

Aptima Specimen Transfer Kit

For *in vitro* diagnostic use.

For US export only.

Intended Use

The Aptima Specimen Transfer Kit consists of transfer tubes containing specimen transport medium (STM) and is intended for use with liquid specimen media to enable testing with Aptima assays and other Hologic products. The Aptima Specimen Transfer Kit allows for Aptima HPV assay and Aptima HPV 16 18/45 genotype assay testing of gynecological specimens collected in ThinPrep Pap Test vials containing PreservCyt solution, and specimens collected in SurePath Preservative Fluid. The Aptima Specimen Transfer Kit may also be used to enable testing of Viral Transport Media (VTM) containing lesion swab specimens. Refer to the appropriate Hologic product package insert for the indicated uses of the Aptima Specimen Transfer Kit for each product.

Reagents

Materials Provided

Aptima Specimen Transfer Kit (Cat. No. 301154C)

Aptima Specimen Transfer Kit — printable (Cat. No. PRD-05110)

Component	Quantity	Description
Aptima Specimen Transfer tubes	100 tubes	1 tube x 2.9 mL STM.

Materials Required But Available Separately

Materials available from Hologic have catalog numbers listed, unless otherwise specified.

Pipettor and tips capable of pipetting 1000 µL

Bleach, 5% to 7% (0.7M to 1.0M) sodium hypochlorite solution

Test tube rack

Plastic-backed absorbent laboratory bench covers

Fisherbrand BloodBloc Super Absorbency Wipes (available from Fisher Scientific)

Lint-free disposable wipes

Aptima Transfer Solution Kit (Cat. No. 303658), for treating SurePath specimens

Pipettor and tips capable of pipetting 300 µL

Pipettor and tips capable of pipetting 25 mL

Water bath capable of maintaining a temperature of 90°C

20-mm-diameter polypropylene water bath balls

Optional Materials

Gyn TransCyt™ Filters (clear) for use with the ThinPrep 2000 System

Kit Storage Requirements

Store specimen transfer tubes at room temperature (15°C to 30°C) prior to use.

Store the Aptima Transfer Solution at 2°C to 8°C (refrigerated) upon receipt.

Do not use reagents beyond expiration date indicated on the vials.

Warnings and Precautions

- A. For handling ThinPrep liquid cytology specimens refer to the ThinPrep 2000 System, ThinPrep 3000 System*, ThinPrep 5000 Processor or ThinPrep 5000 Processor with AutoLoader (ThinPrep 5000 Systems), or ThinPrep Genesis Processor instructions for use.
- B. If the Aliquot Removal procedure will be used, refer to the ThinPrep 2000 System, ThinPrep 3000 System, or ThinPrep 5000 Systems instructions on aliquot removal. (The ThinPrep Genesis Processor performs aliquot removal inside the instrument.)
- C. Use the Aptima Specimen Transfer Kit with Aptima assays or other Hologic products only. Performance has not been evaluated with non-Hologic products.
- D. Do not apply the Aptima specimen transport medium directly to skin or mucous membranes or take internally.
- E. Use only supplied or specified disposable laboratory ware.
- F. Use routine laboratory precautions. Do not eat, drink or smoke in designated work areas. Wear disposable, powderless gloves, protective eye wear, and laboratory coats when handling specimens and reagents. Wash hands thoroughly after handling specimens and reagents.
- G. Specimens may be infectious. Use Universal Precautions when handling specimens. Only laboratory personnel adequately trained in handling infectious materials should perform the procedures described in this package insert.
- H. Take care to avoid cross-contamination during the specimen handling steps. Specimens may contain high levels of organisms. Change gloves frequently and always change gloves when they come in contact with specimen. Discard used materials without passing over open containers. Avoid specimen container contact with one another.
- I. Work surfaces, pipettes and other equipment must be regularly decontaminated with 0.5% sodium hypochlorite solution, made with deionized (DI) water. If DI water is not used in the 0.5% sodium hypochlorite solution, the effectiveness of the solution may be compromised. The pH of tap water varies from lab to lab. Alkaline water can decrease the available chlorine making the sodium hypochlorite less effective for decontaminating equipment. Refer to *ThinPrep Liquid Cytology Specimen Procedural Notes* and *SurePath Liquid Cytology Specimen Procedural Notes*, and *Decontamination Instructions*. The effect of the ThinPrep 2000 System decontamination procedure was not assessed for its impact on cytology results. Prior to implementing the decontamination procedure, laboratories should validate that the decontamination procedure does not impact cytology results.
- J. Only pipette tips with hydrophobic plugs should be used to transfer specimens to the transfer tubes.
- K. Do not use this kit after its expiration date.
- L. Maintain proper temperature conditions during specimen shipping and storage to ensure the integrity of the specimen. Refer to the appropriate Aptima assay or other Hologic product package insert for specific shipping and storage conditions.
- M. Dispose of residual clinical specimens, unused reagents and waste in accordance with local regulations.

*For use with the Aptima HPV assay and the Aptima HPV 16 18/45 genotype assay only.

- N. If testing gynecological specimens processed with the ThinPrep 2000 System, a specific procedure has been validated to mitigate the potential for cross-contamination during cytology processing. Two important steps of the procedure include: (1) soaking the filter cap in 0.5% sodium hypochlorite solution for 1 minute between samples and (2) mandating that the operator change gloves between the handling of each sample. Refer to *ThinPrep Liquid Cytology Specimen Procedural Note C* for a detailed protocol.
- O. Do not transfer and use a SurePath liquid cytology specimen for Aptima HPV assay or Aptima HPV 16 18/45 genotype assay testing if a collection device is not present in the vial.
- P. Use caution when handling the Aptima Transfer Solution (Pro K Reconstitution Solution and reconstituted Pro K Transfer Solution). Avoid direct contact of both skin or mucous membranes and avoid ingestion. Wash with water if these reagents come into contact with skin or eyes. If spills occur, dilute with water and wipe dry.
- Q. Some reagents of this kit may be labeled with risk and safety symbols.

Note: Hazard Communication information for labeling of globally marketed products reflects the US and EU Safety Data Sheets (SDS) classifications. For hazard communication information specific to your region, refer to the region specific SDS on the Safety Data Sheet Library at www.hologic.com.

Specimen Performance

Gynecological Specimens

The assay performance characteristics of gynecologic specimens collected in ThinPrep and SurePath liquid cytology vials are provided in the appropriate Aptima assay package insert. The Aptima assay package inserts may be referenced online at www.hologic.com. The table below identifies the acceptable aliquot procedure for each of the Aptima assays.

Aptima assay	Pre-Processed Aliquot	Post-Processed Aliquot			SurePath Liquid Cytology Specimens
		ThinPrep 2000 System	ThinPrep 3000 System	ThinPrep 5000 Systems	
<i>Chlamydia trachomatis</i> and <i>Neisseria gonorrhoeae</i> (Aptima Combo 2™ assay)	Yes	Yes	No	Yes	No
<i>Chlamydia trachomatis</i> (Aptima CT assay)		Yes	No	No	No
<i>Neisseria gonorrhoeae</i> (Aptima GC assay)		No	No	No	No
<i>Mycoplasma genitalium</i> (Aptima Mycoplasma genitalium assay)		No	No	No	No
<i>Trichomonas vaginalis</i> (Aptima Trichomonas vaginalis assay)		Yes	Yes	Yes	Yes
Human papillomavirus (Aptima HPV assay)		Yes	Yes	Yes	Yes
Human papillomavirus (Aptima HPV 16 18/45 genotype assay)					

VTM Lesion Swab Specimens or Other Liquid Media Specimens

The performance characteristics of VTM lesion swab specimens or other liquid media specimens are provided in the appropriate Aptima assay or other Hologic product package insert. The Aptima assay and Hologic product package inserts may be referenced online at www.hologic.com.

Specimen Transport and Storage

Note: Refer to the appropriate Aptima assay or Hologic product package insert for complete storage and handling information.

Note: Specimens must be shipped in accordance with applicable national and international transportation regulations.

ThinPrep Liquid Cytology Specimens

Gynecological specimens may be stored in the ThinPrep liquid cytology vials for at least 30 days at 2°C to 30°C prior to transfer to Aptima Specimen Transfer tubes. Refer to the appropriate Aptima assay package insert for additional storage and handling information. ThinPrep liquid cytology specimens transferred to the Aptima Specimen Transfer tube may be stored for at least 14 days at 2°C to 30°C prior to testing. Refer to the appropriate Aptima assay package insert for additional storage and handling information.

SurePath Liquid Cytology Specimens

Gynecological specimens may be stored in the SurePath liquid cytology vial for 7 days at 2°C to 25°C prior to transfer to Aptima Specimen Transfer tubes. After the SurePath liquid cytology specimen is transferred to the Aptima Specimen Transfer tube, the specimen may be stored for 7 days at 2°C to 25°C prior to Aptima Transfer Solution treatment. SurePath specimens must be treated prior to testing with the Aptima HPV assay and the Aptima HPV 16 18/45 genotype assay. Refer to the Aptima HPV assay and the Aptima HPV 16 18/45 genotype assay package inserts for additional storage and handling information.

VTM Lesion Swab Specimens

Lesion swab specimens may be stored for 3 days in the VTM tube at 2°C to 8°C prior to transfer to the Aptima Specimen Transfer tubes. Refer to the appropriate Aptima assay package insert for additional storage and handling information. VTM lesion swab specimens transferred to the Aptima Specimen Transfer tube may be stored for up to 30 days at 2°C to 30°C prior to testing. If longer storage is needed, freeze the VTM lesion swab specimen in the Aptima specimen transfer tube for up to 90 days at ≤ -20°C.

Other Liquid Media Specimens

Refer to the appropriate Aptima assay or other Hologic product package insert for acceptable specimen transport and storage information.

ThinPrep Liquid Cytology Specimen Procedural Notes

- A. Preparation of the Specimen Transfer Area
 1. Put on clean gloves.
 2. Wipe down work surfaces and pipettors with 0.5% sodium hypochlorite solution. (Use DI water to dilute 5% to 7% (0.7M to 1.0M) sodium hypochlorite solution. A prepared batch of 0.5% sodium hypochlorite solution will be effective for 1 week if it is properly stored.)
 3. Allow the sodium hypochlorite solution to contact work surfaces and pipettors for at least 1 minute, then follow with a water rinse. Dry the surfaces with paper towels.
 4. Cover the bench with clean, plastic-backed, absorbent laboratory bench covers.
 5. In the specimen transfer area, place a test tube rack containing a sufficient number of Aptima Specimen Transfer tubes corresponding to the number of ThinPrep liquid cytology specimens being tested.

If the ThinPrep aliquot removal procedure will be used, refer to the ThinPrep 2000 System, ThinPrep 3000 System, or ThinPrep 5000 Systems instructions for use on aliquot removal and follow the Hologic Specimen Transfer Procedure as defined in *Procedural Note B*.

Note: This does not apply to the ThinPrep Genesis Processor as that device performs aliquot removal inside the instrument.

If ThinPrep liquid cytology specimens will be transferred into Aptima Specimen Transfer tubes after processing using the ThinPrep 2000 System, perform ThinPrep 2000 System processing according to the instructions in *Procedural Note C* and *Procedural Note D*.

If ThinPrep liquid cytology specimens will be transferred into Aptima Specimen Transfer tubes after processing using the ThinPrep 3000 System, perform ThinPrep 3000 System processing according to the ThinPrep 3000 System instructions for use.

If ThinPrep liquid cytology specimens will be transferred into Aptima Specimen Transfer tubes after processing using either of the ThinPrep 5000 Systems, perform ThinPrep 5000 Systems processing according to the ThinPrep 5000 Systems instructions for use.

If ThinPrep liquid cytology specimens will be transferred into Aptima Specimen Transfer tubes after processing using the ThinPrep Genesis Processor, perform ThinPrep Genesis Processor processing according to the instructions in *Procedural Note D*.

B. Specimen Transfer Procedure for ThinPrep Liquid Cytology Specimen Aliquots Removed Before Processing with the ThinPrep 2000 System, ThinPrep 3000 System, or ThinPrep 5000 Systems

Note: These instructions do not apply to the ThinPrep Genesis Processor as that device performs aliquot removal inside the instrument.

1. Put on clean gloves and transfer specimens to be tested to the specimen transfer area.
2. Uncap the Aptima Specimen Transfer tube, placing the cap on the bench with the threads facing up.
3. Vortex the tube containing the removed aliquot of ThinPrep liquid cytology specimen for 3 to 10 seconds. Uncap the tube, placing the cap on the bench with the threads facing up.
4. Within 1 minute of vortexing, transfer 1 mL of the ThinPrep liquid cytology specimen into the Aptima Specimen Transfer tube.
5. Dispose of the pipette tip in an appropriate biohazard container.
6. Recap the Aptima Specimen Transfer tube tightly. Gently invert the tube 2 to 3 times to ensure complete mixture of the specimen.
7. Recap the tube containing the removed aliquot of ThinPrep liquid cytology specimen for storage for up to 30 days at 2°C to 30°C, if desired.
8. Put on clean gloves and repeat steps 1 through 7 above for the transfer of subsequent specimens. To reduce the risk of contaminating other specimens, work with one ThinPrep liquid cytology specimen at a time.
9. Proceed to the *Test Procedure* section.

C. Processing ThinPrep Liquid Cytology Specimens Using the ThinPrep 2000 System

Refer to the ThinPrep 2000 System instructions for use to perform the standard cytology processing steps and the maintenance of the O-rings at the base of the filter cap.

Note: The following cleaning procedures on the ThinPrep 2000 System are not required for the Aptima HPV assays. See *ThinPrep Liquid Cytology Specimen Contamination Study for Aptima HPV Assay* below for more information.

1. Put on clean gloves.
2. Clean 2 filter caps by soaking them in 0.5% sodium hypochlorite solution for at least 1 minute, rinse the caps in DI water and dry them thoroughly with a lint-free, disposable wipe. Dispose of the wipe.

Note: Using 2 filter caps enables the work flow to continue while 1 filter cap is soaking.

3. Place a clean filter cap on a BloodBloc Super Absorbency Wipe.
 4. Place the fixative bath into the ThinPrep 2000 System.
 5. Create a filter assembly by placing a new Gyn TransCyt Filter in a clean filter cap and insert the filter assembly into the ThinPrep 2000 System. Refer to the ThinPrep 2000 System instructions for use for details on performing this step.
 6. Put a slide in the slide holder. Refer to the ThinPrep 2000 System instructions for use for details on performing this step.
 7. Uncap the ThinPrep Pap Test vial, placing the cap on the bench with the threads facing up. Ensure that the bench is clean, with no bleach residue or foreign particles.
 8. Load the ThinPrep Pap Test vial into the ThinPrep 2000 System. From the ThinPrep system main menu, select "4-GYN" by pressing **4** on the keypad.
 9. Put on clean gloves.
 10. After the slide preparation is finished, open the door, remove the ThinPrep Pap Test vial and recap the vial.
 11. Remove the fixative bath and place the slide in a 95% ethanol bath.
 12. Return the fixative bath to the system.
 13. Remove the filter assembly from the system using one hand to grasp the filter cap and, using a lint-free, disposable wipe as a barrier, separate the filter from the filter cap. Discard the filter, gloves, and disposable wipe. **Do not discard the filter cap.**
 14. Place the filter cap in a container of 0.5% sodium hypochlorite solution for at least 1 minute.
 15. With clean gloves, rinse the filter cap in DI water, then dry it thoroughly with a lint-free disposable wipe. Dispose of the wipe.
 16. Repeat the process for each specimen starting with step 3 of this processing procedure, changing gloves between each specimen, until all of the specimens are processed.
- D. Specimen Transfer Procedure for ThinPrep Liquid Cytology Specimens After Processing with the ThinPrep 2000 System, ThinPrep 3000 System, ThinPrep 5000 Systems, or ThinPrep Genesis Processor
1. Put on clean gloves and transfer specimens to be tested to the specimen transfer area.
 2. Uncap the Aptima Specimen Transfer tube, placing the cap on the bench with the threads facing up.
 3. Vortex the ThinPrep Pap Test vial for 3 to 10 seconds. Uncap the vial, placing the cap on the bench with the threads facing up.
 4. Within 1 minute of vortexing, transfer 1 mL of the processed ThinPrep liquid cytology specimen into the Aptima Specimen Transfer tube.
 5. Dispose of the pipette tip in an appropriate biohazard container.
 6. Recap the Aptima Specimen Transfer tube tightly. Gently invert the tube 2 to 3 times to ensure complete mixture of the specimen.
 7. Recap the ThinPrep Pap Test vial for storage, if desired.
 8. Put on clean gloves and repeat steps 1 through 7 above for the transfer of subsequent specimens. To reduce the risk of contaminating other specimens, work with one processed ThinPrep liquid cytology specimen at a time.
 9. Proceed to the *Test Procedure* section.

SurePath Liquid Cytology Specimen Procedural Notes

- A. Preparation of the Specimen Transfer Area
 1. Put on clean gloves.
 2. Wipe down work surfaces and pipettors with 0.5% sodium hypochlorite solution. (Use DI water to dilute 5% to 7% (0.7M to 1.0M) sodium hypochlorite solution. A prepared batch of 0.5% sodium hypochlorite solution will be effective for 1 week if it is properly stored.)
 3. Allow the sodium hypochlorite solution to contact work surfaces and pipettors for at least 1 minute, then follow with a water rinse. Dry the surfaces with paper towels.
 4. Cover the bench with clean, plastic-backed, absorbent laboratory bench covers.
 5. In the specimen transfer area, place a test tube rack containing a sufficient number of Aptima Specimen Transfer tubes corresponding to the number of SurePath liquid cytology specimens being tested.
 6. Label each Aptima Specimen Transfer tube with the accession number or specimen ID number.
- B. Specimen Transfer Procedure for SurePath Liquid Cytology Specimens
 1. Put on clean gloves and transfer specimen to be tested to the specimen transfer area.
 2. Uncap the Aptima Specimen Transfer tube, placing the cap on the bench with the threads facing up.
 3. Vortex the SurePath liquid cytology vial for 3 to 10 seconds. Uncap the vial, placing the cap on the bench with the threads facing up.
 4. Within 1 minute of vortexing, transfer 0.5 mL of the SurePath liquid cytology specimen into the Aptima Specimen Transfer tube. Refer to *Specimen Treatment Procedure for SurePath Liquid Cytology Specimens* for further details.
 5. Dispose of the pipette tip in an appropriate biohazard container.
 6. Recap the Aptima Specimen Transfer tube tightly. Gently invert the tube 2 to 3 times to ensure complete mixture of the specimen.
 7. Recap the SurePath vial for storage, if desired.
 8. Put on clean gloves and repeat steps 1 through 7 above for the transfer of subsequent specimens. To reduce the risk of contaminating other specimens, work with one SurePath liquid cytology specimen at a time.
 9. Proceed to the *Test Procedure* section.
- C. Specimen Treatment Procedure for SurePath Liquid Cytology Specimens
 1. Prepare Work Surface
 - a. Put on clean gloves.
 - b. Wipe down bench top or work area surfaces with 0.5% sodium hypochlorite solution. (Use DI water to dilute 5% to 7% (0.7M to 1.0M) sodium hypochlorite solution. A prepared batch of 0.5% sodium hypochlorite solution will be effective for 1 week if properly stored.)
 - c. Allow the sodium hypochlorite solution to contact work surfaces for 1 minute and then follow with a water rinse. Dry the surfaces with paper towels.
 - d. Cover the bench with clean, plastic-backed, absorbent laboratory bench covers.
 2. Aptima Transfer Solution Reagent Preparation of a New Kit
 - a. Open the lyophilized Pro K vial (glass).
 - b. Firmly insert the notched end of the reconstitution collar into the glass vial's opening (Figure 1, Step 1).

- c. Open the Pro K Reconstitution Solution bottle (plastic) and set the cap on a clean, covered work surface.
- d. While holding the plastic bottle on the bench, firmly insert the other end of the reconstitution collar into the bottle's opening (Figure 1, Step 2).
- e. Invert the assembled bottle and vial. Allow the solution to drain into the glass vial (Figure 1, Step 3). The volume of liquid should exceed the volume of the glass vial, causing some of the liquid to remain in the reconstitution collar.
- f. Gently swirl the solution in the vial to mix (Figure 1, Step 4).
- g. Wait for the lyophilized reagent to go into solution (approximately 3 minutes).
- h. Invert the assembled bottle and vial (Figure 1, Step 5). Allow all of the liquid to drain back into the bottle.
- i. Remove the reconstitution collar and glass vial (Figure 1, Step 6).
- j. Recap the plastic bottle (Figure 1, Step 7).
- k. Mix by inverting the bottle 5 or 6 times.
- l. Record the operator's initials and reconstitution date on the bottle.
- m. Discard both the reconstitution collar and glass vial (Figure 1, Step 8).

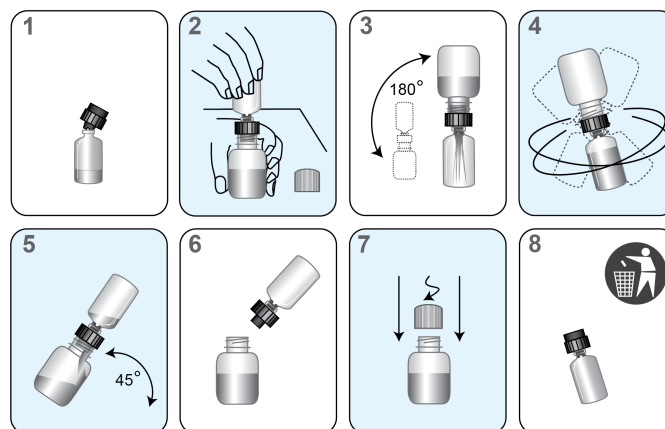


Figure 1. Reconstitution Process

- n. Store the reconstituted Pro K Transfer Solution for up to 30 days at 2°C to 8°C. Do not freeze.
 - o. Discard any reconstituted Pro K Transfer Solution after 30 days or after the kit expiration date, whichever comes first.
3. Aptima Transfer Solution Reagent Preparation of a Previously Reconstituted Kit
 - a. Allow the reconstituted Pro K Transfer Solution to come to room temperature.
 - b. Mix thoroughly by inverting the bottle prior to use.
 4. Reagent Addition
 - a. Place the rack of Aptima Specimen Transfer tubes containing SurePath liquid cytology specimens onto the covered work surface.
 - b. Uncap one specimen tube and place the cap on a clean, covered work surface with the threads facing up.
 - c. Add 300 µL of the reconstituted Pro K Transfer Solution to the specimen tube.
 - d. Recap the specimen tube and gently invert the tube 5 to 6 times to mix.
 - e. Repeat steps b through d for the remaining specimen tubes.

5. Sample Treatment
 - a. Allow a water bath to reach 90°C. The water bath lid can be used to pre-heat the water bath, but should be removed throughout the incubation. Cover the surface area of the water bath with water bath balls to provide surface insulation during the incubation.

Note: Failure to remove the water bath lid during the incubation step could result in compromised Aptima Specimen Transfer tube caps.
 - b. Place the rack of specimen tubes containing the reconstituted Pro K Transfer Solution into the water bath. The water level in the water bath should reach the liquid level in the specimen tubes.
 - c. Incubate the specimen tubes for 15 minutes.
 - d. Remove the specimen tubes from the water bath and let cool to room temperature.
 - e. Treated samples may be stored for up to 17 days at 2°C to 8°C prior to testing with the Aptima HPV assay and the Aptima HPV 16 18/45 genotype assay.

VTM Lesion Swab Specimen Procedural Notes

- A. Preparation of the Specimen Transfer Area
 1. Put on clean powderless gloves.
 2. Wipe down work surfaces and pipettors with 2.5% to 3.5% (0.35 M to 0.5 M) sodium hypochlorite solution.
 3. Allow the sodium hypochlorite solution to contact work surfaces and pipettors for at least 1 minute, then follow with a DI water rinse. Dry the surfaces with clean paper towels.
 4. Cover the bench with clean, plastic-backed, absorbent laboratory bench covers.
 5. In the specimen transfer area, place a test tube rack containing a sufficient number of Aptima specimen transfer tubes corresponding to the number of VTM specimens being tested.
 6. Label each Aptima specimen transfer tube with the accession number or specimen ID.
- B. Specimen Transfer Procedure
 1. To reduce the risk of contaminating other specimens, work with one VTM specimen at a time.
 2. Put on clean powderless gloves and place specimens to be tested in the specimen transfer area.
 3. Obtain one VTM specimen. Uncap the corresponding Aptima specimen transfer tube, placing the cap on the bench with the threads facing up.
 4. Vortex the VTM specimen for 3 to 10 seconds. Uncap the tube, placing the cap on the bench with the threads facing up.
 5. Within 1 minute of vortexing, pipet 0.5 mL of the VTM specimen into the Aptima specimen transfer tube containing 2.9 mL of specimen transport medium.
 6. Dispose of the pipette tip in an appropriate biohazard container.
 7. Recap the Aptima specimen transfer tube tightly. Gently invert the tube 2 to 3 times to ensure complete mixture of the specimen.
 8. Recap the tube containing the leftover VTM specimen for storage at $\leq -70^{\circ}\text{C}$ if desired.
 9. Repeat steps 3 through 8 above for the transfer of subsequent specimens. Change powderless gloves often and especially if they come in contact with specimen.

Other Liquid Media Specimen Procedural Notes

Refer to the appropriate Hologic product package insert for the specimen transfer procedure.

Test Procedure

Test the ThinPrep, SurePath liquid cytology, VTM lesion swab, or other liquid media specimens from the Aptima Specimen Transfer tube according to the instructions in the appropriate Aptima assay or other Hologic product package insert.

Note: SurePath liquid cytology specimens transferred to an Aptima Specimen Transfer tube must be pre-treated prior to testing with the Aptima HPV assay and the Aptima HPV 16 18/45 genotype assay. Refer to the Aptima HPV assay and the Aptima HPV 16 18/45 genotype assay package inserts for further details.

Decontamination Instructions

Note: If ThinPrep liquid cytology specimens are transferred into Aptima Specimen Transfer tubes after processing using the ThinPrep 2000 System, the ThinPrep 2000 System must be decontaminated after 8 hours of use.

- It is important to clean the system from the top of the machine to the bottom and to change gloves as instructed in order to prevent recontamination of cleaned surfaces.
 - Avoid touching the internal instrumentation wiring throughout this process.
 - Only use 0.5% sodium hypochlorite solution to decontaminate the ThinPrep 2000 System.
- A. Decontamination of the ThinPrep 2000 System
1. Put on clean gloves.
 2. Wet a lint-free disposable wipe with 0.5% sodium hypochlorite solution.
 3. Open the sample door, wipe down the slide holder with the disposable wipe, and dispose of the wipe.
 4. Close the sample door.
 5. Move the internal workings of the system into the maintenance position by pressing **7** then **2** and **Enter** on the keypad.
 6. Open the sample door.
 7. Put on clean gloves.
 8. Wet a lint-free disposable wipe with 0.5% sodium hypochlorite solution and wipe down the surfaces from top to bottom. Be sure to thoroughly clean surfaces that are handled during processing such as the slide holder, fixative bath holder, and sample vial holder. Also be sure to clean the cap seal and the inside of the system's door. Dispose of the wipe.
 9. Change gloves. Using a lint-free disposable wipe moistened with 0.5% sodium hypochlorite solution, clean the exterior of the system from top to bottom paying close attention to the door handle and the keypad. Dispose of the wipe.
 10. Allow the 0.5% sodium hypochlorite solution to sit on the equipment for 5 minutes.
 11. Return the system to the working position by closing the sample door and pressing **Enter** on the keypad.
 12. Change gloves and wipe down the slide holder with a lint-free, disposable wipe soaked in DI water. Dispose of the wipe.
 13. Close the sample door and enter **7** then **2** and **Enter** on the keypad to return the system to the maintenance position.
 14. Open the sample door and, working from top to bottom, wipe the interior with a lint-free, disposable wipe soaked in DI water, being sure to thoroughly remove the 0.5% sodium hypochlorite solution from the cap seal. Dispose of the wipe.
 15. Repeat steps 1 through 14 above to ensure that decontamination is complete.

B. Lab Contamination Monitoring Protocol

There are many laboratory-specific factors that may contribute to contamination, including testing volume, workflow, disease prevalence, and various other laboratory activities. These factors should be taken into consideration when contamination monitoring frequency is being established. Intervals for contamination monitoring should be established based on each laboratory's practices and procedures. Each cytology lab must coordinate with an Aptima testing site in order to test samples collected for monitoring contamination and receive the sample results.

To monitor for laboratory contamination, the following procedure may be performed using the Aptima Unisex Swab Specimen Collection Kit for Endocervical and Male Urethral Swab Specimens:

1. Label the swab transport tubes with numbers corresponding to the areas of the lab that will be tested.
2. Remove the specimen collection swab (blue shaft swab with green printing) from its packaging, wet the swab in the swab transport medium and swab the numbered area using a circular motion.
3. Immediately insert the swab into the corresponding transport tube.
4. Carefully break the swab shaft at the score line. Avoid splashing the contents.
5. Re-cap the swab transport tube tightly.
6. Repeat steps 2 through 5 for all areas to be swabbed.
7. Test the swab using instructions found in the *Test Procedure* section of the appropriate assay package insert.

If the results are positive or equivocal (see the *Test Interpretation* section of the appropriate assay package insert), the surface may be contaminated and should be decontaminated by treating with 0.5% sodium hypochlorite solution as recommended in the appropriate Operator's Manual and/or assay package insert.

Contamination Studies

ThinPrep Liquid Cytology Specimen Contamination Study for Aptima Combo 2 Assay

To demonstrate that soaking the filter cap in 0.5% sodium hypochlorite solution ("bleaching") is effective in reducing contamination, 200 negative and 200 high titer ($>1 \times 10^6$ CFU/mL) GC positive samples were alternately processed first without the bleaching steps and, subsequently, with the bleaching steps. The GC positive samples were generated by spiking the liquid cytology sample with cell equivalents of $>5 \times 10^6$ fg GC rRNA. Note that the operators changed gloves between handling each sample for both the first and second stages of the study. The same filter cap was used with all 400 samples. After processing on the ThinPrep 2000 System, 1 mL of the remaining ThinPrep sample was transferred to an Aptima Specimen Transfer tube (this is now referred to as the processed liquid cytology sample) then run in the Aptima Combo 2 assay. These conditions replicate the processes that are expected to be conducted in a typical clinical setting.

Additionally, an aliquot was removed from each sample prior to processing on the ThinPrep 2000 System as a control sample. This aliquot was tested when a sample produced a false positive result to determine if the contamination occurred prior to sample processing. Further, an additional 20 negative ThinPrep liquid cytology samples were added at the end of the second stage to determine if a build up of cells on the system (potentially due to the creation of aerosols) could contaminate negative samples.

Without the bleach step there were 24 false positives and 17 equivocal results among the ThinPrep samples for a false positive frequency of 20.5%. When the filter cap was bleached between samples the false positive frequency was 1.4% (3 false positives out of 220 negative samples). None of the pre-processed aliquots from the samples producing false results were GC-positive. This is consistent

with the notion that the contamination was not introduced prior to processing the sample on the ThinPrep 2000 System; rather, contamination was likely introduced during the cytology processing.

These studies demonstrate that incorporation of a contamination mitigation protocol decreases the potential for cross-contamination introduced by the processing steps of the ThinPrep 2000 System by > 14 fold.

ThinPrep Liquid Cytology Specimen Contamination Study for Aptima HPV Assay

ThinPrep 2000 System Study

A study was conducted to determine the false positive rate observed with the Aptima HPV assay when ThinPrep liquid cytology specimens containing a high concentration of spiked HPV-positive cells, were alternately processed with HPV-negative specimens on the ThinPrep 2000 System.

Negative samples were created by spiking 20 mL of PreservCyt solution with 3×10^5 HPV-negative cultured cells. Prior to processing on the ThinPrep 2000 System, 1 mL of each negative sample was transferred to an Aptima Specimen Transfer tube which served as a 'pre-processed' negative control. High titer HPV-positive samples were created by spiking 7.5×10^4 HPV 16-positive cultured cells and 2.25×10^5 HPV-negative cultured cells into 20 mL of PreservCyt solution. HPV-positive then HPV-negative samples were alternately processed on the ThinPrep 2000 System according to the ThinPrep 2000 System instructions for use. One set of HPV-positive and HPV-negative samples were processed following the filter cap cleaning procedure (described above in *Procedural Note C*) and one set were processed without following the filter cap cleaning procedure. An aliquot of each sample was removed after processing on the ThinPrep 2000 System (post-processed samples) and transferred to an Aptima Specimen Transfer tube. The pre- and post-processed samples were tested with the Aptima HPV assay.

The false positive rate for the pre-processed negative control samples, as well as both sets of post-processed negative samples (with cleaning procedure and without) was calculated, as well as the 2-sided 95% Score confidence interval. Of the post-processed negative samples for which the cleaning procedure was followed, one false positive was observed out of the 120 tested, which resulted in a false positive rate of 0.8% (95% CI 0.2-4.6%, 99.2% specificity). For the post-processed negative samples for which the cleaning procedure was not followed, a total of 2 false positives out of 119 negative samples tested were observed, resulting in a false positive rate of 1.7% (95% CI 0.2%-5.9%, 98.3% specificity). All three samples with false results were negative for the pre-processed negative control sample. The difference in false positive rates was not significant; -0.85% difference (95% confidence interval: -5.16% to 3.00%).

ThinPrep 3000 System Study

A study was conducted to determine the false positive rate observed with the Aptima HPV assay when ThinPrep liquid cytology specimens containing a high concentration of spiked HPV-positive cells, were alternately processed with HPV-negative specimens on the ThinPrep 3000 System.

Negative samples were created by spiking 20 mL of PreservCyt solution with 3×10^5 HPV-negative cultured cells. Prior to processing on the ThinPrep 3000 System, 1 mL of each negative sample was transferred to an Aptima Specimen Transfer tube which served as a 'pre-processed' negative control. High titer HPV-positive samples were created by spiking 2×10^5 HPV 16-positive cultured cells and 1×10^5 HPV-negative cells into 20 mL of PreservCyt solution. HPV-positive then HPV-negative samples were alternately processed on the ThinPrep 3000 System according to the ThinPrep 3000 System instructions for use. An aliquot of each sample was removed after processing on the ThinPrep 3000 System (post-processed samples) and transferred to an Aptima Specimen Transfer tube. The pre- and post-processed samples were tested with the Aptima HPV assay.

The false positive rate for the pre- and post-processed negative samples was calculated, as well as the 2-sided 95% Score confidence interval. The post-processed negative samples resulted in one false positive (1/120, 0.8%, 95% CI 0.02-4.6%), whereas the pre-processed negative samples had no false positive results (0/120, 0%).

ThinPrep 5000 Processor with Autoloader (ThinPrep 5000 System) Study

A study was conducted to determine the false positive rate observed with the Aptima HPV assay when ThinPrep liquid cytology specimens containing a high concentration of spiked HPV-positive cells, were alternately processed with HPV-negative specimens on the ThinPrep 5000 System.

Residual, HPV-negative, ThinPrep liquid cytology specimens were pooled to create HPV-negative samples. HPV-positive samples were prepared by first combining residual ThinPrep liquid cytology specimens into five large negative pools. HPV 16-positive cells (SiHa) and HPV 18-positive cells (HeLa) were spiked together into the pools to achieve a concentration of 1×10^4 cells/mL for each cell line. HPV-positive then HPV-negative samples were alternately processed on the ThinPrep 5000 System according to the ThinPrep 5000 System instructions for use. An aliquot of each sample was removed after processing on the ThinPrep 5000 System (post-processed samples) and transferred to an Aptima Specimen Transfer tube. The pre- and post-processed samples were tested with the Aptima HPV assay.

The false positive rate for the pre- and post-processed negative samples was calculated. The pre- and post-processed negative samples each resulted in one false positive (1/250, 0.4%).

ThinPrep Genesis System Study

A carryover study was conducted to determine the carryover contamination rate observed with the Aptima HPV and Aptima HPV 16 18/45 genotype assays when ThinPrep liquid cytology specimens containing high concentrations of spiked HPV-positive cells were alternately processed with HPV-negative specimens on the ThinPrep Genesis Processor. Residual ThinPrep liquid cytology specimens were screened with the Aptima HPV assay, and specimens determined to be negative were used to create two HPV-negative specimen pools. One pool was used to create HPV-negative specimens, and the second pool was spiked with HPV-16 positive cells (SiHa) and HPV-18 positive cells (HeLa) to achieve a concentration of 1×10^4 cells/mL for each cell line. This second pool was used to create HPV-positive specimens.

Manual aliquots were prepared from all HPV-negative specimens, and then manual aliquots were separately prepared from all HPV-positive specimens. The HPV-positive and HPV-negative specimens were then alternately processed on ThinPrep Genesis Processors. Each specimen was first processed with the "Aliquot + Slide" process (aliquot prepared before cytology), and the remaining vial contents processed with the "Aliquot" process (aliquot prepared post-cytology). All aliquots were tested with the Aptima HPV and Aptima HPV 16 18/45 genotype assays.

The false positive rate for the three aliquots taken from each negative specimen was calculated for the Aptima HPV assay results. The manual aliquot, the pre-cytology ThinPrep Genesis aliquot, and the post-cytology ThinPrep Genesis aliquot resulted in positivity rates of 8/299 (2.7%), 12/299 (4.0%), and 8/299 (2.7%), respectively. Statistical analysis demonstrates that there is no statistically significant difference in positivity rate between these three conditions.

The false positive rate for the three aliquots taken from each negative specimen was calculated for the Aptima HPV 16 18/45 genotype assay results. The manual aliquot, the pre-cytology ThinPrep Genesis aliquot, and the post-cytology ThinPrep Genesis aliquot resulted in positivity rates of 2/299 (0.7%), 1/299 (0.3%), and 0/299 (0.0%), respectively. Statistical analysis demonstrates that there is no statistically significant difference in positivity rate between these three conditions.

The results of the carryover study demonstrate that the ThinPrep Genesis System does not contribute to cross-contamination of samples.

Limitations

- A. Aptima assay performance was not evaluated for testing the same ThinPrep liquid cytology specimen both before and after processing on the ThinPrep 2000 System, the ThinPrep 3000 System, the ThinPrep 5000 Systems, or the ThinPrep Genesis Processor.
- B. ThinPrep liquid cytology samples processed on the ThinPrep 3000 System have not been evaluated for use with the Aptima Combo 2 assay. ThinPrep liquid cytology samples processed on the ThinPrep 3000 System or the ThinPrep 5000 Systems have not been evaluated for use with the Aptima GC and Aptima CT assays.
- C. Post-processed ThinPrep liquid cytology specimens have not been evaluated for use with the Aptima *Trichomonas vaginalis* assay or the Aptima *Mycoplasma genitalium* assay.
- D. The Aptima Specimen Transfer Kit was evaluated using ThinPrep liquid cytology specimens collected with either broom-type or endocervical brush/spatula collection devices. The use of other collection devices was not evaluated for use in Aptima assays.
- E. The effect of the ThinPrep 2000 System decontamination procedure was not assessed for its impact on cytology results. Prior to implementing the decontamination procedure, laboratories should validate that the decontamination procedure does not impact cytology results.
- F. Use of these products is limited to personnel who have been trained in the use of the Aptima Specimen Transfer Kit and/or the Aptima Transfer Solution Kit.
- G. The Aptima Bleach Enhancer has not been validated for the ThinPrep 2000 System decontamination procedure.
- H. Removal of 1 mL of a SurePath liquid cytology specimen prior to cytological processing has not been evaluated for impact to the cytology result.
- I. If a liquid cytology specimen has small amounts of cellular material, uneven distribution of this material may occur, which may affect the ability to detect target organisms in the collected material. If negative results from the specimen do not fit with the clinical impression, a new specimen may be necessary. When compared to direct sampling with Aptima swab specimen transport medium, the additional volume of PreservCyt Solution results in greater dilution of the sample material.
- J. Test results may be affected by improper specimen collection, storage or specimen processing.



Hologic, Inc.
10210 Genetic Center Drive
San Diego, CA 92121 USA

Customer Support: +1 800 442 9892
customersupport@hologic.com

Technical Support: +1 888 484 4747
molecularsupport@hologic.com

For more contact information visit www.hologic.com.

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