Guidelines for Organizing a Quality Assurance Program for Introduction and Routine Use of *care*HPV in Low-Resource Settings

PATH

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Tools to support quality assurance programs are freely available to cervical cancer screening programs from PATH's website or by contacting PATH's offices.

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1. Introduction

This document is based on PATH's experience implementing human papillomavirus (HPV) DNA tests in low-resource settings. It is designed for public health programs conducting screening with *care*HPV™ that wish to implement a quality assurance program and for nongovernmental organizations (NGOs) conducting or supporting screening activities. The document's purpose is to describe basic principles and practical aspects of a quality assurance program and suggest protocols and corrective actions for quality assurance program adherence, based on PATH's experience.

The objective of a quality assurance program is discussed in Section 3: Implementing a Quality Assurance Program. Quality assurance, quality control, and quality assessment constitute an essential part of testing programs and of diagnostic testing in general.

The availability of *care*HPV does not automatically guarantee high-quality results. Many steps are involved in the testing process from collecting, storing, and transporting samples; to storing and running the test; reporting results; and using the results to inform cervical cancer screening programs and control plans. At each step in the process, there is a potential that something can go wrong; therefore, cervical cancer screening programs and control plans should ensure that sufficient support is made available to provide appropriate staff to monitor the program and, if necessary, improve the quality of testing. A well-functioning quality assurance program is an important step in achieving high-quality testing results and eventual control of cervical cancer.

A specialized molecular test, *care*HPV detects 14 high-risk types of HPV DNA when present in cervical or vaginal specimens through hybridization of the virus DNA with RNA, the addition of antibodies to capture the hybrid, and the addition of antibodies and a substrate to amplify the signal of the captured hybrid. The HPV types detected by the test are the high-risk HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68. A validated, skilled lab technician and suitable environmental conditions are necessary to run the assay, which is a 7-step protocol that includes pipetting, decanting, and handling reagents and biological samples.

a. Terminology

To avoid confusion, the following distinctions must be drawn between three commonly used terms:

Quality assurance: The total process that guarantees that the final results reported by a laboratory or testing program are as accurate as possible. This involves specimen integrity, reviewing transcriptional measures, using the most reliable assays, and verifying final reports.

Quality control: The measures that must be included in each step of the test to ensure that it is working properly. This includes operating conditions (e.g., temperature), test controls, etc. Quality control thus indicates whether the test run was valid and has produced acceptable results. It does not, however, indicate that the results are accurate nor if they have been properly reported.

Quality assessment: The means of determining the quality of results. It evaluates effectiveness of a quality assurance program.

2. Establishing a quality assurance program

The purpose of this document is to describe basic principles and practical aspects of a quality assurance program for *care*HPV testing that can be implemented by cervical cancer control programs. The objective of a quality assurance program is to ensure high quality of testing and to provide a mechanism to identify areas for feedback and improvement.

All *care*HPV tests that are used in screening programs should be procured directly through the test manufacturer, QIAGEN, through an authorized local distributor, or through a regional procurement system. The quality assurance program that a country adopts is separate and distinct from design control, quality management systems, and/or quality assurance programs that may be implemented by the manufacturer.

*care*HPV is a trademark of QIAGEN.

An ideal quality assurance program is comprehensive, iterative, and contains the following components:

- **Operator training and proficiency.**
  - ◊ Provider training to collect and store samples properly.
  - ◊ Provider proficiency assessment to determine that each provider collects and stores samples properly.
  - ◊ Lab technician training to run the test properly.
  - ◊ Lab technician proficiency assessment to determine that each lab technician runs the test properly.
  - ◊ Field support and additional resources for lab technicians.
- **Infrastructure requirements: Instrumentation, test kit, and lab supplies functionality.**
- **Quality control and quality assessment.**
  - ◊ Quality control to affirm that the test is running properly.
  - ◊ Quality assessment to affirm that the test performs as intended.
- **Post-marketing surveillance to capture information on the performance of the test in the intended setting.**

Due to scope and responsibility limitations of control programs or of individual program component implementation partners, one entity may not be able to implement a comprehensive quality assurance program on its own. Quality assurance program components can be individually implemented by different entities as appropriate.

A quality assurance program should include a clear description of the roles and responsibilities of those implementing the quality assurance program, including assigning responsibility for tasks to specific individuals. Examples of individuals who may carry out quality assurance activities include ministry of health (MOH) program managers; other MOH personnel such as physicians, nurses, and lab technicians; and NGO implementing partners, among others.

3. Implementing a quality assurance program

a. Operator proficiency

Operator proficiency is comprised of training and proficiency assessment for providers and lab technicians. While only lab technicians run the actual test, providers play a key role in the test continuum by collecting, storing, and transporting samples.

i. Provider training

The objective of provider training is to teach providers offering *care*HPV through clinician-collected or self-collected modalities to properly offer the test to women; collect, store, and transport samples; and report test results to women.

At minimum, provider training should include individuals who will be offering the test to women; collecting, storing, and transporting samples; and reporting test results to women. Ideally, provider training should be expanded to include all individuals whose responsibilities touch the testing continuum, including supervisors, data managers, program coordinators, procurement and supply-chain specialists, inventory managers, logistics planners, individuals reporting data, data analysts, epidemiologists, individuals taking action based on data/results, community enumerators, etc.

Provider training should include instruction about specimen collection by provider- or self-collection modalities, how to counsel women on screening and how to give women test results, principles of the test, how it works, the steps required to conduct the test properly, reporting of results, safety precautions, and appropriate disposal of test materials. Training should be conducted in the setting where samples are intended to be collected, or as similar a setting as possible. Training should apply appropriate evidence-based practices for effective adult learning and must include hands-on practical training for individuals collecting samples. Additionally, provider training should be conducted with the same brush and collection medium to be used in the screening program activities.

Training materials may be available from the test manufacturer, obtained from similar HPV DNA screening programs, obtained from other qualified sources, and/or may need to be developed for the specific context. Training materials must be based on the test product insert. Provider training should also specifically illustrate incorrect specimen collection; anticipated problems and/or errors with specimen collection, transportation, and storage; troubleshooting; and reporting of problems and/or errors.

Materials for provider training should be obtained in the quantity needed to allow demonstration of the procedure as well as to allow each participant to practice conducting the procedure until they are able to independently perform the test procedure correctly. All training materials must be based on the product insert and follow manufacturer procedures and recommendations.

Training frequency: Individuals offering the test to women; collecting, storing, and transporting samples; and reporting test results to women should receive annual refresher training for each test used in the program. If changes are made to a test by the manufacturer that impact specimen collection, retraining should occur before the test is implemented by the program. If problems are identified with providers, training may be conducted at more frequent intervals or ad hoc.

Individuals not directly associated with offering the test to women; collecting, storing and transporting samples; and reporting test results to women should receive training at least once. If changes are made to a test by the manufacturer, retraining should occur.

Records of provider training (i.e., individuals trained and the date of training) should be maintained by the program.

ii. Provider proficiency assessment

The objective of provider proficiency assessment is to determine if each provider collects and stores the samples properly.

Provider proficiency assessment occurs at the end of provider training and may be administered in the form of a written exam, an oral assessment, or a visual observation of providers' performance.

iii. Lab technician training

The objective of lab technician training is to teach lab technicians how to run the test properly.

At minimum, lab technician training should include individuals who will be receiving samples from providers, storing samples in the lab, conducting the test, interpreting test results, and disposing properly of specimens. Ideally, lab technician training should be expanded to include all individuals whose responsibilities touch the testing continuum within the lab, including supervisors, data managers, program coordinators, procurement and supply-chain specialists, inventory managers, logistics planners, individuals reporting data, data analysts, epidemiologists, individuals taking action based on data/results, community enumerators, etc.

Lab technician training should include the following:

- Specimen collection by provider- or self-collection modalities.
- Proper sample storage, handling, and disposal.
- Principles of the test, how it works (hybridization of the virus DNA with RNA, the addition of antibodies to capture the hybrid, and the addition of antibodies and a substrate to amplify the signal of the captured hybrid), the steps required to properly run the test (test protocol), how to properly set-up, operate, and troubleshoot the test system (instrumentation).
- Lab skills required to run the test including pipetting, decanting (discarding the liquid from the test plate by inverting it over a receptacle), adhering and removing plate sealers, and handling the test plate.
- Interpreting, documenting, and reporting of results.
- Safety precautions.
- Appropriate disposal of test materials.

Training should be conducted in the setting where the test is intended to be run, or as similar a setting to this as possible. Training must include hands-on practical training for all individuals who will run the test. Additionally, lab technician training should be conducted with both training panels and real samples to provide a training setting that is consistent with actual screening program activities. Clinical decisions

should not be made based on the results obtained by not-yet-validated lab technicians running real samples in training. For this reason, discarded samples (aliquots remaining from specimens previously tested by a validated lab technician) should be used in the training.

Lab technician training materials may be available from the test manufacturer, obtained from similar HPV DNA screening programs, obtained from other qualified sources, and/or may need to be developed for the specific context. Training materials should be based on the manufacturer's test kit manual and operating procedures. Lab technician training should also specifically illustrate anticipated problems and/or errors with running the test; improper pipetting, decanting, adhering and removing the plate sealer, and handling the test plate; troubleshooting instrumentation failures, power outages, and other environmental problems; and reporting of problems and/or errors.

Materials for lab technician training should be obtained in a quantity sufficient to allow demonstration of the procedure as well as to allow each participant to conduct the procedure until they are able to independently perform the test procedure correctly.

Training frequency: Individuals receiving samples from providers, storing samples in the lab, conducting the test, interpreting test results, and disposing properly of specimens should receive an initial training followed by an annual refresher training by a local master trainer. If changes are made to a test by the manufacturer, retraining should occur before the new modified test is implemented by the program. If problems are identified with lab technicians, training or additional practice in lab skills may be conducted at more frequent intervals or ad hoc.

Individuals not directly associated with receiving samples from providers, storing samples in the lab, conducting the test, interpreting test results, and disposing properly of specimens should receive training at least once. If changes are made to a test by the manufacturer, retraining should occur.

The first lab technician training for a screening program in a specific location should be carried out by a trainer from the test manufacturing company to skilled lab technicians who will later become master trainers for that country screening program. Local master trainers must be validated as trainers by the test manufacturer before independently training others.

Records of lab technician training (i.e., individuals trained and the date of training) should be maintained by the program.

iv. Lab technician proficiency assessment

The objective of lab technician proficiency assessment is to determine that each lab technician runs and interprets the test properly. Lab technician proficiency assessment should include individuals who will be receiving samples from providers, storing samples in the lab, conducting the test, interpreting test results, and disposing properly of specimens.

Initial lab technician proficiency assessment occurs at the end of lab technician training, when lab technicians earn validation after one successful plate run using the training panel followed by two successful plate runs of real samples, observed by a representative of the manufacturer or an in-country master trainer. Each validation plate run using the training panel should disperse the positive test panel samples throughout the plate in a random pattern, where no two positive training panel samples are adjacent. The number of positive training panel samples should be consistent with regional HPV infection rates. Each validation plate run should be a full plate (96 wells, including the 6 control wells in column 1). The location of the positive training panel samples should be noted on the test information form and the results should match exactly. For each validation plate run with real samples, results should comply with the quality assurance recommendations for results interpretation (see Section 3.c). As previously stated, clinical decisions should not be made based on these results.

Lab technician proficiency assessment should be conducted in a laboratory or conducted in the setting where the test is intended to be used. Proficiency assessment should be conducted on the same instrumentation and disposable supplies to be used in the screening program.

Materials for lab technician proficiency assessment should be obtained in a quantity sufficient to allow each operator to perform the proficiency assessment at least once annually.

Each individual directly involved in testing must complete operator proficiency assessment prior to conducting any program activities related to conducting the test. Proficiency assessment is based on each individual's abilities, not as a group or team.

Assessment frequency: Individuals who will be receiving samples from providers, storing samples in the lab, conducting the test, interpreting test results, and disposing properly of specimens should annually conduct proficiency assessment under a supervisor or in-country master trainer. If changes are made to a test by the manufacturer, lab technician training and proficiency assessment should occur before the test is implemented by the program. If problems are identified with lab technicians, those lab technicians should be retrained and complete lab technician proficiency assessment prior to conducting further program activities related to performing the test.

Records of lab technician proficiency assessment should be maintained by the program.

v. Field support and additional resources for lab technicians

The screening program should ensure that options for field support are available to enable lab technicians to respond to any concerns that may arise with running the test. Field support should be provided by the screening program, manufacturer, and relevant implementation partners through communication options such as telephone, SMS, Skype, WhatsApp and email. This support should be available to help troubleshoot issues, share concerns, and reinforce best practices. As noted in the introduction, *care*HPV is a molecular test that requires a validated, skilled lab technician and suitable environmental conditions to run the assay. Support from the screening program, manufacturer, and implementation partners will help to ensure high-quality testing.

Additional resources should be provided to ensure a high skill level is maintained following the validation of lab technicians. These resources can include job aids, checklists, photo guides, videos, etc. Many resources already exist and can be provided in collaboration with the test manufacturer, funder, or other implementation partners. Additional resources should be adapted to the local context while conforming to norms established by the test manufacturer. If changes are made to a test by the manufacturer, these resources should be revised.

b. Infrastructure requirements: Instrumentation, test kit, and lab supplies functionality

The objective of infrastructure requirements is to ensure quality functionality of the instrumentation, test kits, samples, and lab supplies within the testing environment. The test instrumentation (the *care*HPV Test System) includes the Magnetic Plate Holder, Test Shaker, Test Controller, Test Luminometer, and power cables. The test kit includes the test reagents and test plate, and lab supplies include all durable and consumable products procured to run the test.

Environmental considerations: The environment in which the Test System is installed should comply with manufacturer site requirements. The temperature in the lab should stay within the range of 15°C to 30°C at the time when the test in being run. In warmer climates, it may be best to run the tests early in the morning when the lab environment is cooler. Due to temperature considerations, the instruments must be located out of direct sunlight and airflow. Nucleic acids are very sensitive to environmental nuclease degradation. Nucleases are present on human skin and on surfaces or materials handled by humans; therefore, work surfaces must be clean. The lab should be free of excess dust and moisture and protected from the rain, wind, and other elements. The lab must also provide a supply of electricity, a receptacle for decanting the microplate (such as a waste-bin, basin, or sink), and a good source of light. In order for lab technicians to contact field support, it is recommended that the screening program provide internet, telephone, or mobile phone access to the lab technicians.

The Test System must be kept in a secured location within the lab that is accessible to authorized personnel only and locked when not in use. At the time when the test is being run, only the lab technician running the test should be present in the lab or at the bench top area designated for the *care*HPV assay if other lab functions are carried out in the same lab. In addition, all efforts should be made to ensure that the lab technician is not

interrupted or tasked with other duties while running the test. A distractive environment can compromise a quality test run.

Instrumentation functionality: Functionality assurance for the Test System should be carried out when each test system is initially set up in any site, including moving the Test System from one location to another within the same site, such as switching rooms. Instrumentation should be checked to ensure that the setup is in compliance with manufacturer recommendations and the environmental considerations listed above. Additionally, the Test System (including the Test Shaker, Test Controller, and Test Luminometer) must be connected to its power source through an uninterruptable power supply (UPS) at the time of installation. Personnel should ensure that the power cables for the Test System are connected to the designated outlets on the UPS that will provide power to the instrumentation should a power outage occur (the test must never be run without first meeting this condition). To ensure a back-up power supply is available, the UPS device must always be plugged in to the electricity source (outlet) even when the test is not in use, including on evenings and weekends.

Three AC power cables are required for each Test System; for certain regions, these are not provided by the manufacturer and must be procured before Test System installation can occur.

At the first lab technician training for a screening program, the instrumentation procured for that screening program should be set up and tested to ensure functionality.

Operational qualification process for the Test System is ensured through the correct following of the test procedure or protocol. Screening programs should always provide up-to-date copies of the manufacturer's test kit manual in each lab where the test is run.

In case of instrumentation malfunction, screening programs should follow standard troubleshooting protocols provided in the Test System manuals. If the issue persists, programs should contact the test manufacturer's Tech Service and provide the instrument's serial number and a short description of the failure (see Section 3.a.v).

Test kit functionality: Upon receipt, the *care*HPV test kit must be stored between 4°C and 25°C. An ambient thermometer must always be present in the storage area to ensure the test kits are within the temperature range. The thermometer should be calibrated annually to ensure accuracy. The storage environment of the test kits must also be free of excess moisture or condensation and protected from the rain and other elements. Due to temperature considerations, the storage area for the test kits must not be exposed to periods of direct sunlight. In warmer climates, acceptable temperature requirements must be maintained in the storage area at all times; if this is not possible using ice packs, coolers, and other low-tech methods, the test kits must be stored in refrigerators.

Test-kit expiration dates must be clearly monitored in order to ensure that older kits, closer to their expiration dates, are used first.

The *care*HPV test kit should not be used beyond the expiration date on the kit label. The test kit should not be used if it has been exposed to temperatures outside the required range. Expired or heat-exposed test kits are to be disposed of through the non-hazardous waste system of the lab site or clinic.

Prepared reagents must be stored between 15°C and 30°C for no longer than 8 hours. If not used for testing within 8 hours of reagent preparation, the kit and all prepared reagents must be discarded through the non-hazardous waste system of the lab site or clinic. Following a test run, the plate and reagents are to be disposed of through the non-hazardous waste system of the lab site or clinic.

The components in this test kit have been validated as a unit and must not be interchanged with components from other sources or from different test kits.

Sample functionality: Only specimens collected in *care*HPV Collection Medium should be used. Clinical specimens must be stored in *care*HPV Collection Medium either between 15°C and 30°C for 14 days or between 2°C and 8°C for 30 days. It is not possible to store specimens for 14 days between 15°C and 30°C and then transfer those same samples to the 2°C to 8°C temperature range for additional days of storage; programs must select one temperature range for sample storage and store for the corresponding number of days. Programs must not freeze the specimens.

Samples should be stored in foam tube racks; metal racks are also acceptable. If tube racks are not available, they may be bundled into groups of ten with a rubber band and stored upright. Screening programs must ensure that samples with earlier expiry dates are run before samples with later expiry dates. A record should always be kept of the date the oldest sample in a lot was collected and the last day the samples can be run. Samples should be run a minimum of two workdays before their date of expiry. This will allow the lab technician to run the same sample the following day in the event of an invalid plate run. Due to temperature considerations, the storage area for the samples must not be exposed to direct sunlight. Temperature requirements must be maintained in the storage area at all times; if this is not possible using ice packs, coolers, and other low-tech methods, the samples must be stored in refrigerators.

Supplies functionality: Lab supply requirements include the procurement of the correct durable and consumable supplies in the appropriate quantities to allow for routine testing. Screening programs must order only supplies recommended by the test manufacturer. If substitution is required, this can only be done if the replacement supply is validated before use. As mentioned in the introduction, *care*HPV is a specialized molecular test and can only be run with validated lab supplies.

Durable lab supplies required for running the *care*HPV test include a 50-microliter fixed-volume pipet and a repeat pipet. The fixed-volume pipet must be compatible with the extra-long pipet tips, and the repeat pipet must be compatible with the repeat pipet tips. Ensure that both pipets are checked and calibrated according to the manufacturer's recommendations before use.

Two foam specimen-tube racks are also required at each test site. The tube racks must be for 15-mm to 16-mm diameter tubes and able to hold a minimum of 45 tubes each. Tubes must sit firmly in the tube racks so that the racks may be inverted safely during sample preparation without tubes slipping.

A receptacle for decanting the microplate such as a sink, waste-bin, or basin must be provided. A waste-bin is also required for disposing of used towels, packaging, and other waste.

An ambient thermometer must be kept in the same room where the test is run to ensure that temperatures remain between 15°C and 30°C during a test run. The thermometer should be calibrated annually to ensure accuracy. Thermometers intended for use in refrigerators or freezers are not appropriate as these are not designed to measure ambient temperatures.

A lab coat or apron must be worn by the lab technician when operating in the lab. Safety goggles may also be worn according to local laboratory standards.

Each lab site should also supply a digital camera (or mobile phone with a camera) to take pictures of the test controller when it displays the test-results map (for monitoring) and error screens (for troubleshooting assistance). A ballpoint pen, highlighter, and permanent marker should also be available in the lab.

Consumable lab supplies required for running the *care*HPV test include powder-free gloves; plate sealers; paper towels; two types of repeat-pipet tips; and extra-long fixed-volume pipet tips. Each is described below in further detail.

Powder-free gloves must be worn by the lab technician at all times while operating the test. As noted above, nucleases, which are present on human skin, can affect the nucleic acids present in the assay. The gloves should fit the lab technician's hands snugly; oversized gloves may interfere with running the test. Each plate run requires two pairs of gloves. Do not reuse or share gloves.

Plate sealers must be procured from the test manufacturer. Five plate sealers are required for each plate run.

KimTowels, manufactured by Kimberly-Clark, or a product with the same specifications is required to run the test. Note that KimTowels are thicker and more absorbent than KimWipes. Each plate run requires 13 KimTowels.

Two types of repeat pipet tips are required: 1.0 mL and 1.25–2.5 mL volume tips. Both tip types must be compatible with the repeat pipet used in the lab. Each plate run requires four 1.0 mL tips (used to dispense increments of 20 µl and 40 µl) and one 1.25–2.5 mL tip

(used to dispense increments of 25 µl). Other tip sizes may be used, provided they are compatible with the repeat pipet and are capable of dispensing the required volumes.

Extra-large 200 mL pipet tips are required for the fixed-volume pipet and must be compatible with the fixed-volume pipet used in the lab. One box of 96 tips is required for each plate run.

In addition, labs should have the following common consumable supplies on hand: adhesive tape such as masking tape for creating labels as needed; disposal/trash bags including biohazard bags, if required by local waste disposal protocol; and bleach and distilled water for monthly sterilization of the laboratory environment, to avoid potential sources of contamination.

Disposable lab supplies must be procured routinely and in quantities that correspond with the screening volume for the particular program. In the initial six months of a screening program, disposable supplies should be procured with an additional 5 percent for wastage; in addition, extra disposable supplies for use during trainings should be procured. During the first six months, actual rates of usage should be documented by the screening program to inform future procurement. Forecasting schedules and other tools should be used to help avoid stock-outs that will halt testing. Screening programs should always provide support and oversight to each lab site to ensure the sustained availability of required supplies.

c. Quality control and quality assessment

The objective of quality control is to affirm that the test is working properly at the point of use. Testing should be conducted by operators who have been trained and deemed to be proficient at conducting the test.

Each lot of the *care*HPV test kit is tested before release against predetermined specifications to ensure consistent product quality. Acceptable ranges have been established specifically for the *care*HPV Test System.

The *care*HPV test includes three positive and three negative calibrators or controls in each test kit. The calibrators that are required for assay calibration verification must be included with each performance of the test. As part of the test protocol, the calibrators are added to the test plate in column 1, wells A–F. The *care*HPV Test Controller performs assay calibration verification to ensure that the reagents and furnished calibrator materials are functioning properly, permitting accurate determination of the test result. When the quality control standards are met, the test results are valid and the *care*HPV Test Controller displays the "Results" screen at the end of the assay. When the quality control standards are not met, the test results are invalid and the *care*HPV Test Controller displays an "Invalid" screen. If the "Invalid" screen is displayed, all samples from that plate must be run again to obtain a valid result.

Quality control measures for results interpretation include comparing the positivity rate of the test result to the expected positivity rate within the population. Positivity rates will vary between plate runs; however, a test run with a positivity rate that varies drastically from the expected rate would not meet quality standards. Reviewing the distribution of test results to ensure that the positive results do not present in large groupings, such as in an entire column(s) or row(s), is also a quality control measure for suspected contamination. Positive results should be dispersed throughout the plate without groupings large enough to meet the threshold as being suspicious for well-to-well contamination. If the results of an assay do not meet quality assurance standards for positivity rate and the distribution of positive results, it is recommended that the plate be repeated. A photo of the results screen should also be shared with the monitoring personnel.

d. Post-marketing surveillance to capture information on the performance of the test in the intended setting

Periodic evaluation of tests that have been procured by the program should be conducted. This would include unused tests that remain after they have been deployed to the field and unused tests that remain in storage, yet to be deployed to the field. In addition, periodic evaluation of tests used in the field (i.e., results of plate runs) should also be conducted.

If problems with tests used in the field are reported or suspected, evaluation of these tests should be conducted, similar to the quality assessment. All reported or suspected problems, investigations, and outcomes should be reported to the appropriate chain of command

in the program, to the test manufacturer, other key stakeholders, and to the funder, if appropriate.

Potential areas of concern for the test process may include:

- The availability of resources, such as a lab technician with dedicated time to run the *care*HPV test in an uninterrupted fashion and a back-up lab technician to perform the test when the primary lab technician is not present.
- The availability of required lab supplies at each testing site, such as the timely fulfillment of order requests from the lab and accurate forecasting for procurement of supplies at the central level.
- The execution of manual lab techniques as part of the test protocol, including pipetting samples and reagents; washing the plate with Reagent 5; and decanting the plate.
- Contamination of plate wells; lab technicians may take photos of each plate result for documentation and to allow monitoring personnel to spot-check the plate for suspected contamination. Photos should be taken of any plate where contamination is suspected.

Performance qualification is the process of ensuring that the Test System continues to function properly, through monitoring of test results and valid plate runs.

4. Off-label use of tests

Use of the test for purposes other than those described in the test product insert or validated by quality assessment and regulatory approval should be avoided.

Off-label use of the test includes, but is not limited to, using expired tests, using tests exposed to temperatures outside of the specified range, using different specimen types (e.g., saliva, urine), different sample collection media, different brushes, different sample volumes, deviating from the test and sample storage protocol, deviating from test run protocol, testing unintended populations, individual diagnosis of disease, interpretation as a cancer test, etc.

5. Feedback and improvements

Quality assurance programs benefit from regular review and updating in order to remain relevant and useful. Feedback should be provided to the authors of this document. Users of this document should regularly verify that the document to which they are referring is the most current. Documents are tracked by revision number and effective date.

A quality assurance program requires monitoring against a standard. This means that the methodologies utilized should be relevant. A good quality assurance program also monitors the standard to assure relevance and prevent drift of the standard from its original intent.

References

This document has been created specifically by PATH for the *care*HPV test by drawing from materials created for other diagnostic tests.

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