



GUIDELINES FOR ORGANIZING A QUALITY ASSURANCE PROGRAM FOR OV16 SEROLOGICAL RAPID TESTS

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Introduction

These guidelines are designed for policymakers and program planners wishing to implement a quality assurance program for serological tests detecting IgG4 antibodies specific to the Ov16 antigen from *Onchocerca volvulus*. They describe some important basic principles and the main practical aspects of a quality assurance program. The objectives of a quality assurance program are discussed in this document. It is now widely accepted that quality assurance, quality control, and quality assessment constitute an essential part of testing programs and of diagnostic testing in general.

The availability of Ov16 rapid tests does not automatically guarantee high-quality results. Many steps are involved between selecting a test, how and when testing will occur, conducting the test, reporting results, and how the results are used to inform control and elimination programs. At each step in the process, there is the potential that something can go wrong. Therefore, onchocerciasis control and elimination programs should ensure that sufficient support is made available to provide a suitable program to monitor and, if necessary, improve the quality of testing. A well-functioning program is an important step toward achieving high-quality testing results and eventual elimination of onchocerciasis.

As of the publication date of this document, only one rapid test serology for detection of IgG4 antibodies specific to Ov16 antigen exists: Alere SD BIOLINE Onchocerciasis IgG4 Rapid Test.

Terminology

In order to avoid confusion, distinctions need to be drawn between three commonly used terms:

Quality assurance (QA) is 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 (QC) comprises those measures that must be included during each test run to verify that the test is working properly. This includes ensuring correct operations conditions (e.g., temperature), kit controls,

etc. Thus QC indicates whether the test run was valid and has produced acceptable results. QC does not, however, indicate that the results are accurate, nor that they have been reported properly.

Quality assessment is a means of determining the quality of results. It is usually an external evaluation of a laboratory's performance using proficiency panels. Quality assessment is undertaken to evaluate the effectiveness of the quality assurance program. A good QA/QC program may make quality assessment in some situations less important; however, quality assessment is never a substitute for good QA/QC. Failure with quality assessment specimens usually indicates that there is a problem with QA/QC procedures. Furthermore, quality assessment schemes are much more efficient at detecting differences in performance between participating laboratories than differences between test methods and techniques.

Establishing a quality assurance program

The objective of this document is to describe a quality assurance program for Ov16 rapid tests that can be implemented by onchocerciasis control and elimination programs. The objective of such a program is to assure high quality of testing and to provide a mechanism to identify areas for feedback and improvement and a means to implement the necessary changes.

Ov16 rapid tests that are selected for use in onchocerciasis control and elimination programs should be: produced by a reputable manufacturer under good manufacturing practices; demonstrated to have utility for the intended use; and commercially available. This quality assurance program is separate and distinct from design control, quality management systems, and/or quality assurance programs that may be implemented by the manufacturer(s) of Ov16 rapid tests.

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

- Operator training to conduct the test properly.
- Operator proficiency assessment to determine that each operator conducts the test properly.

- Quality assessment to affirm that the test performs as intended.
- Lot testing to confirm that the tests perform as intended when received from the manufacturer.
- Quality control to affirm that the test is working properly.
- Post-market surveillance to capture information on the performance of the test in the intended setting.

Due to limited scope and responsibilities of control programs or individual program component-implementation partners, one entity may be unable to implement a comprehensive quality assurance program. Individual quality assurance program components can be implemented as suitable and appropriate.

Implementing a quality assurance program

Operator training

The objective of operator training is to teach and inform individual test users how to properly conduct the test.

Operator training minimally should include individuals who will be collecting sample(s) for testing, individuals conducting the test in the field or laboratory, and individuals interpreting results. Ideally, operator 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, and community enumerators.

Example of specifications for sample panels supporting QA program operator training, operator proficiency assessment, and quality assessment modules.

Tools to support QA programs are freely available to onchocerciasis control programs from PATH's website or by contacting PATH's offices.

	Training Panel	Proficiency Panel	QA Panel
Purpose	Teach and inform individual test users how to properly conduct the test.	Provide assurance that the user correctly interprets the test results.	Affirm test performs as intended. Panel should not be prepared by test manufacturer.
Intended user	Individuals who will be collecting samples for testing, conducting the test in the field or laboratory, and/or interpreting results.	Trained individuals who will be collecting samples for testing, conducting the test in the field or laboratory, and/or interpreting results.	Highly trained and proficient operators of the test, generally at the program reference laboratory.
Contents (Panel members)	High to low positive, negative.	Mixture of range of positives and negatives.	Range of positives, very low positive, and negative.
Shipping conditions	Ambient	Ambient	Ambient
Storage conditions	2°C-8°C.	2°C-8°C.	2°C-8°C.
Setting	Conducted where the test is intended to be used, or as close to this as possible.	Conducted either in a controlled laboratory setting or where test is intended to be used.	Conducted in a controlled laboratory settings or similar controlled setting.
Recommended use	Training technical personnel in the performance of tests.	Panel is blinded and must be run and read correctly to be qualified as a proficient operator.	Assessment of all lots of tests prior to use.
What happens to results	Results indicate the success of training materials and the ease with which an individual runs the test without error.	Records of operator proficiency assessment should be maintained by the program using the tests.	Testing should be 100% complete with expected results before routine testing is conducted. Results are collected over time and used to determine functional issues with the test, including lot variability.

Operator training should include instruction about the principles of the test, how it works, the steps required to conduct the test properly (including specimen collection, conducting the test, and interpreting results), reporting of results, safety precautions, and appropriate disposal of test materials. Training should be conducted in the setting where the test is intended to be used, or as close to this as possible. Training must include hands-on practical training for individuals collecting samples, conducting the test, and interpreting results. Other individuals included in operator training should receive hands-on practical training as appropriate, which may be conducted outside of the setting where the test is intended to be used.

Training materials may be available from the test manufacturer, obtained from similar onchocerciasis control programs, obtained from other qualified sources, and/or may need to be developed for the specific context. Training materials should be based on the test product insert. Operator training should also specifically illustrate incorrect use of the test, anticipated problems with testing and/or errors with the test, troubleshooting, and reporting of problems and/or errors.

Operator training should be conducted on the same test to be used in the control and elimination program activities. Training panel samples should minimally include a negative, positive, and a positive which is weakly reactive, but ideally include three to six samples. Training panels may contain blood or plasma samples obtained from humans and/or synthetic/recombinant samples. Training panels may be available from the test manufacturer or other qualified sources, but care should be taken when selecting a training panel in order to select a panel that is useful for the test that is to be used. Examples of invalid tests should be included in operator training.

Materials for operator training should be obtained in the quantity 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 collecting samples, conducting the test, and interpreting test results should receive annual training for each test used in

the program. If changes are made to a test by the manufacturer, retraining should occur before the test is implemented by the program. If problems are identified with operators, training may be conducted at more frequent intervals or ad hoc.

Individuals not directly associated with collecting samples, conducting the test, and interpreting test results should receive training at least once. If changes are made to a test by the manufacturer, retraining should occur.

Records of operator training (individuals trained and the date of training) should be maintained by the program.

Operator proficiency assessment

The objective of operator proficiency assessment is to determine that each operator is able to conduct and interpret the test properly.

Operator proficiency assessment is part of operator training and is different from external laboratory proficiency testing as part of quality assessment. Operator proficiency assessment should include individuals who will be collecting sample(s) for testing, individuals conducting the test in the field or laboratory, and individuals interpreting results.

Proficiency panels should consist of four to ten samples containing blood or plasma obtained from humans and/or synthetic/recombinant samples. The proficiency panel should include a mixture of negative samples and positive samples that have yield varying reactivity/intensity on the test. The identity of each sample and its expected test result should be blinded from the test user. Proficiency panels may be available from the test manufacturer, obtained from similar onchocerciasis control programs, or obtained from other qualified sources.

Operator proficiency assessment can be conducted in a controlled setting (e.g., laboratory) or conducted in the setting where the test is intended to be used. Proficiency assessment should be conducted on the same test to be used in the control and elimination program activities.

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

Each individual directly involved in testing should 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. Proficiency assessment is an activity that occurs after operator training. Proficiency assessment is implemented by providing each individual with the blinded proficiency panel, the required number of tests, and the appropriate test instructions. Individuals will complete the tests and report their results. After results are reported, the proficiency panel is unblinded. An individual is deemed proficient in the test procedure if he/she correctly identifies 100% of the samples in the proficiency panel as negative, positive, or invalid.

Operator proficiency assessment frequency:

Individuals collecting samples, conducting the test, and interpreting test results should annually conduct proficiency assessment for each test product selected to be included in the program. If changes are made to a test by the manufacturer, operator training and proficiency assessment should occur before the test is implemented by the program. If problems are identified with operators, those operators should be retrained and complete operator proficiency assessment prior to conducting further program activities related to performing the test.

Records of operator proficiency assessment should be maintained by the program.

Quality assessment

The objective of quality assessment is to affirm that the test performs as intended. Quality assessment is not intended to replace performance evaluations (laboratory and/or field) conducted by the test manufacturer or program which may or may not have been used for regulatory approval or licensed for use in a particular country/setting.

There are a number of panels that can be included for quality assessment. These can be conducted individually or as a group, depending on local or programmatic needs. Frequency of testing may also vary depending on local or programmatic needs.

Quality assessment should be conducted for each Ov16 test product selected for use by the program. Should the manufacturer make changes or modifications to the

product, quality assessment may need to be repeated. Quality assessment can be conducted in a controlled setting (e.g., laboratory) and does not need to be conducted in the setting where the test is intended to be used.

Quality assessment should be conducted by trained and proficient operators with appropriate backgrounds.

Quality assessment panels that may be appropriate for use include: serum/plasma quality assurance panel, performance panel, titration panel, low titer panel, geographic panel, specificity panel, whole blood panel, and IgG4 panel.

Quality assessment panels may be obtained from reference sample banks, in-country resources, local control and elimination program, qualified researchers, other control and elimination programs, or other qualified sources. It is not recommended that these panels be obtained from the test manufacturer. Quality assessment panels should be well characterized by accepted standards which may include reference lot testing, other laboratory methods, and/or clinical endpoints. The Ov16 rapid test may be specifically designed for use with fingerstick, whole-blood samples; however, it is often impractical to conduct quality assessment testing with such samples. Therefore, it is important to utilize serum or plasma samples. It may be appropriate to prepare contrived whole-blood quality assessment samples from well-characterized serum/plasma samples and whole-blood or prepared red blood cells.

Results of the quality assessment should be recorded in a log (test lot, samples, operator, results, date) and records maintained by the program. Results should be monitored over time to identify any trends and problems that may emerge.

Any problems observed with quality assessment testing should be reported to program management and to the test manufacturer.

Lot testing

Routine lot testing should be conducted for each lot and each order received from the manufacturer by a program prior to using the tests for operator training, operator proficiency, or use of the test by the program in the field or laboratory.

The serum/plasma quality assurance panel may be used for lot testing. Lot testing should minimally include a negative, strong positive, and weak positive. Samples used for lot testing should be well characterized, including performance with approved or reference lots of the test.

The number of tests to be performed with each sample should be determined based on a valid and supported sampling plan.

Pass/Fail criteria for the test should be determined prior to testing.

Lot testing can be conducted in a controlled setting (e.g., laboratory) and does not need to be conducted in the setting where the test is intended to be used.

Lot testing should be conducted by trained and proficient operators with appropriate backgrounds.

Results for each lot evaluated should be recorded in a log (test lot, samples, operator, results, date) and records maintained by the program. Failed lots should be immediately reported to the appropriate chain of command in the program, to the test manufacturer, other key stakeholders, and to the funder, if appropriate.

Quality control

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.

Quality control testing should be conducted at the point where testing will be performed. Each operator who will be conducting testing should conduct quality control tests each day prior to conducting tests. Quality control testing should be repeated if a new lot of tests is used.

Quality control panels should consist of at least one negative and one positive sample containing blood or plasma obtained from humans and/or synthetic/recombinant samples. Quality control panels may be available from the test manufacturer, obtained from similar onchocerciasis control programs, or obtained from other qualified sources.

Quality control testing should be complete and demonstrate 100% correlation with expected results before routine testing is conducted.

Results of quality control testing should be recorded in a log (test lot, quality control panel lot, operator, date, location). Results should be monitored over time to identify any trends and problems that may emerge.

Any problems observed with quality assurance testing should be reported to program management and to the test manufacturer.

Post-market surveillance

Periodic evaluation of tests that have been procured by the program should be conducted. This would include tests that remain after they have been deployed to the field and tests that remain in storage, yet to be deployed to the field. This testing should be similar to the quality assessment and lot testing described in this document.

If problems with tests used in the field are reported or suspected, evaluation of these tests should be conducted, similar to the quality assessment described in this document. Panels selected for this evaluation may vary depending on the suspected problem. 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. Additional resources for post-market surveillance of in vitro diagnostics are available from World Health Organization.

Off-label use of tests

Use of the test for purposes other than 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 different specimen types (e.g., dried blood spots, saliva, urine), different sample-transfer devices, different sample volumes, interpreting the test before or after the time recommended by the manufacturer, testing on populations not intended, individual diagnosis of infection or disease, interpretation for test of cure, etc.

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 document authors. Users of the 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 sample panels utilized should be well curated, and 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/purpose.

References

This document has been created specifically for Ov16 serological rapid tests by drawing from materials that are currently in use and available from WHO/UNAIDS.

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