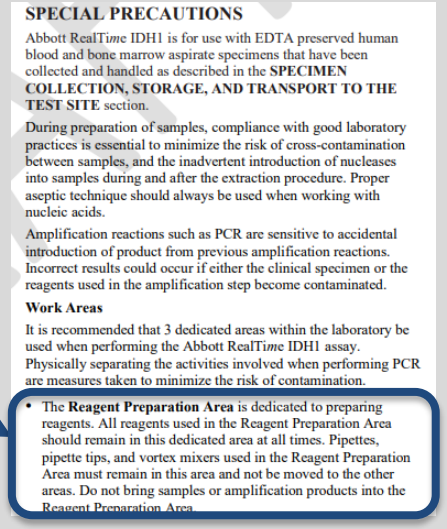
Statement of warnings or precautions for users as established in the regulations contained in 16 CFR part 1500 (Hazardous Substances) and any other warnings appropriate to the hazard presented by the product

Statement "For In Vitro Diagnostic Use"

Any other limiting statements appropriate to the intended use

The limiting statement appropriate to the intended use of a prescription in vitro diagnostic product shall bear the symbol statement "Rx only" or "℞ only" or the statement "Caution: Federal law restricts this device to sale by or on the order of a ___", the blank to be filled with the word "physician", "dentist", "veterinarian", or with the descriptive designation of any other practitioner licensed by the law of the State in which the practitioner practices to use or order the use of the device.

Example: Abbott RealTime IDH1



SPECIAL PRECAUTIONS

Abbott RealTi*me* IDH1 is for use with EDTA preserved human blood and bone marrow aspirate specimens that have been collected and handled as described in the **SPECIMEN COLLECTION, STORAGE, AND TRANSPORT TO THE TEST SITE** section.

During preparation of samples, compliance with good laboratory practices is essential to minimize the risk of cross-contamination between samples, and the inadvertent introduction of nucleases into samples during and after the extraction procedure. Proper aseptic technique should always be used when working with nucleic acids.

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 in the amplification step become contaminated.

Work Areas

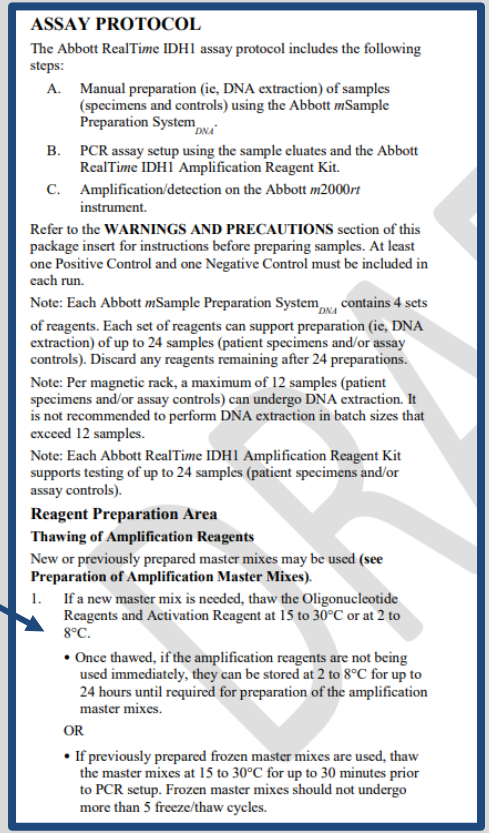
It is recommended that 3 dedicated areas within the laboratory be used when performing the Abbott RealTi*me* IDH1 assay. Physically separating the activities involved when performing PCR are measures taken to minimize the risk of contamination.

- The **Reagent Preparation Area** is dedicated to preparing reagents. All reagents used in the Reagent Preparation Area should remain in this dedicated area at all times. Pipettes, pipette tips, and vortex mixers used in the Reagent Preparation Area must remain in this area and not be moved to the other areas. Do not bring samples or amplification products into the Reagent Preparation Area.

Reagents

809.10(b)(5)(iii)

Adequate instructions for reconstitution, mixing, dilution, etc.



ASSAY PROTOCOL

The Abbott RealTime IDH1 assay protocol includes the following steps:

A. Manual preparation (ie, DNA extraction) of samples (specimens and controls) using the Abbott *m*Sample Preparation System$_{DNA}$.

B. PCR assay setup using the sample eluates and the Abbott RealTime IDH1 Amplification Reagent Kit.

C. Amplification/detection on the Abbott *m*2000*rt* instrument.

Refer to the **WARNINGS AND PRECAUTIONS** section of this package insert for instructions before preparing samples. At least one Positive Control and one Negative Control must be included in each run.

Note: Each Abbott *m*Sample Preparation System$_{DNA}$ contains 4 sets of reagents. Each set of reagents can support preparation (ie, DNA extraction) of up to 24 samples (patient specimens and/or assay controls). Discard any reagents remaining after 24 preparations.

Note: Per magnetic rack, a maximum of 12 samples (patient specimens and/or assay controls) can undergo DNA extraction. It is not recommended to perform DNA extraction in batch sizes that exceed 12 samples.

Note: Each Abbott RealTime IDH1 Amplification Reagent Kit supports testing of up to 24 samples (patient specimens and/or assay controls).

Reagent Preparation Area

Thawing of Amplification Reagents

New or previously prepared master mixes may be used **(see Preparation of Amplification Master Mixes)**.

1. If a new master mix is needed, thaw the Oligonucleotide Reagents and Activation Reagent at 15 to 30°C or at 2 to 8°C.

   • Once thawed, if the amplification reagents are not being used immediately, they can be stored at 2 to 8°C for up to 24 hours until required for preparation of the amplification master mixes.

   OR

   • If previously prepared frozen master mixes are used, thaw the master mixes at 15 to 30°C for up to 30 minutes prior to PCR setup. Frozen master mixes should not undergo more than 5 freeze/thaw cycles.

Example: Abbott RealTime IDH1

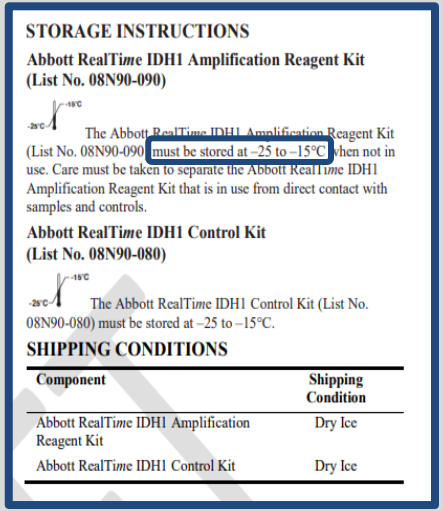
Reagents

809.10(b)(5)(iv)

Appropriate storage instructions

- Adequate to protect the stability of the product
  - As applicable, conditions such as temperature, light, humidity, other pertinent factors
- For products requiring manipulation, such as reconstitution and/or mixing before use, appropriate storage instructions shall be provided for the reconstituted or mixed product. The basis for such instructions shall be determined by reliable, meaningful, and specific test methods such as those described in 21 CFR 211.166

Example: Abbott RealTime IDH1



STORAGE INSTRUCTIONS

Abbott RealTime IDH1 Amplification Reagent Kit (List No. 08N90-090)

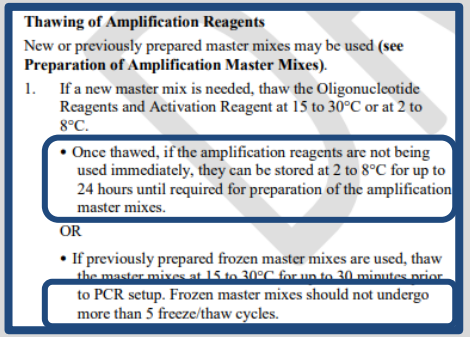
The Abbott RealTime IDH1 Amplification Reagent Kit (List No. 08N90-090) must be stored at –25 to –15°C when not in use. Care must be taken to separate the Abbott RealTime IDH1 Amplification Reagent Kit that is in use from direct contact with samples and controls.

Abbott RealTime IDH1 Control Kit (List No. 08N90-080)

The Abbott RealTime IDH1 Control Kit (List No. 08N90-080) must be stored at –25 to –15°C.

SHIPPING CONDITIONS

Component	Shipping Condition
Abbott RealTime IDH1 Amplification Reagent Kit	Dry Ice
Abbott RealTime IDH1 Control Kit	Dry Ice



Thawing of Amplification Reagents

New or previously prepared master mixes may be used **(see Preparation of Amplification Master Mixes)**.

1. If a new master mix is needed, thaw the Oligonucleotide Reagents and Activation Reagent at 15 to 30°C or at 2 to 8°C.
   - Once thawed, if the amplification reagents are not being used immediately, they can be stored at 2 to 8°C for up to 24 hours until required for preparation of the amplification master mixes.

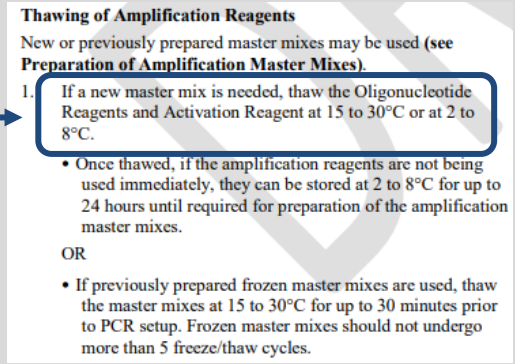
   OR
   - If previously prepared frozen master mixes are used, thaw the master mixes at 15 to 30°C for up to 30 minutes prior to PCR setup. Frozen master mixes should not undergo more than 5 freeze/thaw cycles.

Reagents

809.10(b)(5)(v)

Statement of any purification or treatment required for use

Example: Abbott RealTime IDH1



Thawing of Amplification Reagents

New or previously prepared master mixes may be used **(see Preparation of Amplification Master Mixes)**.

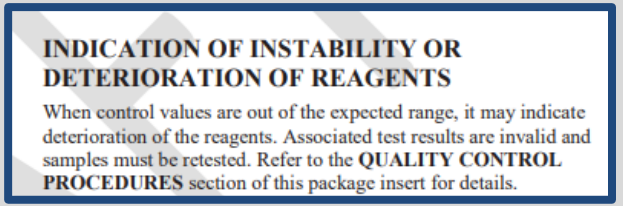
1. If a new master mix is needed, thaw the Oligonucleotide Reagents and Activation Reagent at 15 to 30°C or at 2 to 8°C.
   - Once thawed, if the amplification reagents are not being used immediately, they can be stored at 2 to 8°C for up to 24 hours until required for preparation of the amplification master mixes.

   OR

   - If previously prepared frozen master mixes are used, thaw the master mixes at 15 to 30°C for up to 30 minutes prior to PCR setup. Frozen master mixes should not undergo more than 5 freeze/thaw cycles.

809.10(b)(5)(vi)

Physical, biological, or chemical indications of instability or deterioration



INDICATION OF INSTABILITY OR DETERIORATION OF REAGENTS

When control values are out of the expected range, it may indicate deterioration of the reagents. Associated test results are invalid and samples must be retested. Refer to the **QUALITY CONTROL PROCEDURES** section of this package insert for details.

Instruments

For LDTs, this information might be in the test protocol, the instrument's Operations Manual, or other laboratory documents.

809.10(b)(6)

(i) Use or function

(ii) Installation procedures and special requirements

(iii) Principles of operation.

(iv) Performance characteristics and specifications

(v) Operating instructions

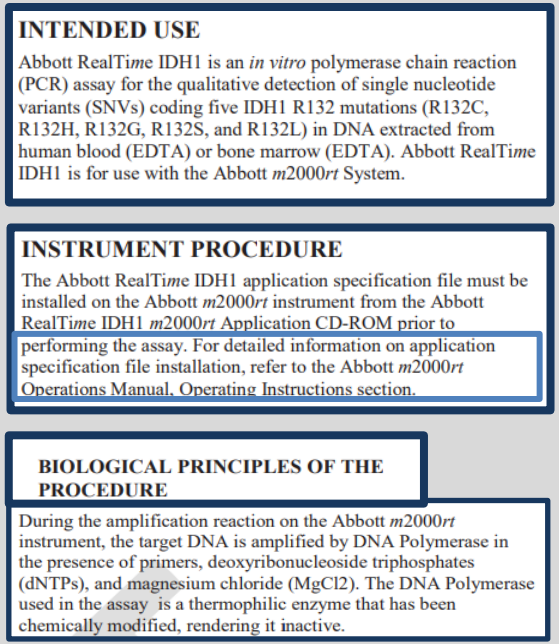
(vi) Calibration procedures including materials and/or equipment to be used

(vii) Operational precautions and limitations

(vii) Hazards

(ix) Service and maintenance information

Example: Abbott RealTime IDH1



INTENDED USE

Abbott RealTi*me* IDH1 is an *in vitro* polymerase chain reaction (PCR) assay for the qualitative detection of single nucleotide variants (SNVs) coding five IDH1 R132 mutations (R132C, R132H, R132G, R132S, and R132L) in DNA extracted from human blood (EDTA) or bone marrow (EDTA). Abbott RealTi*me* IDH1 is for use with the Abbott *m*2000*rt* System.

INSTRUMENT PROCEDURE

The Abbott RealTi*me* IDH1 application specification file must be installed on the Abbott *m*2000*rt* instrument from the Abbott RealTi*me* IDH1 *m*2000*rt* Application CD-ROM prior to performing the assay. For detailed information on application specification file installation, refer to the Abbott *m*2000*rt* Operations Manual, Operating Instructions section.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

During the amplification reaction on the Abbott *m*2000*rt* instrument, the target DNA is amplified by DNA Polymerase in the presence of primers, deoxyribonucleoside triphosphates (dNTPs), and magnesium chloride (MgCl2). The DNA Polymerase used in the assay is a thermophilic enzyme that has been chemically modified, rendering it inactive.

Instruments

809.10(b)(6)

(i) Use or function

(ii) Installation procedures and special requirements

(iii) Principles of operation.

(iv) Performance characteristics and specifications

(v) Operating instructions

(vi) Calibration procedures including materials and/or equipment to be used

(vii) Operational precautions and limitations

(viii) Hazards

(ix) Service and maintenance information

The list of performance characteristics required under 809.10(b)(6) for instruments used in a test system are the same as those described under 809.10(b)(12).

Instruments labeled for clinical diagnostic use include instrument specifications in compliant labeling accompanying the instrument.

When an LDT uses an instrument not previously labeled for clinical diagnostic use, labeling accompanying the LDT must include instrument-specific specifications.

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Instruments

809.10(b)(6)

(i) Use or function

(ii) Installation procedures and special requirements

(iii) Principles of operation.

(iv) Performance characteristics and specifications

(v) Operating instructions

(vi) Calibration procedures including materials and/or equipment to be used

(vii) Operational precautions and limitations

(viii) Hazards

(ix) Service and maintenance information

Example: Abbott RealTime IDH1

INSTRUMENT PROCEDURE

The Abbott RealTi*me* IDH1 application specification file must be installed on the Abbott *m*2000*rt* instrument from the Abbott RealTi*me* IDH1 *m*2000*rt* Application CD-ROM prior to performing the assay. For detailed information on application specification file installation, refer to the Abbott *m*2000*rt* Operations Manual, Operating Instructions section.

Abbott *m*2000*rt* Initiation and Test Order Creation

48. Switch on and initialize the Abbott *m*2000*rt* instrument.
49. Create an 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 specification file corresponding to the Abbott RealTi*me* IDH1 assay.
50. A 12-sample setup (2 controls and 10 specimens) for the Abbott 96-well reaction plate is shown in Figure 1 below.

Figure 1: Example of a 12-Sample Setup for Abbott 96-Well Optical Reaction Plate.

Example Plate Setup

	1	2	3	4	5	6	7	8
A	NEG	NEG	#7	#7				
B	POS	POS	#8	#8				
C	#1	#1	#9	#9				
D	#2	#2	#10	#10				
E	#3	#3						
F	#4	#4						
G	#5	#5						
H	#6	#6						

Oligo 1 master mix

Oligo 2 master mix

Oligo 1 master mix

Oligo 2 master mix

Figure 1 represents a partial image of the Abbott 96-Well Optical Reaction Plate.

Instruments

809.10(b)(6)

(i) Use or function

(ii) Installation procedures and special requirements

(iii) Principles of operation.

(iv) Performance characteristics and specifications

(v) Operating instructions

(vi) Calibration procedures including materials and/or equipment to be used

(vii) Operational precautions and limitations

(viii) Hazards

(ix) Service and maintenance information

Example: Abbott RealTime IDH1

Abbott *m*2000*rt* Optical Calibration

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. Optical calibration of the Abbott *m*2000*rt* instrument is required for the accurate measurement and discrimination of dye fluorescence during the Abbott RealTi*m*e IDH1 assay.

The following Abbott *m*2000*rt* Optical Calibration Plates are used to calibrate the Abbott *m*2000*rt* instrument for the Abbott RealTi*m*e IDH1 assay:

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

Instruments

809.10(b)(6)

(i) Use or function

(ii) Installation procedures and special requirements

(iii) Principles of operation.

(iv) Performance characteristics and specifications

(v) Operating instructions

(vi) Calibration procedures including materials and/or equipment to be used

(vii) Operational precautions and limitations

(viii) Hazards

(ix) Service and maintenance information

Example: Abbott RealTime IDH1

Procedural Precautions

- Read the instructions in this package insert carefully before processing samples. The Abbott RealTi*me* IDH1 Amplification Reagent Kit is intended for use with the Abbott RealTi*me* IDH1 Control Kit and the Abbott *m*Sample Preparation System$_{DNA}$ for sample processing, and the Abbott *m*2000*rt* instrument for amplification and detection.
- For a detailed description of how to operate the Abbott *m*2000*rt* instrument, refer to the Abbott *m*2000*rt* Operations Manual, **Operating Instructions** section.
- Laboratory personnel must be trained to operate the Abbott *m*2000*rt* instrument. The operator must have thorough knowledge of the assay application run on the instrument and must follow good laboratory practices.

Safety Precautions

Refer to the Abbott *m*2000*rt* Operations Manual, **Hazards** section, for instructions on safety precautions.

Summary

- Labeling requirements for IVDs under 21 CFR 809.10(b) are intended to help ensure that IVD labeling has a consistent set of information
  - Consider the intended use of the IVD
  - Focus on clarity and completeness of information for the intended user
- Most IVDs offered as LDTs are generally expected to comply with FDA's labeling requirements by May 6, 2026.
  - As described in the preamble to the LDT final rule, there are targeted enforcement discretion policies that may apply to certain IVDs offered as LDTs, and for certain policies, FDA intends to request labeling for those IVDs at the time of device listing.
- There are many examples of IVD labeling publicly available on FDA's website for LDT manufacturers to reference, including different approaches used to comply with the labeling requirements
  - FDA anticipates that, for LDTs, the required labeling information may be encompassed in more than one document, such as a primary labeling document and the test protocol, test report template, and test menu

Laboratory Developed Tests | FDA

Date
October 24, 2024

Time
1:00 – 2:00 PM ET

Topic
FDA's Total Product Life Cycle Approach to In Vitro Diagnostic Products

Resources and References

Slide Number	Cited Resource	URL
	Labeling - Regulatory Requirements for Medical Devices	Labeling - Regulatory Requirements for Medical Devices (FDA 89-4203) | FDA
3	Laboratory Developed Tests	www.fda.gov/medical-devices/in-vitro-diagnostics/laboratory-developed-tests
5	21 CFR Part 801	eCFR :: 21 CFR Part 801 -- Labeling
5	21 CFR 809.10	www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-809
11, 14-18, 29	FoundationFocus™ CDxBRCA	P160018C.pdf (fda.gov) www.accessdata.fda.gov/cdrh_docs/pdf16/P160018C.pdf
12, 19, 21, 28, 30-31, 36	ARUP Laboratories AAV5 DetectCDx	www.accessdata.fda.gov/cdrh_docs/pdf19/P190033C.pdf

Resources and References

Slide Number	Cited Resource	URL
13	*KIT* D816V Mutation Detection by PCR for Gleevec Eligibility in Aggressive Systemic Mastocytosis	www.accessdata.fda.gov/cdrh_docs/pdf14/H140006C.pdf
19	Alinity m HR HPV AMP	www.accessdata.fda.gov/cdrh_docs/pdf23/P230003C.pdf
22, 24-27	PartoSure Test	P160052C.pdf (fda.gov) www.accessdata.fda.gov/cdrh_docs/pdf16/P160052C.pdf
23, 27, 30	ADVIA Centaur Anti-HBe2 assay	www.accessdata.fda.gov/cdrh_docs/pdf20/P200017C.pdf
26, 36-43, 45-47	Abbott RealTi*me* IDH1 assay (using Abbott *m*2000*rt* instrument)	www.accessdata.fda.gov/cdrh_docs/pdf17/P170041C.pdf


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