
Establishing External Quality

Assessment Programmes for

Screening of Donated Blood

for Transfusion-Transmissible

Infections

Implementation Guide



**World Health
Organization**

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Introduction

External quality assessment (EQA) is an important component of quality systems for blood transfusion services. EQA is the external assessment of a laboratory's overall performance in testing exercise material of known, but undisclosed, content and comparison with the performance of other laboratories that have tested the same material. In laboratories that screen donated blood for transfusion-transmitted infections (TTI), participation in EQA helps to monitor and raise standards of performance. Information generated by EQA provides an opportunity for continual quality improvement through the identification of laboratory errors and the implementation of measures to prevent their recurrence. Thus EQA plays a vital role in making blood safer.

The World Health Organization (WHO) plays an advocacy role in promoting the establishment of national EQA programmes and encourages participation by TTI screening laboratories in these programmes. National health authorities are urged to recognize the importance of EQA and support the implementation of these programmes throughout a country's TTI screening network. Professional bodies are encouraged to endorse and support the establishment of EQA programmes.

Establishing external quality assessment programmes for screening of donated blood for transfusion-transmissible infections: implementation guide aims to support WHO Member States in establishing and operating EQA programmes for screening donated blood for TTI. The guide has been designed for use by national health authorities and EQA organizing institutions in the development of EQA programmes that can be implemented at national, state, provincial and district levels. It will also give participating laboratories an insight into the organization of EQA programmes for TTI screening and an understanding of the benefits of participation.

This guide is intended to be a companion to the WHO publication *External quality assessment of transfusion laboratory practice: guidelines on establishing an EQA scheme in blood group serology* (WHO/EHT/04.09). Hence, much of the present guide mirrors the information included in the earlier publication. This is because general principles of external quality assessment are the same irrespective of discipline.

The scope of the guidance described here includes mandatory serology screening of all blood donation for HIV, hepatitis B and C, and syphilis.

It may also be used to guide implementation of EQA for other agents for which mandatory screening is required in a particular country or region.¹ Although screening for HIV, hepatitis B and hepatitis C using nucleic acid testing is undertaken in some Member States, establishing an EQA programme for nucleic acid testing is outside the scope of this guidance, as it would require different approaches to sample acquisition, characterization and analysis, additional infrastructure and stringent logistical conditions.

This guide is designed to support the establishment of EQA programmes by organizing institutions that are in different stages of development. A phased approach should be considered if it is not possible initially to implement all the elements described here. The establishment of even a basic, small programme can have a significant impact in raising standards. When establishing an EQA programme in TTI screening, assessment of the most clinically important tests should be included first; the range of tests assessed can then be expanded as the programme is further developed.

The guide describes the principles for establishing and operating an EQA programme for TTI screening. EQA programmes should be organized in accordance with these principles, although due consideration should also be given to regulatory and quality system mechanisms that may exist within a country for laboratories conducting TTI screening.

¹ *Screening donated blood for transfusion-transmissible infections: recommendations.* Geneva: World Health Organization; 2010.

1

External quality assessment

The transfusion of safe, compatible blood and blood products involves a number of processes. There is a risk of error in each process from the selection of blood donors, the collection, processing and testing of donated blood, the testing of specimens from potential transfusion recipients, and the issue of compatible blood and its administration to the recipient. The laboratory plays a key role in this transfusion chain and quality system failures in screening donated blood for TTI can have serious implications for the recipients of blood and blood products.

Haemovigilance programmes, such as the Serious Hazards of Transfusion (SHOT) programme in the United Kingdom, have shown that laboratory errors can lead to major morbidity and mortality in transfusion recipients.

Errors in the laboratory may be due to a number of deficiencies, including:

- inadequate procedures for identification of donor specimens
- incorrect storage or use of inappropriate reagents
- inadequate equipment maintenance
- poor testing practices
- inaccuracies in recording or transcription
- inadequate procurement practices
- inadequate staff training.

Errors often result from a combination of factors, with the original error being compounded by inadequate checking procedures in the laboratory.

The aim of screening donated blood for TTI is to provide safe blood and blood products for transfusion. The implementation of a quality system in the TTI screening laboratory seeks to ensure this aim is achieved by minimizing errors.

Accurate screening for TTI is essential for providing safe blood and blood products. Along with the performance of a test, it is equally important that the results are transcribed, collated and interpreted correctly so that safe blood products are issued for transfusion.

1.1 EQA AS PART OF A QUALITY SYSTEM IN THE SCREENING OF DONATED BLOOD FOR TTI

External quality assessment forms an integral part of the monitoring of the overall quality system in a laboratory in which TTI screening is performed. National authorities should determine the standards with

which quality systems in laboratories should comply. These standards can be developed nationally based on international standards or relevant international standards can be applied.

The key elements of a quality system are:

- organizational management, including:
 - quality policy and plan
 - clear organizational structure
 - designated individual(s) with responsibility for establishing and managing the quality system
 - job descriptions for all staff;
- accurate and complete documentation, including standard operating procedures, and a functioning document control system;
- training, mentoring and continued professional development of staff;
- equipment validation, maintenance and calibration;
- validation of reagents, consumables, techniques and, where applicable, software;
- assessment, including:
 - internal quality control
 - internal and external audit
 - external quality assessment.

Documentation: Written policies, instructions and records involved in providing a product or service.

Standard operating procedure: Specified way to carry out an activity or a process that is documented, implemented and maintained – ISO 9000:2006

Internal quality control: Procedures that verify the attainment of the intended quality of results – ISO 15189:2013. These may include procedures to monitor the day-to-day reproducibility of test results and detect major errors in the analytical process.

Audit: Systematic, independent and documented process for obtaining evidence and evaluating it objectively to determine the extent to which audit criteria are fulfilled – ISO 9000:2006.

Effectiveness: Measure of the extent to which planned activities are realized and planned results achieved – ISO 9000:2006.

Validation: Confirmation and provision of objective evidence that the requirements for a specific intended use or application have been fulfilled – ISO 9000:2006.

Competency assessment: Process to assess an individual's ability to apply knowledge and skills.

1.2 ASSESSMENT

Continuous quality improvement requires ongoing monitoring and review of the effectiveness of all elements of the quality system, using both internal and external mechanisms, to ensure that the defined quality standards are being met consistently.

Internal assessment of the quality system in the laboratory includes:

- full validation of all activities, processes, procedures, equipment, reagents and software prior to their introduction and use;
- regular monitoring of all critical activities where continuous measurement of the outcomes is both possible and appropriate.
- use of specific control measures, such as quality control samples, to monitor the performance of critical activities;
- staff competency assessment;
- development of an internal audit system, using relevant standards or other regulatory and licensing requirements;
- development of a system for the reporting, investigation and analysis of errors, with effective corrective and preventive action.

External assessment of the quality system in the laboratory includes:

- participation in an appropriate EQA programme;
- external audit by a recognized independent body.

1.3 EXTERNAL QUALITY ASSESSMENT

Participation in EQA programmes is one of several effective mechanisms for identifying deficiencies or improvement opportunities within a laboratory's processes and periodically provides an objective view of performance relative to that of other laboratories. Other EQA mechanisms include monitoring through supervisory visits or audits or sample exchange programmes. In the latter, materials are exchanged between laboratories and tested in a coded fashion. The results are analysed to determine whether all laboratories participating in the sample exchange achieve the same results.

Participation in EQA involves testing sets of exercise materials of known, but undisclosed, content that are sent to participating laboratories by the EQA programme provider. Each participating laboratory receives an identical set of exercise materials, which should be processed in the same way as routine blood donor specimens to ensure that the laboratory's performance in EQA accurately reflects its usual performance. Once the EQA exercise materials are tested, participating laboratories send the test results obtained back to the EQA programme provider. Following the collation and analysis of results, each laboratory receives feedback on its own results, together with the anonymized results for all other participating laboratories and the reference results, which enables it to compare its performance with that of other participants.

The assessment of performance through EQA enables a laboratory to determine either that their systems are operating effectively or that deficiencies exist that require correction. As a result, corrective and preventive measures can be implemented as necessary. Thus, information generated by the programme helps to improve the overall quality of the laboratory and the safety of the blood and blood products it issues for transfusion.

Even if a complete quality system is not in place, EQA can still be introduced as part of a process of continual quality improvement.

1.4 OBJECTIVES AND BENEFITS OF EQA

The overall objective of EQA is to measure, maintain and improve as necessary the standards of performance in laboratories. Support for the national adoption of EQA can be achieved by raising awareness of the need for improvement, demonstrating the benefits of best practice, and providing information, education and support for improvement.

Benefits to participating laboratories

The benefits of EQA to participating laboratories include:

- identification of opportunities for improvement relating to laboratory processes;
- comparison of a laboratory's own performance with that of other participating laboratories;
- comparison of performance between different testing systems;
- provision of information and education to improve performance;
- encouragement of best practice;

- opportunities to enhance the credibility of the laboratory and increase public confidence;
- access to a network of laboratories for the exchange of information.

Benefits to health and regulatory authorities

The benefits of EQA to health and regulatory authorities include:

- establishment of a network of blood transfusion laboratories with a known standard of performance;
- training and education of laboratory staff;
- provision of useful information to assist in:
 - setting standards
 - reviewing testing strategies
 - postmarket surveillance of test kits, reagents, instruments
 - using resources effectively
 - improving public confidence in the blood transfusion service
 - supporting systems of accreditation.

Accreditation: Procedure by which an authoritative body gives formal recognition that an organization is competent to carry out specific tasks – ISO 15189:2013

EQA is most effective in raising standards when the need for quality is recognized. This must be accompanied by commitment from senior management to support the changes needed to improve performance. Participation in EQA can be an effective means of driving quality forward in situations where quality systems are not in place. EQA results can reveal poor performance and assist in identifying the need for standards, guidelines, education and training, and the resources required to support them.

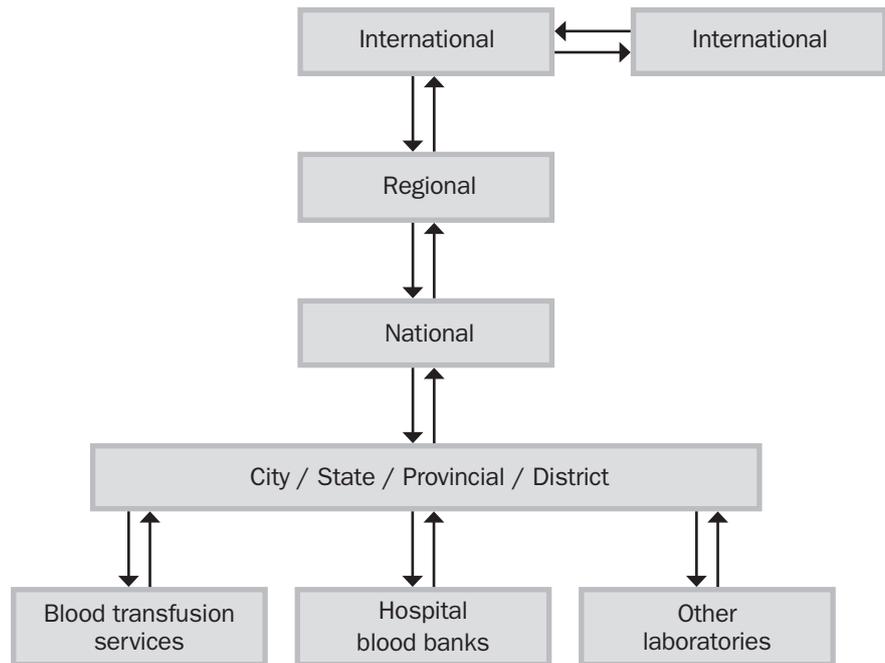
1.5 EQA PROGRAMMES

EQA should be organized as a formal and structured programme to ensure effective planning and organization. This will ensure the uniform provision of exercise materials for testing and a standardized approach to both the analysis and reporting of results and the monitoring of performance of participating laboratories. If it is possible for the EQA organizing institution to be accredited to or comply with the principles of ISO/IEC 17043:2010, *Conformity assessment: general requirements for proficiency testing*, this will assist in achieving the standardization required.

EQA should be made available to all laboratories in which TTI screening is performed, regardless of their size, workload or the complexity of the tests performed. Depending on the policy and regulatory systems in place, laboratories could participate in EQA on either a voluntary or a mandatory basis. Where participation is voluntary, laboratories should be actively encouraged to register for EQA all tests that they routinely perform.

Figure 1 shows one model for a network of EQA programmes developed at international, regional and national levels. At each level, the programme provides the EQA exercise materials, advice and support to its participating laboratories and, in turn, has its own performance monitored through participation in another EQA programme. Another model may encourage TTI screening laboratories to participate in as many EQA programmes as is feasible to challenge their systems as comprehensively as possible.

Figure 1: Network of EQA schemes



Nevertheless, in this model, the principle of the EQA organizing institutions having their own performance assessed still remains paramount.

Based on country needs, WHO advocates establishment of EQA programmes at the regional, national or provincial levels with the aim of facilitating participation by all laboratories undertaking TTI screening of blood donors, irrespective of the type of institution with which they are associated.

When establishing an EQA programme, it can be helpful to seek information and support from WHO or other well-organized EQA programmes. At national level, it is advisable to investigate existing EQA programmes in other areas of pathology and the possibility of sharing of organizational infrastructure, facilities and resources.

2

Establishing EQA programmes for TTI screening

The establishment of an EQA programme could be initiated by the national health authority, blood transfusion service, professional body or interested individuals. An organizing institution and a team of individuals within the institution should be identified to manage and operate the programme. An advisory committee should be constituted to oversee the establishment of the programme and provide guidance on planning and organization.

An effective EQA programme requires the commitment and support of the national health authority or authorities, professional bodies, the organizing institution and relevant staff, the supplier of material for EQA exercises and participating laboratories. The success of the programme depends on the trust and cooperation of all involved. In particular, the involvement of participating laboratories is vital in the organization of the programme.

The roles and responsibilities of all involved should be clearly defined in order to ensure the effective operation of the programme.

2.1 ORGANIZING INSTITUTION

The organizing institution should be a reputable institution with suitable facilities and expertise in the relevant field. Ideally the institution should be designated by the ministry of health and have access to funds allocated specifically for the operation of the EQA programme to ensure the programme's independence and sustainability. Organizing and managing an EQA programme requires a large commitment of time and must therefore be adequately recognized and resourced if the programme is to be successful. To avoid any conflict of interest, an organization with commercial interests in supplying laboratory equipment or reagents should not be designated as the organizing institution.

Establishing an EQA programme provides an opportunity for the organizing institution to become part of a network of laboratories for the exchange of information; this may also bring recognition to the institution.

The organizing institution should participate in a recognized international or regional EQA programme in the relevant field. It should be able to demonstrate satisfactory performance and also show that an effective quality system is in place. The organizing institution should strive for international accreditation to ISO 17043:2010: *Conformity assessment: general requirements for proficiency testing*.

The facilities and resources required to implement an EQA programme include:

- space
- different test kits and methodologies
- access to supplemental or confirmatory testing
- equipment
- staff
- technical support
- administrative support
- reliable source of exercise material
- information management system
- adequate funding.

Ideally, all the required facilities and resources will be provided by the organizing institution. However, it is important to avoid compromising the quality of the programme by attempting to obtain all the resources from within one institution, if this is not feasible. If facilities such as logistical support need to be sought from different institutions for an EQA programme, an effective system of coordination will be required.

Within the organizing institution a team of appropriately qualified individuals with a designated leader (EQA programme team leader) should be dedicated to providing the EQA programme. (Hereafter this team of individuals will be referred to as the EQA programme provider.) The EQA programme provider should have extensive experience and knowledge of best-practice TTI screening, and be aware of common approaches in different types of laboratories. In-depth knowledge and understanding is crucial to ensure the planning of effective exercises, as is insight into possible causes of error and ability to offer effective advice when required.

Responsibilities

The EQA programme team leader is responsible for the general management, operation and ongoing development of the programme, including the following activities:

1. General management:
 - identifying the number of staff required and their training needs;
 - selecting staff and allocating staff time;
 - financial management of the programme;
 - convening advisory committee meetings;
 - communicating with suppliers, participating laboratories, the advisory committee, regulatory authorities, the media and, where applicable, accreditation authorities;
 - selecting laboratories to conduct confirmatory testing or validate programme exercise material if necessary;
 - ensuring the provision and use of a suitable information management system (manual or computerized) for the programme to collate participant information and results;

- implementing, maintaining and auditing the programme's quality system;
- preparing annual reports;
- preparing annual financial statements if necessary;
- handling complaints and taking corrective action;
- attending and presenting data at meetings of participating laboratories and conferences;
- promoting the programme.

2. Operation of the programme:

- devising exercises and sourcing exercise material;
- distribution of the exercise materials;
- keeping track of results return and sending reminders;
- verifying data entry, analysing results, assigning scores and preparing individual and composite reports;
- reporting to participating laboratories any identified problems and advising on ways of improving performance;
- providing troubleshooting advice to participating laboratories;
- reporting to the ministry of health on de-identified laboratory performance and any issues with policy implications;
- monitoring trends in laboratory and test kit performance;
- maintaining up-to-date information about participating laboratories.

3. Ongoing development of the programme:

- keeping up to date with developments in transfusion laboratory practice in TTI testing;
- initiating and implementing changes, as required, to ensure the continued relevance of the programme;
- exploring improved methods for data management and provision of information;
- developing the education and training function of the programme.

2.2 ADVISORY COMMITTEE

An advisory committee is invaluable in the design, planning and implementation of the programme. The membership of the advisory committee should comprise:

- EQA programme team leader;
- selected experts in the relevant discipline;
- representatives of:
 - national blood centre
 - participating laboratories
 - professional bodies
 - confirmatory laboratories, if used
 - health and regulatory authorities.

Once the EQA programme is established, the advisory committee should continue to give direction for its effective continuation.

To ensure effective decision-making and communication, the size of the committee should be limited and members who will participate actively should be selected. The number and timing of advisory committee meetings will depend on the size of the programme and the frequency of the distribution of exercises, but at least two meetings per year will be required.

The committee should make annual plans in advance for the aims of the exercises to facilitate the procurement of exercise material. Members of the advisory committee should maintain confidentiality of programme information, including any details about the exercises, especially if their own laboratory participates in the programme.

Functions and responsibilities

The functions and responsibilities of the advisory committee include:

1. Setting policy on:
 - strategy and direction of the programme;
 - rules of participation;
 - analytes and markers to be included for assessment;
 - ensuring regulations are in place for safe transport of exercise material;
 - principles of scoring and defining poor or unsatisfactory performance;
 - action to be taken on unsatisfactory performance;
 - reviewing complaints;
 - actions to be taken to rectify lost or damaged panels;
 - promotion of the programme;
 - role of the programme in education and training;
 - providing a source of independent expert advice to help poorly performing laboratories.
2. Providing professional and scientific guidance on operational matters, including:
 - planning the aims of each exercise;
 - establishing the algorithms by which exercise material is characterized;
 - establishing the methods by which the reference results are determined;
 - agreeing on the content of reports;
 - reviewing laboratory performance in each survey;
 - dealing with specific questions;
 - reflecting the views of participating laboratories;
 - promoting the educational and training role of the programme.

2.3 TECHNICAL AND ADMINISTRATIVE SUPPORT

Adequate technical and administrative support is required to ensure adherence to the EQA programme schedule. This may be obtained within the organizing institution by the redesignation of existing staff,

the appointment of suitably qualified staff or by contracting to outside agencies.

Technical and administrative tasks include:

- acquiring and characterizing material;
- processing material;
- testing exercise material to ensure its suitability and documenting the results;
- dispensing and labelling exercise material;
- packing and dispatching questionnaires, exercises and final reports;
- organizing couriers and postal services;
- entering and analysing results and other information;
- invoicing participating laboratories for registration fees, if applicable.

2.4 INFORMATION MANAGEMENT SYSTEM

The requirements for information processing will depend on the scale and scope of the programme. It is possible to operate an EQA programme without any information technology, but the use of a computerized system makes essential tasks such as producing results forms much easier and allows for a more complex analysis of results.

It is *essential* to be able to:

- create a database (manual or electronic) of the details of participating laboratories, including contact names, addresses, confidential registration codes and tests to be assessed;
- prepare exercise documentation, including letters, instructions, results forms and address labels;
- record the results from participating laboratories, using confidential registration codes;
- perform basic analyses, including comparison of each individual participating laboratory's results with the expected results and the collation of the overall results;
- analyse results within defined groups, such as laboratories using a particular technique;
- prepare reports with the expected results, the individual results of each participating laboratory and other overall analyses or comments.

It is *desirable* to be able to:

- report data in different formats, such as histograms and scatter charts;
- generate scores for performance monitoring and cumulative scoring;
- search the database using specified criteria.

Specialized computer software is available or can be developed, but many of these functions can also be achieved by the use of standard commercial software packages.

2.5 FINANCES

The resources required to establish and operate an EQA programme must be identified, the costs estimated and funding sought. Tables 1 and 2 show the broad categories of capital and recurrent costs and examples of the facilities and resources required for the establishment and operation of an EQA programme. Possible sources of establishment funding include government, health authorities, professional bodies, nongovernmental organizations and organizations providing research funds.

A regular source of funds will be required for the ongoing and successful operation of the programme. An EQA programme could recover all or part of the operational costs by charging a fee to participating laboratories. While paying a fee may make participating laboratories appreciate the programme, the fee amount needs to be such that it is not a barrier to a laboratory's participation. Health authorities should allocate adequate resources to ensure the programme's sustainability, allowing the contribution from laboratories to be affordable.

Care should be exercised if commercial companies are involved, as the programme should be seen to be independent.

Table 1. Initial capital costs

Category	Examples
Accommodation	<ul style="list-style-type: none"> ■ Purchase or lease of premises or modifications to an existing building for: <ul style="list-style-type: none"> – office – laboratory – cold storage – packing and distribution facilities – record storage
Staff	<ul style="list-style-type: none"> ■ Recruitment ■ Initial training, if necessary
Capital equipment	<ul style="list-style-type: none"> ■ Laboratory: <ul style="list-style-type: none"> – water purification system – centrifuge – incubator – refrigerator – freezer – TTI test kit-specific equipment, e.g. microtitre plate washer and reader ■ Processing and dispensing: <ul style="list-style-type: none"> – magnetic stirrer – lyophilizer (optional) – laminar flow cabinet – clamp stands – pump – racks ■ Storage, package and dispatch: <ul style="list-style-type: none"> – cold room or refrigerator – heat sealer ■ Office: <ul style="list-style-type: none"> – photocopier – telephone – fax ■ Information technology: <ul style="list-style-type: none"> – computer

Pilot study	<ul style="list-style-type: none"> ■ Raw material and staff time for: <ul style="list-style-type: none"> – study design – processing – dispensing and dispatch – analysis and reporting
IT consultancy (optional)	<ul style="list-style-type: none"> ■ Design of software programs for: <ul style="list-style-type: none"> – registration – invoicing – analysis of results – production of reports

Table 2. Continuing recurrent costs

Category	Examples
Accommodation	<ul style="list-style-type: none"> ■ Rent ■ Maintenance ■ Overheads
Staff	<ul style="list-style-type: none"> ■ Salaries and benefits ■ Training and education ■ Travel and related costs ■ Conference fees
Equipment	<ul style="list-style-type: none"> ■ Maintenance contracts ■ Replacement and repairs
Exercise material	<ul style="list-style-type: none"> ■ Raw material <ul style="list-style-type: none"> – acquisition – processing, including filtration
Laboratory testing	<ul style="list-style-type: none"> ■ Reagents ■ Consumables, e.g. tubes and pipettes
Office	<ul style="list-style-type: none"> ■ Telephone ■ Stationery ■ Consumables for printing and photocopying
Information technology	<ul style="list-style-type: none"> ■ Development of software ■ IT support ■ Internet connection
Dispensing, packing and dispatch	<ul style="list-style-type: none"> ■ Bottles ■ Packaging ■ Postage, courier
Meetings	<ul style="list-style-type: none"> ■ Advisory committee ■ Annual meeting of participants ■ Workshops
Consultancy fees	<ul style="list-style-type: none"> ■ Statistician ■ IT development ■ Transfusion specialist

2.6 QUALITY SYSTEM OF THE EQA PROGRAMME

It is essential that the EQA programme itself has a good quality system. Elements of the organizing institution's own quality system could be utilized for this purpose. It will, however, be necessary to implement a specific, effective quality system for the programme, with a quality policy stating how it will provide EQA services to meet the needs of participating laboratories. This policy should be included in the programme's quality

manual, with references to all processes and procedures in the quality system, including those specific to the EQA programme and those in common with the organizing institution.

There are a number of different processes involved in organizing an EQA programme. Therefore, it is important to ensure that appropriate documents and records for each step of the programme exercise are generated for traceability. These include quality plans, standard operating procedures, production protocols, worksheets, checklists, forms, exercise material characterization results, test kit interpretations, and details and results reported by participating laboratories. All documents and records must be kept confidential, stored securely and be readily accessible.

The EQA programme provider may consider the following mechanisms to demonstrate quality of processes:

- WHO/CLSI/CDC *Laboratory quality management system: handbook*
- ISO 15189:2012 *Medical laboratories: requirements for quality and competence*
- ISO 17043:2010 *Conformity assessment: general requirements for proficiency testing*
- ISO 9001:2008 *Quality management systems: requirements*
- ISO 17025:2005 *Accreditation for testing and calibration laboratories*
- Continuing and satisfactory performance in an appropriate international EQA programme.

2.7 PARTICIPATING LABORATORIES

When organizing an EQA programme, the advisory committee should define the profile of laboratories that should be encouraged or required to participate. The programme should be actively promoted to encourage full participation, but the most effective mechanisms for promotion will depend on whether it is a voluntary or mandatory programme.

It is important to be aware of the number and type of laboratories that intend to participate, as this will have an impact on the organization of the EQA programme.

Potential participating laboratories should be sent a preliminary questionnaire to identify:

- staffing levels
- overall workload
- range of tests routinely undertaken
- techniques and reagents used
- quality system in place.

This information can be used to ensure a suitable design for the format of EQA exercises (section 4) and may be also be useful for categorizing laboratories for performance monitoring (section 6). An example of a preliminary questionnaire to obtain general information about participating laboratories is included as Annex 1.

2.8 PILOT STUDY

A pilot study should be undertaken to test the structure of the EQA programme, proposed methods of operation and design of exercises. The purpose of a pilot study is to expose any unforeseen logistical problems and identify solutions before scaling up the operation of the programme and offering formal participation.

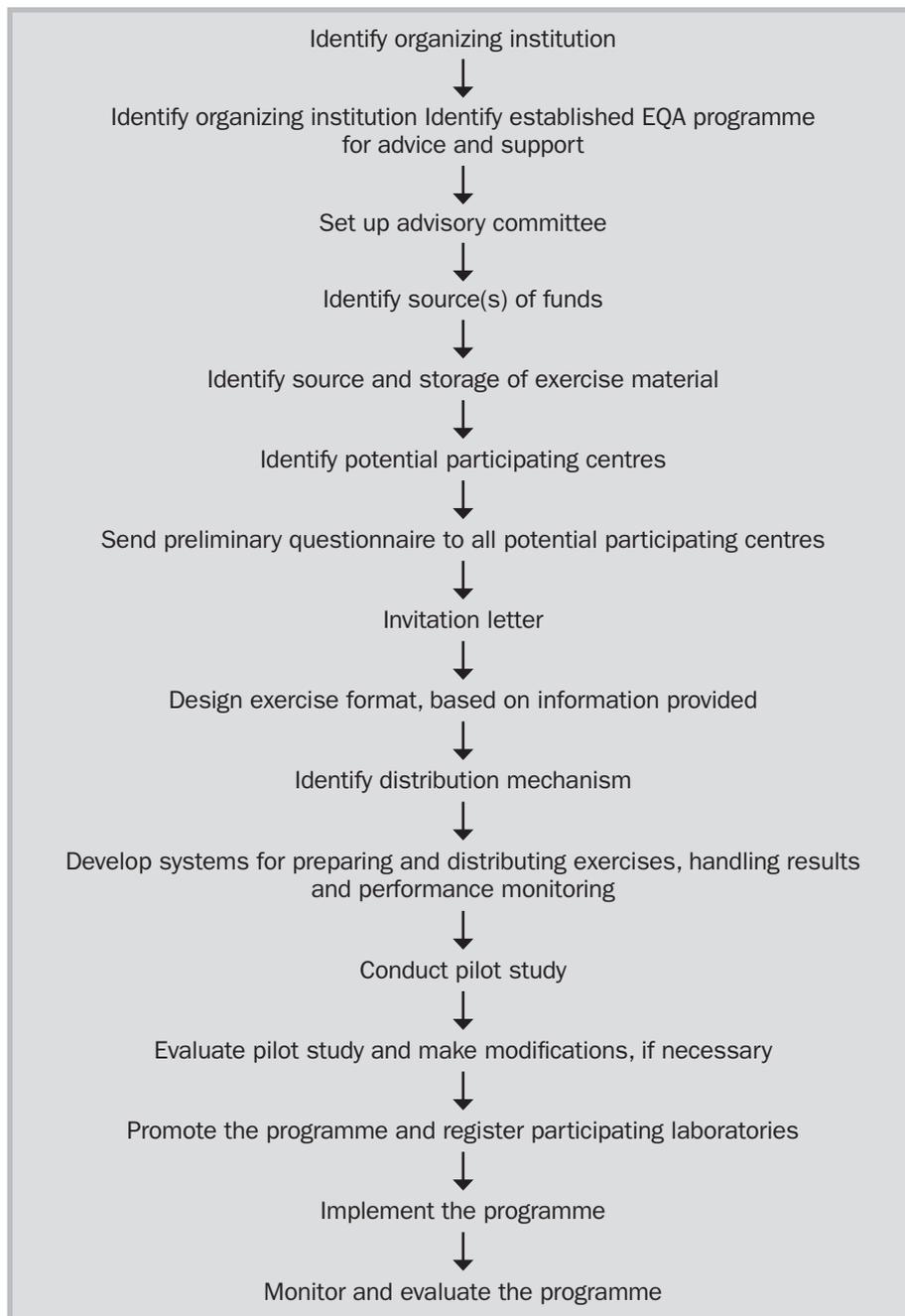
At least two pilot exercise distributions should be sent to a limited number of participating laboratories. These laboratories should be selected to represent different groups of participants in terms of their distance from the organizing institution, the size of their laboratories or the techniques they use.

Participating laboratories should be asked to comment on any problems they encountered and to make suggestions for improvement. At the completion of the pilot study, a review should be made of problems experienced in the operation of the programme and comments from participants. Adjustments can then be made to the design of the programme and to the estimate of operating costs, if necessary.

2.9 PRACTICAL STEPS IN ESTABLISHING AN EQA PROGRAMME

An outline of the practical steps to be taken in establishing an EQA programme is shown in Figure 2. Detailed discussion of each of these steps is found in the ensuing sections.

Figure 2. Steps in establishing an EQA programme



3

Participating laboratories

In order to participate effectively in an EQA programme, participating laboratories should recognize the need for quality and the role of EQA within a quality system in the TTI screening laboratory. Understanding the benefits of EQA and the way in which the programme works will encourage compliance with the rules of participation. This will enhance the value of the programme to the individual participating centres and the overall quality of the information generated.

All staff in participating laboratories should have access to the EQA reports distributed by the programme. Any problems identified should be discussed openly in regular meetings and dealt with as problems relating to laboratory procedures and practices rather than as criticism of individual members of staff. Analysis of the root causes of errors in EQA provides the opportunity for participating laboratories to implement changes to prevent similar errors being made.

Once the programme is established and open to participation, a formal registration process is required in order to gather contact details and other essential information from participating laboratories and also to provide them with the information they need for effective participation. This information should be provided in the form of an EQA programme information manual. The EQA programme provider may also consider organizing seminars for potential participants to explain the programme.

3.1 EQA PROGRAMME INFORMATION MANUAL

An information manual should be developed to explain the management and operation of the programme and give practical instructions for participation. The information manual should be distributed with a registration form.

The information manual should include:

- aims of the EQA programme;
- description of and contact details for the EQA programme provider;
- details of the advisory committee;
- explanation of the commitment needed from participating laboratories and the benefits of participation;
- rules of participation;
- description of the exercises offered;
- explanation of the performance monitoring and scoring system;

- definition of unsatisfactory performance and action to be taken in the event of unsatisfactory performance.

3.2 RULES OF PARTICIPATION

Clear rules of participation in the programme should be determined by the advisory committee. These rules should set out:

- what is expected of participating laboratories;
- the service to be provided by the programme;
- how the information collected, including performance data, will be used.

Participating laboratories should agree to these rules at the time of registration. Examples of rules of participation are given in Boxes 1 and 2.

Box 1. Example of rules for laboratory participation in an EQA programme

To maximize the benefit to participating laboratories and ensure the validity of programme data:

- Only those techniques and technologies that are used in routine algorithms should be used to test the EQA exercise material.
- EQA exercise material should not be tested only by the most senior or experienced staff.
- EQA exercise material should be tested alongside routine specimens; it should not be kept aside for testing separately.
- Exercise material should not be tested more than once and the results compared unless all specimens are also routinely tested in this way.
- Excess exercise material may be used for other purposes such as staff training or competency assessment once the EQA results have been submitted.
- Results must be returned by the closing date specified for the exercise.
- There must be acceptance of agreed procedures for performance monitoring and follow-up of unsatisfactory performance.
- Copyright of programme data must be observed to ensure that they are not published or presented out of context; permission must be sought from the programme provider or advisory committee before data are used.

Box 2. Examples of rules for the programme

To ensure the effective operation of the programme:

- The confidentiality of performance data must be maintained between the programme provider, the advisory committee and the participating laboratory, unless there is an obligation by legislation or prior agreement for them to be disclosed to a third party.
- Exercise material provided should have reliable quality.
- There must be a clear time scale for the distribution of exercises and the return of the report.
- The exercise material must be safe.
- EQA programme reports must include suggestions for improving performance.
- The EQA organizer must be available to address participating laboratories' questions or concerns.
- Exercise material must not be sent to another laboratory for testing, or communication entered into with another participating laboratory about the results.

3.3 REGISTRATION

At registration, all interested laboratories should be sent a registration form, together with the information manual. The registration form should request the following information:

- Contact details for the delivery of exercise materials and reports:
 - name of the participating laboratory
 - name of contact person
 - full postal address
 - telephone number
 - fax number
 - email address, where available.
- The name and address of an additional person such as the head of participating laboratory or institution may be given for correspondence regarding performance, if required.
- The relevant tests used by the participating laboratory and on which it wishes to be assessed should be included, enabling the programme to identify the tests for which exercise results can be expected from each laboratory. Ideally, participating laboratories should be assessed for all tests that they routinely perform.

The registration form should also include a section to be signed by the participating laboratory, indicating its agreement to abide by the rules of participation. Examples of registration forms are included in Annex 2.

Each participating laboratory should be allocated a confidential registration code for use in correspondence with the programme to ensure confidentiality of results and performance data. This code and the information on the registration form for each laboratory should be entered into the programme's information management system. If a

computer database is used, each component of these details (such as the registration code and each line of the address) should be entered as separate fields to facilitate searches on the data.

Information on participating laboratories should be kept up to date by annual re-registration; a new registration form should be distributed with a copy of the current registration details for confirmation. This will enable the programme to obtain updated technical information and contact details.

4

Practical considerations in establishing an EQA programme

Information obtained from the preliminary questionnaires completed by potential participating laboratories should be used to design EQA exercises. Whenever possible, each EQA exercise should have an educational function, exploring areas where wide variation in testing is known to occur or suspected to be challenging to laboratories.

The following practical aspects of the programme should be considered during its design:

- scope
- EQA programme and exercise format
- objectives of the programme
- sourcing and processing exercise material
- exercise documentation
- analysis and communication of results.

4.1 SCOPE

A TTI EQA exercise should meet the needs of the participating laboratories and assess the tests routinely performed for screening of donated blood. This can be ascertained from the laboratories' responses to the preliminary questionnaire. Screening for markers such as HIV-1/2 antibodies, hepatitis C antibodies, hepatitis B surface antigen and *Treponema pallidum* antibodies may be considered standard in a TTI laboratory and therefore should be included in EQA programme exercises. Depending on the scope of testing of the participating laboratories and the national regulatory requirements for screening of TTI, the markers included may be expanded to include HIV-1 p24 antigen, hepatitis B core antibodies or other markers such as *Trypanosoma cruzi*, malaria and HTLV-I/II antibodies.

4.2 EQA PROGRAMME EXERCISE FORMAT

The number of EQA exercises to provide in a year should be sufficient to allow adequate assessment of laboratory procedures and practices and to gather sufficient data for cumulative performance monitoring. At least two exercises should be distributed to participating laboratories each year to give a minimum level of confidence in the laboratories' performance.

The number of exercise materials that will be included in an EQA exercise should enable detection of potential errors in laboratory processes. An exercise consisting of a small number of materials (for example 1–4) may be able to detect random errors but will have limited capacity to detect systematic errors. Panels that consist of a larger number of exercise materials (for example 5–10) will have greater capacity to detect both random and systematic errors.

4.3 EQA PROGRAMME OBJECTIVES

Each EQA exercise should address specific questions or objectives; the EQA panel should be constructed to address these objectives. A good EQA programme will provide participating laboratories with education on good laboratory practice and will be able to identify different laboratory errors that may occur.

Some possible objectives and mechanisms are shown in Table 3.

Table 3. EQA programme objectives and mechanisms

Objective	Mechanism
Can the participating laboratory correctly identify the status of specimens?	Do the participating laboratory's results match the reference results?
Does the participating laboratory follow the manufacturer's kit protocols?	Collect details of testing on the results form, for example variations in test kit control results, reading time
Does the participating laboratory produce consistent results?	Include replicates of the same exercise material
Does the participating laboratory produce consistent results over time?	Include replicates of the same exercise material over different exercises
Does the participating laboratory have a process for rejecting unsuitable specimens?	Include haemolysed or other unsuitable exercise materials and assess if the participating laboratory proceeds to test the materials
Can the participating laboratory identify administrative errors?	Include exercise materials that have been purposely mislabelled
Compare performance of different testing systems	Analyse the results according to different systems and technologies
Verify coverage of mandatory screening for TTI	Include all mandatory markers Check the laboratory report

Exercise materials:

Materials that have been prepared from samples and that make up an EQA panel.

Panel: A set of EQA exercise materials.

Sample: A specimen, preferably of large volume, that has been processed, tested, and stored in a sample bank for potential use as exercise material.

Specimen: Discrete portion of a body fluid, breath, hair or tissue taken for examination, study or analysis of one or more quantities or properties assumed to apply for the whole (ISO 15189:2013).

4.4 SOURCES OF EXERCISE MATERIAL

Exercise material should preferably be obtained from blood transfusion services, since donor blood is ideal as exercise material. It is readily available in large volumes and is tested for TTI in accordance with local regulations. However, the ethics surrounding its use should be clarified. Ideally, informed consent should be obtained from the donors to use their blood for EQA purposes.

Finding the required number of donations positive for TTI could prove to be difficult. When no suitable donor material is available and patient material has to be used, informed consent must be obtained.

Blood transfusion service algorithms may prescribe that donations reactive on a TTI screening test kit are discarded, that is, confirmatory testing is not performed. In those cases, the reactivity may be true or false, and if the donations are to be used as exercise material, confirmation may be undertaken by the EQA programme provider or a designated expert laboratory. Efforts should be made to ensure that donations provided as potential exercise material confirm as positive when confirmatory testing is undertaken. This is important because of the costs involved in transporting plasma packs in accordance with regulations and in confirmatory testing. These investments are wasted if the reactivity of plasma packs is not as expected. Measures the programme provider can implement include:

- Consider the prevalence of the TTI in the donor population from which the plasma packs are being sought. Preference should be given to obtaining plasma packs from blood transfusion services where the prevalence of the particular TTI is higher, so the positive predictive value of the reactive result in the screening test kit is higher.
- Choose suppliers with good quality systems in place so that the quality of their test results can be trusted.

Suppliers of exercise material should be selected according to their ability to make reliable provision of the quantity of material required and assure its quality. There should be a formal agreement between the EQA programme provider and the supplier or suppliers to ensure that the supply of exercise material is reliable and meets all the specifications set by the programme.

It is essential that the EQA programme provider or an expert laboratory, if used, is able to characterize the exercise material accurately, even if participating laboratories are not required to undertake extensive testing (see section 5.3 on the selection of exercise material).

Candidate samples for TTI exercise material may be organized into a “sample bank” – a repository of a large number of large-volume samples with varying characteristics. This is possible because, in the case of TTI, the most common exercise material is plasma or serum, which can be stored frozen for prolonged periods without compromising its serological reactivity. Significant and ongoing resources are required to establish and maintain a sample bank.

4.5 ESTABLISHING A SAMPLE BANK

Establishing a TTI sample bank for serum or plasma to be used as exercise material should be commenced well in advance of the first EQA programme exercise. Candidate sera and plasmas should be processed in a timely manner and stored appropriately. Upon receipt, a unique laboratory identification number should be allocated to each serum and plasma. A candidate serum or plasma obtained in large volume should be dispensed into smaller practical volumes aimed at reducing the number of freeze/thaw cycles. Serum and plasma should be stored frozen at or below -20°C in polypropylene containers of appropriate volume with leak-proof screw lids containing a sealant such as an O-ring.

The containers should be clearly labelled using high-quality adhesive labels. The exercise material should be carefully characterized through validated testing strategies to determine the true serological status of the material, and the information stored in a database (see subsection on characterizing and testing EQA exercise material, in section 4.6).

A sample bank database is an inventory of biological material in a repository. The information in the inventory should be updated on a regular basis, as it will need to be accessed each time an EQA exercise is planned. The type of information that should be recorded in a sample bank database includes:

- unique laboratory identification number
- reference number or code
- date collected
- date received
- type of material (e.g. serum, plasma)
- volumes and number of vials (if dispensed into smaller volumes)
- clinical information and provider's test results
- characterization test results
- location in sample bank freezer
- sample tags²
- number of freeze/thaw cycles.

Once the sample bank is established, it is recommended that allocation of resources continues in order to maintain the appropriate number and volumes of exercise materials required for future EQA exercises.

4.6 PROCESSING CANDIDATE EXERCISE MATERIAL

Although plasma is an appropriate biological material for TTI EQA exercises, there are aspects that must be considered when it is used as EQA exercise material (for example limitations in volume, and formation of clots regardless of filtration or centrifugation steps). In some cases defibrinated plasma or serum may be considered as an alternative to plasma. Which biological material to use as TTI EQA exercise material should take into account the needs of the participating laboratories and the validity of the material for use in TTI test methods. Manipulations may be performed to increase the volume or quality of biological materials used for EQA exercises. It should be stressed that EQA exercise materials should be as representative of "normal" donor specimens as possible. Each manipulation performed will cause deviation from "normality". Further, a manipulation may have an adverse effect on the results produced by different test methods. Thus, each method of manipulation should be extensively validated for its effect before applying it to EQA exercise material.

² It is useful to consider the allocation of a "tag" or code to each serum or plasma to help search and identify materials in the database.

Conversion of plasma to serum

Plasma collected in donor collection bags will contain an anticoagulant such as citrate-phosphate-dextrose (CPD), and thus conversion to serum naturally is not possible. However, plasma can be converted to defibrinated plasma (in effect serum) by artificially initiating the clotting cascade through the addition of thrombin followed by removal of the resulting clot. Once the clot is removed, microfiltration of the serum should be considered to remove any bacterial contamination.³

Filtration

Biological materials can be filtered using either vacuum or pressure filtration apparatus, in a stepwise reduction of pore size (prefilter, 0.8 microns, 0.45 microns and a final 0.22 microns). Filtration will remove any microparticulate matter, ranging from microclots to bacterial contamination.⁴

As a note of caution, the conversion of plasma to serum and filtration processes are cumbersome, labour intensive and potentially hazardous. Therefore, these processes should be conducted in biohazard cabinets by personnel with adequate personal protective equipment including gowns, gloves and face masks or goggles.

Nevertheless, effort must be made to provide exercise material free of contamination, particulate material and clots. Without conversion of plasma to serum, reasonably satisfactory exercise materials can be produced by centrifugation of the material to remove particulate matter and clots. To maintain sterility without filtration, exercise material should be handled in a class II biosafety cabinet, paying attention to aseptic techniques to the extent possible and using sterile equipment and containers.

Use of biocides

The use of biocides may be considered to reduce the potential for bacterial growth and preserving the quality of the biological material. An example of a biocide is ProClin 300 (1.5% methylisothiazolinone, methylchloroisothiazolinone). Sodium azide, which was once used extensively as a biocide, is no longer recommended owing to safety concerns. Thorough validation of any biocide should be undertaken to identify potential interference with TTI test methods.⁵

Pooling

For large EQA programmes, pooling can be considered an option for increasing the volume of exercise material available (where the volume

³ Ratnoff OD. "An accelerating property of plasma for the coagulation of fibrinogen by thrombin", *Journal of Clinical Investigation*. 1954;33:1175–82.

⁴ Bobbitt JA, Betts RP. "The removal of bacteria from solutions by membrane filtration". *Journal of Microbiological Methods*. 1992;16(3):215–20.

⁵ ProClin: http://www.sigmaaldrich.com/content/dam/sigma-aldrich/docs/SAFC/General_Information/proclin_efficacy.pdf.

requirement for the number of participants exceeds that normally found in a single blood donation). Pooling samples involves mixing individual samples together to create a mixed pooled sample. However, in pooling samples, a dilution effect may be created – in other words, dilution of the individual constituents of each sample used in the pool. This risk may be reduced by selecting samples of similar antibody or antigen profiles, as ascertained by testing, thus only pooling samples with similar test result profiles or characteristics. Pooling has the benefit of extending the volume of exercise material while seeking to maintain the reactivity of key constituents in the samples contributing to the pool. Sometimes, pooled negative sera or plasmas can show an increased tendency to false reactivity. Therefore, pooled exercise materials, whether they are negative or positive, should be tested extensively before use in an EQA programme.

Dilution

Dilution with negative plasma or another isotonic diluent to create exercise materials should be avoided where possible. Dilution of biological material to increase the volume may be possible if the material is only diluted to the extent required to create the additional volume. Dilution to mimic early infection profiles or “weak” results creates a final exercise material that does not have a serological profile representative of that seen in undiluted donor specimens. In addition, the ability of some tests to detect diluted antibodies or antigens that would normally be detected when undiluted may be reduced. The EQA programme provider must test diluted exercise materials in a large number of test kits that are likely to be used in the programme to ensure that they behave as expected.

Dilution of quantifiable markers – for example, hepatitis B surface antigen (HBsAg) or HIV-1 p24 antigen – may be considered as options to produce serological exercise materials representative of early infection, where it is difficult to find naturally occurring biological material of sufficient volume. In the case of HBsAg, care must be taken to not overdilute other early hepatitis B markers (anti-HBc IgM), should these be markers that the EQA programme is assessing.

Further, the diluent must be free of hepatitis B surface antibody as it is likely to complex with HBsAg and render it unavailable in the testing system.

Dried tube samples

Transportation conditions are major contributors to poor-quality exercise materials. In addition, transportation costs may be too high, adding a financial burden to the EQA programme.

Some EQA programmes for resource-limited settings are provided as dried tube samples (DTS). These are small volumes of positive or negative serum or plasma that have been dried in air over 12–24 hours.⁶

⁶ Parekh BS, Anyanwu J, Patel H et al. “Dried tube specimens: a simple and cost-effective method for preparation of HIV proficiency testing panels and quality control materials for use in resource-limited settings”. *Journal of Virological Methods*. 2010;163(2):295–300.

Only small volumes can be dried over this period (for example 20 microlitres), but the dried pellet is reconstituted in a ten-times greater volume, usually in phosphate-buffered saline, resulting in exercise material that is tenfold diluted and having a different matrix from true serum or plasma specimens. It is not advisable to use weakly positive samples in DTS EQA programmes because the dilution may cause false negative reactions in all or some test kits. The EQA programme provider must reconstitute and test the DTS in a large number of test kits that are likely to be used in the programme to ensure that the exercise materials behave as expected.

Despite these different approaches that contravene conventional EQA norms, using DTS makes providing some form of quality monitoring possible in situations where conventional EQA programmes are not feasible.

It must be noted that if DTS are provided as exercise materials for an EQA programme, the participating laboratories must reconstitute them before testing. This is an additional variable, the potential impact of which must be considered when analysing and scoring results.

Characterizing and testing EQA exercise material

The key attributes of exercise material in TTI EQA are:

- that the specimen type is generally approved by the manufacturers of test kits that are used by the programme participants, for example serum or plasma;
- that the exercise materials are homogenous, and stable for the period over which the exercise is under way;
- that the true status of an exercise material is known for the markers under assessment.

Instructions for use that accompany test kits for TTI usually specify the specimen types that are appropriate for use in the tests. It is important that the exercise materials provided in the EQA programme mimic as closely as possible a specimen type that is allowed by all the tests, otherwise aberrant results may be obtained if a specimen type differs significantly from those recommended. For example, as mentioned earlier, the appropriateness of phosphate-buffered saline reconstituted DTS as a specimen type must be confirmed by the programme provider as appropriate in all the test kits used by the programme participants.

Characterization of samples is usually achieved using a testing strategy and a defined algorithm. A testing strategy defines the range and types of tests used to determine the status of a sample; an algorithm specifies the names of the tests and the order in which they are used. A testing strategy includes a first test to identify negative samples, and one or more supplemental tests that are used to confirm whether those samples that are reactive in the first test are positive or not. This confirmation of positive reactivity is performed because all tests for TTI give a small proportion of false positive results. Testing in a second test assists with ensuring that samples in the sample bank that are assigned a positive status are truly positive.

The first test in an algorithm must be of high sensitivity, especially because it will identify negative samples, that is, a negative result from

the first test will be assumed to be correct and no other testing will be performed to “confirm” the material’s negative status before its status is assigned in the sample bank. Therefore the programme provider needs to be confident that the first test kit used to characterize sample bank samples is as sensitive as is available and will not misclassify positive samples that could be detected by other test kits used by laboratories participating in the EQA programme.

The EQA programme provider needs to consider carefully the way sample bank samples are characterized. For example, if any participating laboratories have indicated that they use HIV combination assays, which detect both antibodies to HIV and HIV p24 antigen, the EQA exercise materials must be characterized for both of these markers. Similarly, if participating laboratories use specific or non-specific treponemal tests for syphilis, the status of the EQA exercise materials for both of these markers should be known.

The key attributes to consider when choosing tests for characterization of samples and testing of EQA exercise materials are:

- **Tests available.** Most countries will have a list of tests that can be procured for each marker.
- **Test characteristics.** Information about a test’s performance (sensitivity and specificity), its ease of use, requirements for equipment, and other characteristics is necessary. Such information may be found on the WHO website.⁷ Peer-reviewed publications are another source of information.
- **Purpose of testing.** An EQA programme provider may be performing testing for purposes other than characterization of EQA material. It is this testing that will drive the choice of tests, for example, what is the throughput of testing; what is the required turnaround time; what is the shelf life of the reagents; and is there access to refrigeration if necessary.

4.7 EXERCISE DOCUMENTATION

Each EQA exercise requires accompanying documents, which may include:

- instructions on how to handle, test and report results for the EQA exercise material;
- results forms;
- feedback questionnaires, included periodically to enable continual improvement of the programme.

Exercise instruction sheets that are generated for each exercise should provide general information on how to handle, test and store the exercise materials and how to report the results to the EQA programme provider. The participating laboratories should be reminded to treat the exercise materials as routine specimens and subject them to the same testing and processes. The instruction sheets generally include the following information:

⁷ http://www.who.int/diagnostics_laboratory/evaluations/en/.

- number and identifiers of exercise materials
- exercise code
- deadline date for returning the results
- storage and handling instructions
- testing instructions
- reporting instructions
- biological safety precautions
- EQA programme provider contact information.

An example of an exercise instruction sheet is given in Annex 3.

The EQA programme provider should prepare a form for the collection of EQA exercise results. The EQA results form may be provided electronically or in paper form. Whichever mechanism is used, the form will allow for a standardized approach to collecting EQA test results and information from participating laboratories.

A paper-based data collection form requires the EQA programme provider to design a results collection form that is sent to the participating laboratories with the exercise panel. Upon completion of testing for the exercise the laboratories must submit the completed results form to the EQA programme provider by mail or fax. This format is simple to develop and allows for flexibility in the information that can be provided by the participating laboratories. A disadvantage of paper-based data collection is that results from all of the participating laboratories must be collated by the EQA programme provider, a process that is time consuming and vulnerable to error.

An electronic data collection form can be sent electronically to the participating laboratories. When the testing for the exercise is complete, the participating laboratory enters the results into the form and can return it to the EQA programme provider electronically. The EQA programme provider can then copy and collate the data electronically, reducing the time required for data entry. Although this format can reduce the likelihood of data entry error, validation checks are necessary to ensure that data have been copied accurately.

A further adaptation of electronic data collection is an Internet-based format. This method requires the design and maintenance of an online data collection system. Participating laboratories can enter the EQA exercise results directly into the online database. In this format no data entry is required by the EQA programme provider, eliminating the time taken and potential for error at this step. A disadvantage of this data collection format is the need for resources to design and maintain a functional website. Furthermore, participating laboratories will require the information technology infrastructure to use the system.

Whichever format is chosen for the collection of EQA exercise results, the results forms should generally include the following information:

- participating laboratory code and name
- receipt date and condition in which the exercise material was received
- name of test method or reagents used

- reagent lot number and expiry date
- date of testing and name of person doing the test
- test results and interpretations
- additional comments.

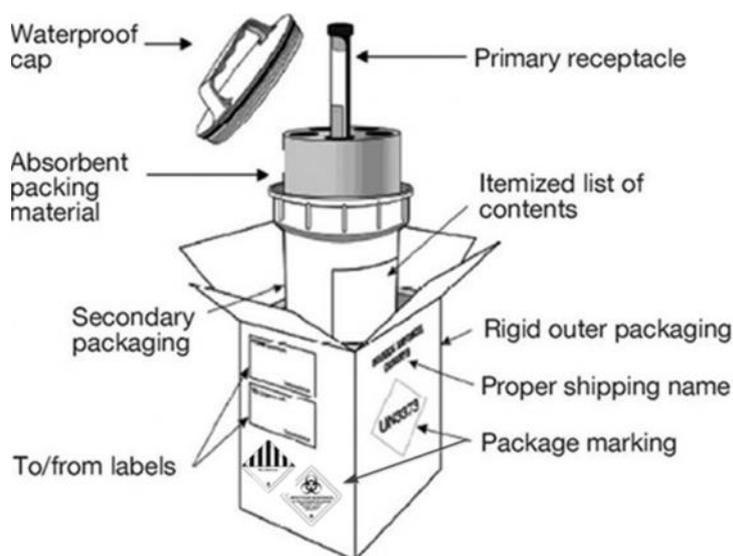
Examples of exercise results forms are given in Annex 4.

4.8 LOGISTICS

Based on local infrastructure, the EQA programme organizer will need to decide upon the mode of transport for the EQA panels to be delivered to the participating laboratories. Health and safety issues should be considered for all groups of workers who may be exposed to exercise material, including postal and courier workers. These people must be trained how to handle the exercise material safely should the packaging be damaged or there is leakage. EQA programme exercises should be packed and labelled in conformity with local or international postal or air regulations, such as those of the International Air Transport Authority (IATA), as applicable. For IATA purposes, exercise materials can be shipped as diagnostic samples and not as dangerous goods.

IATA regulations require specific triple packaging and labelling. In brief, vials containing exercise material are sealed in a watertight secondary package that contains sufficient absorbent material to soak up the total volume of exercise material within the package in case of leakage or breakage. The secondary package should be placed in further packaging that is capable of protecting the contents from physical damage while they are in transit (Figure 3).

Figure 3. Schematic of triple packaging for IATA-compliant shipping of diagnostic samples



Source: IATA, Montreal, Canada.

The external packaging should be labelled to indicate that it contains pathological material. The name and address of the EQA programme should be written on the outside as well as the name and address of the participating laboratory to which the exercise material is being sent.

5

Planning and operating an EQA programme for TTI testing

There are two types of plan required to guide the provision of an EQA programme. One is an annual plan, which describes the main features of the programme and the activities of the programme provider over a year of the programme. The other plan is a detailed description of the activities required from beginning of material production to the finalization of the EQA programme report. A plan of this type is required for each EQA exercise.

5.1 DEVELOPING AN ANNUAL EQA PROGRAMME PLAN

Before the commencement of an EQA programme, the programme provider should identify and plan the processes for the EQA programme year. Plans should be documented and contain information that addresses the objectives and design for each exercise of the EQA programme year. Annual plans should contain references to standard operating procedures, protocols and other documents that contain more detailed information.

Typically, annual plans for EQA programmes should address the following information:

- name, address and contact details of the EQA programme provider;
- name, address and contact details of subcontractors involved in the EQA programme, if applicable;
- any specific objectives of the EQA programme for the year – for example, an annual objective could be to examine the laboratories' abilities to obtain reproducible results on different occasions when testing the same materials;
- activities to ensure samples in the sample bank are adequate to meet the needs for the year's exercises;
- the number and type of participants expected to be enrolled in the EQA programme;
- participation fee or funding mechanisms;
- information on what materials and analytes participating laboratories are to identify, measure or test for in each exercise of the EQA programme;
- requirements for the production, quality control, storage and distribution of EQA exercise material;

- schedules and dates for production of EQA exercises, dispatch to participating laboratories and deadlines for submission of results by participants;
- procedures for homogeneity and stability testing;
- description of the statistical analysis to be used if applicable and criteria for the evaluation of performance of participating laboratories;
- expected dates when reference results and final reports will be made available to participating laboratories.

5.2 DEVELOPING THE PLAN FOR A SPECIFIC EQA EXERCISE

While the annual EQA programme plan is a high-level document that defines broadly the attributes of the programme, a specific plan is required to guide the preparation of each EQA exercise. This more specific plan will document how each individual exercise will be executed.

The specific plan should address the following information for each exercise:

- responsibilities of individual staff in preparation of the exercise;
- aim(s) of the exercise;
- number of laboratories enrolled in the exercise;
- selection criteria and volume requirements for each of the exercise materials to satisfy the aim of the exercise;
- exercise name, panel number and code;
- identifiers for individual exercise materials;
- detailed production processes and verification testing;
- schedule and dates for production of the exercise panels, dispatch to participating laboratories, and deadline for submission of results and report distribution;
- references to protocols for homogeneity and stability specific to each exercise;
- references to all documents, forms and records involved in the exercise.

It is recommended that a process checklist and timeline be designed alongside the specific EQA exercise plan; this ensures that processes occur in a systematic manner and provides traceability of the entire EQA process.

5.3 SELECTION OF MATERIAL FOR EQA EXERCISES

Appropriate samples that will satisfy the aims of the specific EQA exercise should be selected from the sample bank. Each exercise should contain materials that are of highest quality, each with a defined serological status, based on the characterization testing results recorded in the sample bank database (see section 4).

An EQA exercise will consist of a number of negative and positive exercise materials. The number of negative and positive exercise materials and the order in which they are presented in the panel should vary from exercise to exercise to avoid the participating laboratories predicting the exercise composition.

Sufficient vials should be prepared to meet both the requirements of participating laboratories and to allow the programme provider to retain spare vials in storage. Spare vials are needed in case participating laboratories require replacements due to loss or breakage, or for repeat testing following an error. Additional vials will also be required by the programme provider for in-house testing throughout the duration of the exercise for stability purposes, for archiving or for future use.

The total volume required for each exercise material is calculated by taking into consideration the following:

- total number of participating laboratories in the exercise;
- number of additional exercise panels that will be prepared (to be used as replacement panels or for investigation purposes);
- number of vials of each exercise material required for homogeneity and stability testing;
- volume required for each vial;
- volume loss or error allowance during panel production (through centrifugation and dispensing).

5.4 PREPARATION OF EXERCISE MATERIALS

Once appropriate samples have been identified, they are removed from the sample bank. The removal of the samples should be updated in the sample bank database.

Samples will need to be thawed prior to use. For smaller volumes, plasma can be thawed in a water bath at 30–37°C, for as long as it takes to thaw (normally no more than 30 minutes). Thawing time will vary according to the temperature of the water bath and the volume of plasma.⁸ Once thawed, volumes of the same sample should be combined if the sample was stored in more than one vial. If pooled samples are to be used in the EQA exercise, the pooling process would take place during this stage.

Separate aliquots of the same sample or aliquots of different samples identified for pooling must be well mixed before further processing.

The total volume of each sample is centrifuged to pellet particulate matter and the supernatant decanted into a separate sterile vial. Each sample should be tested again before dispensing into individual vials to create exercise materials, and cross-checked with the original sample bank characterization results. This verifies that there has been no mix-up and that there has been no degradation during storage. If any results differ from those expected, the sample is not appropriate for use in the exercise and it is recommended to select an alternative sample.

5.5 DISPENSING EXERCISE MATERIAL

Screw-capped external thread polypropylene vials of appropriate volume should be prelabelled prior to dispensing, with adhesive labels that have

⁸ *Extended life plasma: a framework for preparation, storage and use*, 2nd edition. Australian and New Zealand Society of Blood Transfusion Ltd; 2013.

been validated to demonstrate adherence to the vials through fluctuating temperatures and storage conditions. Adhesive vial labels should contain the following information:

- EQA programme name
- exercise number or code
- identifier of the exercise material
- volume of the material contained in the vial.

It is recommended that the information on the labels be printed electronically if possible to minimize transcription errors. Labelling of all tubes for one exercise material should be segregated to avoid mix-up of labelled tubes.

Dispensing all the vials for one exercise material should be completed before moving on to the next to reduce the risk of contamination, of mix-up between materials, or of dispensing into an incorrect vial. It is recommended that negative materials be dispensed first followed by positive materials. Manipulation of biological material is ideally performed inside a biological safety cabinet.

Once exercise materials are dispensed into vials, the panels can be assembled into labelled panel packaging. Packaging labels should contain the following information:

- EQA programme name
- exercise number or code
- number of exercise materials in the panel
- recommended storage temperature
- expiry date
- biohazard symbols.

The assembled exercise panels should be stored between 2°C and 8°C until ready for dispatch, which should occur as soon as possible after the production has been completed.

5.6 VERIFYING HOMOGENEITY AND STABILITY

Regardless of the biological material used, it is necessary to ensure that exercise materials are adequately mixed and all participating laboratories receive equivalent material that is uniform in composition with minimal variation (homogeneous material). Verification of the materials' homogeneity should be completed for each EQA exercise distribution. It is performed:

- by testing a random selection of representative numbers of final vials of each exercise material;
- after processing and dispensing of the exercise material into vials but before dispatch to participating laboratories.

The number of vials chosen for homogeneity testing should be sufficient to assess possible variation in the exercise material. For each exercise material that has been dispensed an appropriate number of vials is selected randomly. ISO 17043 states: "Where appropriate, the provider or its subcontractors shall use a statistically random selection of a

representative number of samples from a batch of test material to assess the homogeneity of the material.” There is no defined number of vials required for homogeneity testing, though, as a guide, it is usual to select a minimum of 10% or 10 of the vials produced, whichever is the greater. However, the number of vials chosen for homogeneity testing should not exceed the capacity of a single test run to avoid interrun variation.

It is important to ensure that the reactivity of the material has not changed in any of the vials selected and tested for homogeneity. An extensive homogeneity protocol must be undertaken and all records documented. For homogeneity testing, it is recommended that the first test method in the programme provider’s validated testing strategy for the appropriate marker is used. If a single vial does not produce the expected result, it may result in all vials containing the particular exercise material being removed from the exercise. An example of a protocol for homogeneity testing is included in Annex 5.

5.7 VERIFYING STABILITY

It is necessary to validate the stability of materials in order to ensure that they are fit for use when they arrive in participating laboratories and no loss of material integrity has occurred. Temperature, time, biological material type, pathogen properties and other factors can contribute to loss of material integrity. The stability of materials can be tested by different mechanisms:

- leaving vials unopened, at ambient temperature, for the length of time that exercise materials are expected to spend during distribution, followed by retesting to confirm reactivity;
- conducting accelerated stability studies at different temperatures in the laboratory;
- simulating real-time stability studies.

Preparation and execution of a stability protocol will monitor and assess the rate of possible deterioration of the exercise materials. The stability of the exercise material should be monitored from the time of completion of EQA exercise material production through to, at least, the closing date of the exercise.

The number of vials chosen for stability testing should be sufficient to allow testing to occur at regular intervals for the duration of the exercise. Regular monitoring will help pinpoint the time of deterioration, should it occur. It is recommended that stability continues to be monitored for a short period of time after the closing date of the exercise, in the event of any troubleshooting that may be required.

Like homogeneity testing, it is recommended that the first test in the programme provider’s testing strategy for the appropriate marker to characterize the exercise material is used for stability testing. A stability protocol needs to be documented before the commencement of stability testing, taking into consideration the timeline of the exercise and factors that may influence the stability of the exercise material. Acceptance criteria must also be documented in the stability protocol outlining the actions taken if results show that the stability of an exercise material has deteriorated. In developing the acceptance criteria it is important to

allow for intrarun and interrun variation when analysing stability results. An example of a protocol for stability testing is included in Annex 6.

Sending material to one or more distant participating laboratories that then return it for retesting is also sometimes used for stability testing. However, this only verifies the stability of the material while it is in transit, unless it is held at the participating laboratories for the duration of the exercise before it is returned.

5.8 PACKING AND DISPATCH

Documentation appropriate to the specific EQA exercise should be included within the package. These include the instructions for handling the exercise materials and the forms for recording the results, if hard copy results forms are used. Although templates for this documentation will have been developed at the outset of the programme, it is important to proofread and check all documents before distribution to ensure that there are no contradictions, ambiguities or omissions in the information, and that the information pertains to the specific exercise being distributed. Accompanying documents should be sealed within a protective pouch and attached to the outside of the secondary package.

If the EQA programme provider has decided to use electronic results forms, these should be emailed to the participants at the same time as the exercise materials are dispatched.

A list of participating laboratories' registration codes is helpful when packing exercises to ensure that no laboratory is missed. It is also important to have a protocol for packing, including checking that the correct combination of exercise materials and documents has been packed for each participating laboratory. Annex 7 contains an example of a record of exercise distributions and returned results that can be used as a packing checklist. If exercises are all distributed on a single day, it is sufficient to note the date and place a tick in the columns "Documentation packed", "Materials packed" and "Exercise distributed" against each participating laboratory. The date of packing and distribution should be recorded for any participating laboratory to which exercises are sent on other dates.

5.9 COLLECTION OF AND DEADLINE FOR EQA RESULTS

Participating laboratories are expected to submit the completed exercise results form to the EQA programme provider by the specified deadline date for the acceptance of results. Results received after this time should not be accepted, especially if stability validation processes do not extend beyond the deadline date. In order to encourage and remind participating laboratories, the EQA programme provider may contact participating laboratories a week before the deadline to remind participating laboratories to submit their results.

Upon receipt by the EQA programme provider, the completed results forms should be date-stamped and filed in a manner that allows for easy retrieval. The EQA programme provider may choose to do a quick review of the results forms received to ensure the forms have been completed and that all information is legible and identify any gross errors.

5.10 COLLATION OF EQA RESULTS

EQA exercise results from the participating laboratories should be collated in a manner that facilitates analysis. The approach for collating the results from an EQA exercise will depend upon how the data were collected and the type of data submitted.

EQA exercise results should be collated in a single location that is a physically safe and confidential environment. Although manual-based collation of the results is possible, an electronic system is preferable to allow for ease of storage and analysis. It is essential that the EQA programme provider has a quality data management process in place. Manual-based systems will require higher levels of management to ensure that errors in transcription and data entry are minimized. The number of times data are handled should also be reduced to avoid errors. For both manual and electronic methods of results collation, secure data storage and maintenance of records (including adequate backup of electronic data) are required.

The type of test results submitted by the participating laboratories (qualitative or quantitative) from one or more test methods needs to be considered in designing a system for collation and analysis. Whether each piece of supporting information (such as test method name, lot numbers, expiry dates, operator, test date, etc.) should also be included will depend on the way the data will be analysed.

5.11 ANALYSING EQA RESULTS

In order to analyse the EQA exercise results, the reference result for each exercise material needs to be determined by the EQA programme provider. This reference result will usually be assigned based on characterization testing performed during the production of the EQA exercise material. However, occasionally, the reference result may be assigned based on a consensus of results from a group of laboratories. Ideally, this should occur rarely when an exercise material behaves in an unexpected manner and gives results that deviate from the characterization results. The reference results should be made clear to the participating laboratories.

The complexity of the results analysis performed may depend on:

- the maturity of the EQA programme and the technical knowledge of the EQA programme provider;
- the aims of the EQA exercise;
- the resources available to the EQA programme provider.

Another important consideration is the time frame for providing feedback and reports to participating laboratories. Timely communication of laboratory performance in the EQA exercise may be more useful than an in-depth analysis that requires a prolonged time to complete.

A simple approach to analysing EQA exercise results should highlight:

- participating laboratories that reported results that differed from the reference results;
- test methods that produced results that differed from the reference results.

Advanced approaches to analysing EQA exercise results may include:

- investigating the performance of various test methods by grouping the data into subsets based on common test methods;
- investigating the performance of the different reagent lots used by participating laboratories;
- analyses of quantitative results using statistical tools.

Each participating laboratory should receive an individual analysis of its performance for the exercise. The individual laboratory report should clearly highlight any results reported by the participating laboratory that differed from the reference results determined by the EQA programme provider. It is important to remember that only laboratory codes should be used when reporting or assessing the performance of participating laboratories, in order to maintain confidentiality.

When analysing data sets or using statistical tools, it is important to be aware that making comparisons between small numbers of results may not be valid.

5.12 STATISTICAL ANALYSIS OF EQA EXERCISE RESULTS

Quantitative results can be statistically analysed to determine whether any of the participants' results for an exercise material differ significantly. To perform this type of analysis, data must be divided into like groups so that the data set analysed contains only results that were generated from the same test method (peer group). It is necessary to remove statistically outlying results that can skew the calculation of the average and standard deviation of a data set. Statistical methods for identifying outlying results include Grubbs' test and Tukey's filter.⁹

The summary statistics of the data set describing the mean, standard deviation and coefficient of variation can then be determined. This information provides the "target" values and allows a participating laboratory to compare its performance with that of the other participating laboratories using the same test method. EQA programme providers should consider that when the number of results in a data set is less than five the statistical profile generated may not provide an accurate representation of the results expected for the sample on that test method. Therefore, for small data sets, reporting a statistical profile is not useful or appropriate.

Robust statistics are also commonly used for analysing EQA peer group results and are recommended by ISO 13528:2005, *Statistical methods for use in proficiency testing by interlaboratory comparisons*.

⁹ Barnett V, Lewis T. *Outliers in statistical data*, 3rd edition. Wiley; 1994. Tukey's filter: <http://www.statisticshowto.com/tukey-iqr-test/>.

5.13 PREPARATION OF EQA REPORTS

The outcomes of the analysis of results submitted for the exercise should be documented in a report that is made available to all of the participating laboratories. To maintain confidentiality of the participating laboratories, only identification codes should be used within the report. In this way information about the overall quality of testing among the participating laboratories can be communicated without breaching confidentiality.

A short turnaround time for providing the EQA exercise report to the participating laboratories is a priority. An EQA exercise captures a snapshot of each participating laboratory's performance at a particular point in time. Prompt feedback allows participating laboratories to investigate and take necessary corrective action on any identified deficiency whilst the problem is still relevant for the laboratory. Delays in feedback about performance may reduce the value of extensive analysis of the results performed. In situations where prompt feedback is unachievable for the EQA programme provider, an alternative procedure of sending out a preliminary report soon after the exercise closure, followed by the exercise report at a later date, may be acceptable to the participating laboratories.

5.14 PRELIMINARY REPORT

The preliminary report is a summary of the composition of the materials in the EQA exercise. It does not contain any analyses of results, and hence can be prepared in advance. A preliminary report should contain:

- the EQA exercise name, date and code;
- characterization test results;
- the reference results assigned to each exercise material.

The information in the preliminary report allows participating laboratories to promptly review their performance in the exercise and implement corrective action if necessary.

5.15 FINAL REPORT

The EQA exercise report should contain the following information:

- the name and contact information for the EQA programme provider;
- the name and code of the EQA exercise;
- a description of the materials provided in the EQA exercise, including production methods and details of how the reference results were obtained;
- the characterization test results for each exercise material;
- the aims of the EQA exercise;
- a description of the data analysis methods used;
- the number of participating laboratories in the exercise;
- individual assessment of participating laboratory results, highlighting those that differed from the reference results.

In addition, the following information can enhance the value of the EQA programme:

- a summary of the results reported for each exercise material by test method used;
- systematic problems relating to a specific test method or reagent lot number used by participating laboratories;
- advice to participating laboratories on how to troubleshoot laboratory errors;
- general comments and discussion on the results submitted for the exercise.

Care needs to be taken to make the EQA exercise report clear and informative. Developing a template that forms the basis of the report ensures consistency of the information delivered for each exercise and increases the efficiency of the report writing process. Comments and recommendations made by the EQA programme provider about the results submitted for an exercise should be non-judgemental, constructive and evidence based. The report of the EQA exercise can provide advice and suggestions for preventive action when reasons for error are able to be deduced. Depending on the type, frequency and severity of errors detected in EQA exercises, the programme provider may choose to offer additional action to assist a participating laboratory to rectify its testing processes (see section 6). Examples of a preliminary report and analyses that can be included in the final EQA exercise report are included in Annex 8.

5.16 CERTIFICATES OF PARTICIPATION

Participation in EQA programmes is an important element of a laboratory's quality management system. As such, laboratories may be required to demonstrate evidence of such participation and their performance. Although EQA reports and demonstration of corrective action following identified errors in EQA are the best evidence, many participating laboratories may also request a certificate of participation.

The issue of an annual certificate of participation, detailing the number of exercises undertaken, can be a positive means of encouraging continued participation.

Certificates of participation may be issued in a number of ways. For example, certificates may be issued after each EQA programme exercise or yearly. The EQA provider will need to define what constitutes "participation". Certificates may be granted for participation in EQA, regardless of performance, or may be granted based on meeting minimum levels of performance. In either case, the EQA programme provider should predefine minimum levels of participation or performance and communicate these requirements to the participating laboratories.

6

Monitoring laboratory performance, feedback and education

Performance monitoring involves setting standards of acceptable performance and identifying participating laboratories that fail to reach these standards. The EQA programme's objective in identifying unsatisfactory performance is to offer advice and support to assist these laboratories in improving their performance.

The need for monitoring of the performance of individual laboratories – and the initiation of appropriate corrective and preventive action in cases of persistent unsatisfactory performance – will be determined by the place of EQA within the existing national quality system.

6.1 SETTING STANDARDS OF ACCEPTABLE PERFORMANCE

The first step in performance monitoring is to define standards of satisfactory, unsatisfactory and, possibly, “borderline” performance. The potential clinical significance of errors must be considered when defining standards of acceptable performance. When establishing an EQA programme, it is therefore advisable to operate the programme for a defined period, such as one year, with initial follow-up of errors as described below, but with no formal performance monitoring or scoring. During this time, information can be gathered on current levels of performance within each category of testing, such as rapid or test kit performance for TTI. This process will allow realistically achievable standards of acceptable performance to be set whilst ensuring that major errors, such as a false negative TTI result, are defined as unsatisfactory.

For performance monitoring, there should be no differentiation between incorrect results due to technical or procedural errors (such as the incorrect transcription of results or the transposition of exercise materials), although they may be analysed and reported separately. An incorrect result in the blood transfusion laboratory or hospital blood bank can have the same serious consequences, regardless of the reason for the error. For this reason, it is advisable to base performance monitoring – and numerical scoring, if used – on interpretations made rather than on serological reactions recorded for each test. Along with incorrect results, non-return or late return of results also constitutes unsatisfactory performance.

Performance standards should be agreed independently by the advisory committee, which includes representatives of participating laboratories

and experts in the field. The advisory committee should also be responsible for regularly reviewing the definitions of unsatisfactory performance and making changes, where necessary, to reflect improvements in overall performance.

6.2 NUMERICAL SCORING SYSTEMS FOR PERFORMANCE MONITORING

Scoring systems can be developed to allow the performance of individual laboratories to be monitored. While such scoring systems can objectively show what progress is being achieved, scoring can have the disadvantage of causing laboratories to collude or “cheat” for fear of obtaining an inadequate score. Such behaviour severely limits the value of EQA programme participation. Therefore it is important for the EQA programme provider to emphasize, to participating laboratory staff, their supervisors and their heads, the importance of non-punitive approaches to EQA performance.

A scoring system using penalty points is easiest to weight for clinical significance and to use for the identification of unsatisfactory performance on a cumulative basis. Scoring can be “weighted” to reflect the potential clinical significance of errors made. The scoring system should be determined up front and communicated to participating laboratories as part of the EQA programme information manual.

Cumulative scores can be used to identify persistent unsatisfactory performance as well as laboratories with “borderline” performance. Once the system is established, cumulative scores should be given with each exercise report. If this is not possible, cumulative scores can be provided for each laboratory in an annual summary to show trends in individual performance.

Examples of numerical scoring systems for performance monitoring are included as Annex 9.

6.3 FOLLOW-UP OF UNSATISFACTORY PERFORMANCE

Any follow-up actions by the EQA programme should comply with the procedures laid down by the advisory committee. While it is the role of an EQA programme to perform follow-up actions, the extent of these interventions should be documented and consistent with the resources available to the EQA programme provider. For example, an initial contact could be made by the EQA provider to determine possible causes of error and offer advice.

If the EQA programme provider’s interventions yield no subsequent improvement in performance, a letter should be sent to the head of the laboratory to report the situation, formalize the advice that has been offered and suggest possible solutions. Procedures should be put in place to ensure that, once a laboratory becomes an unsatisfactory performer, its progress is then monitored until consistent satisfactory performance is achieved. Programme personnel should be non-judgemental and constructive regarding unsatisfactory performance. Any advice offered should be evidence based and in line with national standards or guidelines, where these exist.

Examples of severe errors include false negative results for any markers or multiple false positive results, failure to identify an intentional clerical error or sample mix-up. Options for ongoing assistance may include:

- providing specific, long-term and recurrent advice on improvement opportunities;
- providing additional EQA exercise material for troubleshooting;
- providing hands-on laboratory training;
- facilitating a supervisory visit or audit at the participating laboratory to identify deficiencies, including communication with the laboratory's head.

The programme provider's ability to undertake these activities will depend on the resources allocated to them. The advisory committee should advocate strongly that these resources be provided, as the benefit of participation in EQA can be maximized only when these support activities are available.

On an annual basis, a longitudinal review of performance of participating laboratories should be conducted. This will ensure that any participating laboratory with consistent problems from one EQA exercise to another is followed up adequately. To help monitor the performance of participating laboratories, the EQA programme provider may choose to keep a log of performance of participating laboratories in a logbook or spreadsheet for ease of review.

6.4 SELF-ASSESSMENT

In the absence of any performance monitoring or follow-up by the EQA programme, a comparison of an individual laboratory's results with those obtained by other laboratories is a useful means of highlighting the need for improvement. This process can often raise standards with no intervention from an external source.

6.5 EDUCATION

The main purpose of an EQA programme is to improve performance and to provide assistance to address any problems detected. Education should therefore be inherent in all activities of an EQA programme. It can be provided to laboratories on an individual basis as well as to all participating laboratories and other relevant professionals.

The programme has a particularly important educational role regarding errors made in EQA exercises by individual participating laboratories. When resources are available, EQA programme personnel can help laboratories identify the root causes of errors and make suggestions for changes in practice and procedures to prevent their recurrence. Errors in EQA exercises may be due to specific technical issues; however, apparently simple errors, such as transcription errors resulting in the recording of an incorrect TTI result, can be indicative of wider problems and deficiencies in a laboratory's quality system.

Education can be provided more widely in the form of reports on the overall performance of different techniques and technologies, which provide specific learning points on best practice. Once a programme is

well established it may also be possible, with the help of the advisory committee, to organize an annual scientific meeting or a workshop for participating laboratories to address issues highlighted by the EQA exercises.

The programme provider should, where possible, communicate information generated by the programme not only to participants but also to a wider audience, by making presentations at local, national and international meetings and through publications. EQA programme data can also be used as a basis for the writing and review of guidelines, making education accessible to all those working in the field of blood transfusion.

7

Monitoring and evaluating an EQA programme

For an EQA programme to progress, it is important to monitor its development and evaluate its impact on a regular basis. This evaluation will also provide objective evidence in support of the programme's continuation and be crucial for its sustainability. Evaluation should be undertaken at least once a year and a report produced.

7.1 INDICATORS

Process and outcome indicators that could be used to assess the success of a programme are listed below. It should be recognized, however, that an improvement in relation to outcome indicators could be influenced by factors not directly related to participation in an EQA programme, such as the introduction of improved reagents or technology.

Process and output indicators

Examples of process and output indicators to be collected annually include:

- frequency of advisory committee meetings and attendance;
- proportion of participating laboratories;
- proportion of laboratories returning results for each exercise – late and not at all;
- number of laboratories registering for assessment of results on additional tests;
- number of problems recorded in relation to the operation of the programme;
- number of complaints received and resolved regarding the operation of the programme;
- number of times exercise material fails to meet documented requirements;
- positive feedback from participants;
- troubleshooting and educational activities undertaken;
- publications or presentations by the programme.

Outcome indicators

Examples of outcome indicators include:

- proportion of satisfactory and unsatisfactory performance;

- change in overall scores, if applicable;
- trends in performance with the same material over several exercises;
- improvement or changes in testing used by participating laboratories;
- participating laboratories receiving accreditation.

7.2 IMPACT

By analysing outcomes, the impacts that the programme has over a period of time can be determined. For example, the proportion of satisfactory versus unsatisfactory performance or the change in overall scores can infer the reduction in erroneous results on donor specimens obtained and therefore the minimization of transmission risk; the improvement in testing practices can be translated into savings in costs and in technologist time. When stakeholders and those providing the funding for the programme learn of these impacts, continued funding of the programme becomes simple to justify.

7.3 ANNUAL REPORT

An annual report on the programme should be compiled and distributed to stakeholders, including ministry of health, advisory committee and other interested parties, such as participating laboratories. Its contents may include:

- summary of the exercises distributed;
- summary of overall performance, highlighting any trends;
- summary of process indicators;
- learning points from the exercises;
- details of developments and challenges within the programme;
- overall assessment of the impact of the programme;
- human and financial resources, if appropriate and applicable.

Glossary

This glossary has been prepared using definitions included in ISO 9000:2006, *Quality management systems: fundamentals and vocabulary*, or ISO 15189:2013, *Medical laboratories: requirements for quality and competence*. Where definitions were available in these standards, the document reference has been provided. Definitions in *italics* are intended to define the use of the relevant word or phrases within this document and how the terms relate to each other.

Accreditation

Procedure by which an authoritative body gives formal recognition that an organization is competent to carry out specific tasks (ISO 15189:2013).

Audit

Systematic, independent and documented process for obtaining evidence and evaluating it objectively to determine the extent to which audit criteria are fulfilled (ISO 9000:2006).

Competence

Demonstrated ability to apply knowledge and skills (ISO 9000:2006).

Competency assessment

Process to assess an individual's ability to apply knowledge and skills.

Documentation

Written policies, instructions and records involved in providing a product or service.

Effectiveness

Extent to which planned activities are realized and planned results achieved (ISO 9000:2006).

Exercise materials

Materials that have been prepared from samples and that make up an EQA panel.

External quality assessment (EQA)

The external assessment of a laboratory's performance using exercise materials of known, but undisclosed, content and comparison with the performance of other laboratories.

External quality assessment programme

A formal programme organized by a recognized institution. This can be a local programme or organized at national, regional or international level.

Haemovigilance

The monitoring, reporting and investigating of adverse incidents related to all blood transfusion activities.

Internal quality control

Procedures that verify the attainment of the intended quality of results (ISO 15189:2013). These may include procedures to monitor the day-to-day reproducibility of test results and detect major errors in the analytical process.

Management system

System to establish a quality policy and quality objectives and to achieve those objectives (ISO 9000:2006).

Marker

Specific characteristics of exercise materials included in the EQA programme, e.g. HIV antibody, HIV antigen, Treponema antibody.

Panel

A set of EQA exercise materials.

Procedure

Specified way to carry out an activity or a process (ISO 9000:2006).

Process

Set of interrelated or interacting activities that transform inputs into outputs (ISO 9000:2006).

Quality

The degree to which a set of inherent characteristics fulfils requirements (ISO 9000:2006).

Quality management

Coordinated activities to direct and control an organization with regard to quality (ISO 9000:2006).

Sample

A specimen, preferably of large volume, that has been processed, tested, and stored in a sample bank for potential use as exercise material.

Specimen

Discrete portion of a body fluid, breath, hair or tissue taken for examination, study or analysis of one or more quantities or properties assumed to apply for the whole (ISO 15189:2013).

Standard operating procedure

Specified way to carry out an activity or a process that is documented, implemented and maintained (ISO 15189:2013).

Test

Determination of one or more characteristics according to a procedure (ISO 9000:2006).

Validation

Confirmation through the provision of objective evidence that the requirements for a specific intended use or application have been fulfilled (ISO 9000:2006).

Annexes

The following annexes are provided for information and as examples on which prospective EQA programme providers may wish to base their documentation and other aspects of the design of their programme, with appropriate local modifications.

1. Preliminary questionnaire for potential participating laboratories
 2. EQA registration form
 3. Exercise instruction sheet
 4. Exercise results form
 5. Protocol for homogeneity testing of exercise material
 6. Protocol for stability testing of exercise material
 7. Record of exercise distributions and returned results
 8. Exercise analysis and report
 9. Numerical scoring systems
-

Annex 1

Preliminary questionnaire for participating laboratories

External quality assessment programme for TTI screening of donated blood

Please complete this questionnaire regarding transfusion-transmissible infections screening and general quality measures in your laboratory.

Part 1. Contact details

Institution name: _____

Contact name: _____

Department: _____

Address: _____

Telephone: _____

Facsimile: _____

Email address: _____

Part 2. Laboratory information

1. Number of staff:

2. Number of specimens processed per year from:

Blood donors

Others (please specify)

3. Please indicate the TTI screening performed in your laboratory and the test method(s) used

	Mandatory screening*						
	HIV	HCV	HBV	Syphilis	Chagas	HTLV I/II	Malaria
The TTI screened in your laboratory	<input type="checkbox"/>						
The TTI for which your laboratory would like an EQA programme	<input type="checkbox"/>						

* Screening as mandated by the country

Annex 2

EQA registration form

Institution name: _____

Contact name: _____

Department: _____

Postal address: _____

Shipping address: _____

Telephone: _____

Facsimile: _____

Email address: _____

Additional contact for receiving report if required _____

Email address: _____

Please indicate the EQA programmes in which your laboratory would like to enrol. Each exercise includes five exercise materials. Participation in two exercises each year is considered the minimum acceptable.

Exercise number	HIV	HCV	HBV	Syphilis	Chagas	HTLV I/II	Malaria
1	<input type="checkbox"/>						
2	<input type="checkbox"/>						
3	<input type="checkbox"/>						

Annex 3

Exercise instruction sheet

Intended use

This is a coded panel of exercise materials each with known reactivity for: [insert markers included in the panel for assessment]. It is intended to be used for the assessment of the performance of laboratories undertaking routine TTI screening of blood donations.

Materials provided

- X (insert number) vials of serum exercise materials of Y [insert volume] labelled: 1A, 1B, ...
- Result sheets

Instructions for storage, handling and testing of exercise materials

- Vortex, then centrifuge all exercise materials prior to testing.
- Process the exercise materials alongside routine donor specimens and in the same way as they would usually be processed by your laboratory.
- **Warning:** The exercise materials are potentially infectious and should be handled using universal safety precautions.
- Materials are to be stored at 2–8°C for the duration of the exercise.

Instructions for testing of exercise materials

- Test the exercise materials in the same way as routine donor specimens would normally be tested, using the testing strategy in use in your laboratory.

Instructions for completing the results form

- Please tick the relevant box where you have been given a choice of response.
- Report only the results of one test kit on each page. Photocopy the relevant page(s) for additional results.
- Definitions of abbreviations used in the form: (*example*)
 - R: Reactive
 - N: Negative
 - INC: Inconclusive

Instructions for returning the results

- Ensure the return of the results before closing date.

Annex 4

Exercise results form

Exercise identification code: 01/04 (example)

Laboratory registration code: _____

Contact name: _____

Institution name: _____

Telephone number: _____

Email: _____

Date on which your laboratory received the panel: _____

Were the materials received in good condition? Yes No

Comments: _____

(If panels were received in an unsatisfactory condition, replacement panels can be obtained by contacting the EQA programme provider on the details listed below).

The closing date for exercise 01/04 is DD/MM/YYYY

Please return completed results forms to [insert EQA provider's details]:

EQA programme provider: _____

EQA contact name: _____

Address: _____

Telephone: _____

Facsimile: _____

Email: _____

EXERCISE RESULTS FORM: EIA

Exercise 01/04	Laboratory registration code: _____										
Test kit name: _____											
1st run											
Operator: _____											
Date of testing: _____ Kit lot number: _____ Kit expiry date: _____											
2nd run											
Operator: _____											
Date of testing: _____ Kit lot number: _____ Kit expiry date: _____											
Supervisor: _____											
Results											
Exercise material ID	S/Co ratio (1st run)			S/Co ratios (2nd run)					Test kit interpretation		
	OD (A)	Cut-off (B)	S/Co (A÷B)	OD (A)		Cut-off (B)	S/Co (A÷B)				
				Rep 1	Rep 2		Rep 1	Rep 2			
1A									<input type="checkbox"/> R	<input type="checkbox"/> N	<input type="checkbox"/> INC
1B									<input type="checkbox"/> R	<input type="checkbox"/> N	<input type="checkbox"/> INC
...									<input type="checkbox"/> R	<input type="checkbox"/> N	<input type="checkbox"/> INC
...									<input type="checkbox"/> R	<input type="checkbox"/> N	<input type="checkbox"/> INC
1X									<input type="checkbox"/> R	<input type="checkbox"/> N	<input type="checkbox"/> INC
Comments: _____											
Name of operator reporting results: _____											

EXERCISE RESULTS FORM: RAPID TEST

Programme name / ID: _____

Participant ID: _____

Test kit lot number: _____

Test kit expiry date: _____

Operator initials: _____

Exercise material ID	Test date	First reader				Second reader				Final result interpretation ^c
		Reader ID ^a	Ab bar / spot ^b	Ag bar / spot ^b	Control bar / spot ^b	Reader ID ^c	Ab bar / spot ^b	Ag bar / spot ^b	Control bar / spot ^b	

^a Initials.

^b Neg, Pos, Not Applicable (N/A).

^c Negative, Reactive, Invalid.

Annex 5

Protocol for homogeneity testing of exercise material

- *Example:* Panel composition of exercise panel ID: 01/04 contains 5 exercise materials labelled 1A, 1B, 1C, 1D and 1E.
- 80 vials of each exercise material were produced and aliquoted during production.
- 10 representative vials of each EQA exercise material (refer section) are selected for homogeneity testing.
- Using a random number generator, record the 10 vial numbers selected for homogeneity testing (e.g. vials 15, 25, 31, 47, 58, 66, 70, 80, 12, 22).
- The same vial numbers are to be set aside for each exercise material.
- The selected vials need to be renumbered with new homogeneity codes to ensure traceability during testing (e.g. 1A:H1, 1A:H2 1A:H10, etc.)
- Store vials for homogeneity testing at 2–8°C until the testing is performed.
- Test each vial once on the appropriate test kit in the same test run.
- Any exercise material found to have a result that is different from the reference result must be retested in duplicate. The final test interpretation for this exercise material will be based on the consensus of the three test results. Record results in the appropriate form (see following table).
- Before disposal, store the homogeneity vials at 2–8°C until homogeneity results are reviewed and accepted by the EQA programme provider.
- **Acceptance criteria:** An exercise material shall be accepted for inclusion in a panel if all of the test result interpretations for each vial agree with the reference result.

EXAMPLE: HOMOGENEITY TESTING RESULTS FOR EXERCISE PANEL ID: 01/04

Exercise material:	1A	1B	1C	1D	1E
Reference: result	Reactive	Negative	Negative	Reactive	Reactive
H1	Reactive	Negative	Negative	Reactive	Reactive
H2	Reactive	Negative	Negative	Reactive	Reactive
H3	Reactive	Negative	Negative	Reactive	Reactive
H4	Reactive	Negative	Negative	Reactive	Reactive
H5	Reactive	Negative	Negative	Negative*	Reactive
H6	Reactive	Negative	Negative	Reactive	Reactive
H7	Reactive	Negative	Negative	Reactive	Reactive
H8	Reactive	Negative	Negative	Reactive	Reactive
Acceptance:	Pass	Pass	Pass	Fail*	Pass

* Repeat testing required in duplicate. The final test interpretation for this exercise material will be based on the consensus of the three test results.

Annex 6

Protocol for stability testing of exercise material

- *Example:* Panel composition of exercise panel 01/04 contains 5 exercise materials labelled 1A, 1B, 1C, 1D and 1E.
- 80 vials of each exercise material were produced and aliquoted during production, which included 6 vials of each exercise material to be selected for stability testing.
- The selected vials need to be renumbered with new stability codes to ensure traceability during testing (e.g. 1A:S1, 1A:S2, 1A:S3, 1A:S4, 1A:S5 and 1A:S6).
- Identify the time and temperature conditions that the exercise material will be exposed to for the duration of the exercise.

EXAMPLE: ACTIVITY AND SCHEDULE FOR EXERCISE PANEL ID: EXERCISE MATERIAL 1A 01/04

Activity	Schedule	Exercise material	Storage temperature conditions
Post-production	Day 0		2–8°C
Start of dispatch	Day 4	S1	37°C
End of dispatch	Day 11	S2	37°C
Opening date of exercise	Day 12	S3	2–8°C
Middle date of exercise	Day 25	S4	2–8°C
Closing date of exercise	Day 32	S5	2–8°C
7-day storage after closing date	Day 39	S6	2–8°C

- Store stability vials at 2–8°C for 4 days until exercise panels are dispatched to the participating laboratories. Remove stability vial **1A:S1** on day 4, test on the appropriate test kit for the analyte.
- Move the remaining 5 stability vials to 37°C ± 1°C and store for 7 days.
- Remove stability vial **1A:S2** on day 11, test on the appropriate test kit for the marker.
- Move the remaining 4 stability vials and store at 2–8°C. Test the following vials on the appropriate test kit for the analyte as follows:
 - **1A:S3** on day 18
 - **1A:S4** on day 25
 - **1A:S5** on day 32
 - **1A:S6** on day 39.
- Any exercise material found to have a result that is different from the reference result must be retested in duplicate. The final test interpretation for this exercise material will be based on the consensus of the three test results. Record results in the appropriate form (see below).

- **Acceptance criteria:** Criteria for suitable stability should be based on the effect that instability will have on the uncertainty of the participant's result, and thereby on the evaluation of the acceptability of a participant's results.

EXAMPLE: STABILITY TESTING RESULTS FOR EXERCISE PANEL ID: 01/04

Exercise material:	1A	1B	1C	1D	1E
Reference: result	Reactive	Negative	Negative	Reactive	Reactive
S1	Reactive	Negative	Negative	Reactive	Reactive
S2	Reactive	Negative	Negative	Reactive	Reactive
S3	Reactive	Negative	Negative	Reactive	Reactive
S4	Reactive	Negative	Negative	Reactive	Negative*
S5	Reactive	Negative	Negative	Reactive	Negative*
S6	Reactive	Negative	Negative	Reactive	Negative*
Acceptance:	Stable	Stable	Stable	Stable	Unstable

* Repeat testing required in duplicate. The final test interpretation for this exercise material will be based on the consensus of the three test results.

Annex 7

Record of exercise distributions and returned results

PANEL ID NUMBER:

Laboratory code	Documentation packed	Materials packed	Exercise distributed	Results received	Comment
0001					
0002					
0003					
0004					
0005					
0006					
0007					
0008					
0009					
0010					
0011					
0012					
0013					
0014					
0015					
0016					
0017					
0018					
0019					
0020					
0021					
0022					
0023					
0024					

Annex 8

Exercise analysis and report

PRELIMINARY REPORT

Material ID*	Sample type	Comments	Anti-HIV-1 status	p24 reference result
1	Plasma		Negative	Negative
2	Pooled plasma		Positive	Negative
3	Pooled plasma		Positive	Negative
4	Pooled plasma		Negative	Negative
5	Pooled plasma		Positive	Negative
6	Plasma		Negative	Negative
7	HIV-1 culture supernatant diluted in negative human plasma	The sample contains ~5000 pg/mL of subtype B cell culture supernatant	Negative	Positive
8	Plasma		Negative	Negative
9	Pooled plasma		Positive	Negative
10	Plasma		Negative	Negative

* Identification.

CHARACTERIZATION OF THE SAMPLES THAT COMPRISED ANTI-HIV EQA PANEL ID

Material ID	Murex HIV-1.2.0 Ag/Ab EIA (S/Co ¹)	Bio-Rad Genetic Systems HIV-1 Ag ^{**} EIA (S/Co)	Bio-Rad Genetic Systems HIV-1 Ag confirmatory	HIV-1 western blot							Test result interpretation	Anti HIV-1 status	p24 reference result
				p18	p24	p31	p34	gp41	p53	p68			
1	0.41	0.20	Not tested	Not tested							Not applicable	Negative	Negative
2	14.96	0.24	Not tested	-	++	-	+	++	++	+++	Positive	Positive	Negative
3	15.21	0.21	Not tested	-	+++	-	++	+++	+++	+++	Positive	Positive	Negative
4	0.48	0.25	Not tested	Not tested							Not applicable	Negative	Negative
5	18.82	0.24	Not tested	+++	+++	++	++	+++	+++	+++	Positive	Positive	Negative
6	0.39	0.25	Not tested	Not tested							Not applicable	Negative	Negative
7	0.31	40.66	37.83	Not tested							Not applicable	Negative	Positive
8	0.37	0.26	Not tested	Not tested							Not applicable	Negative	Negative
9	18.57	0.25	Not tested	++	+++	++	++	+++	+++	+++	Positive	Positive	Negative
10	0.41	0.20	Not tested	Not tested							Not applicable	Negative	Negative

* Sample: cut-off ratio, where ≥ 1 is reactive.

** Antigen.

ANALYSES FOR INCLUSION IN FINAL EXERCISE REPORT

Percentage of false negative and false positive results by marker

	False positive	%	False negative	%
Syphilis	0	0	0	0
	TND = 100		TPD = 28	
HIV	10	9.80	0	0
	TND = 102		TPD = 68	
Anti-HTLV-I/II	0	0	0	0
	TND = 56		TPD = 19	
HCV	0	0	0	0
	TND = 85		TPD = 26	
HBsAg	0	0	2	7.1
	TND = 90		TPD = 28	
Total	10	2.2	2	1.1
	TND = 448		TPD = 175	

TND = Total of determinations performed in negative samples.

TPD = Total of determinations performed in positive samples.

Participants' performance by marker

Participant ID	HIV	HBsAg	Syphilis	HCV	anti-HTLV-I/II
1	A	A	A	A	A
2	A	A	A	A	–
3	A	A	A	A	A
4	A	A	A	A	A
5	A	A	A	A	A
6	A	A	A	A	A
7	A	A	A	A	A
8	A	A	A	A	A
9	A	A	A	A	–
10	A	A	A	A	–
11	B ²	A	A	A	A
12	B ²	A	A	A	A
13	B ²	A	A	A	–
14	A	C	A	A	–

A = 100% of concordance.

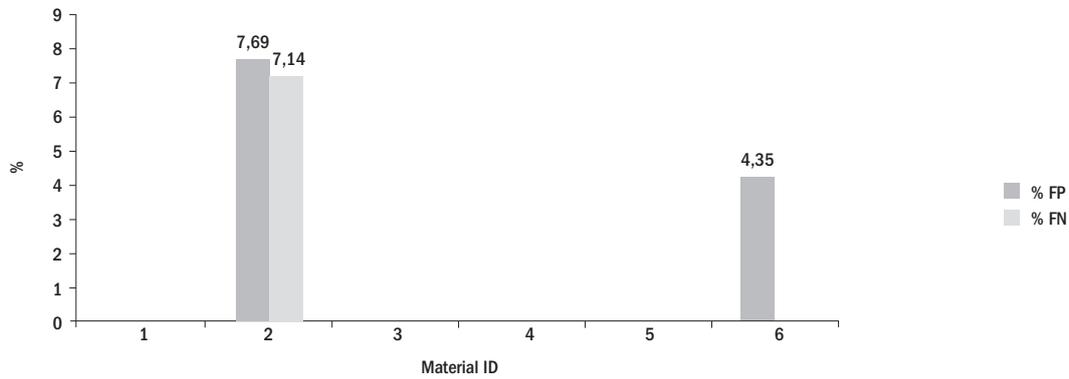
B¹ = False positive result was reported ($\leq 5\%$ of the total of individual participant's determinations).

B² = False positive result was reported ($> 5\%$ of the total of individual participant's determinations).

C = False negative result.

– = Not performed

False positive and false negative results (%) reported for each exercise material



ANALYSIS BY TEST KIT

Example table below shows the number of false results reported for each syphilis test kit used by the participants. Similar tables can be created for the other markers.

Test kits	FPR	%	TND	FNR	%	TPD
Architect syphilis TP	0	0	30	0	0	9
Murex ICE syphilis	0	0	15	0	0	3
Macrovue RPR card	0	0	10	0	0	2
Trepanostika TP recombinante	0	0	10	0	0	5
Total	0	0	65	0	0	19

TND = Total of determinations performed in negative samples.

TPD = Total of determinations performed in positive samples.

FPR = False positive results.

FNR = False negative results.

Annex 9

Numerical scoring systems

SIMPLEST SCORING METHOD EVALUATES ONLY THE FINAL STATUS OF EACH MATERIAL WITH TOTAL SCORE OF 100%

EQA panel ID _____ Year _____						Score
Expected results	Positive	Negative	Negative	Positive	Positive	
Material ID	1	2	3	4	5	
Participant results	Negative	Positive	Negative	Negative	Positive	80%

SCORING METHOD FOR BOTH TEST RESULT AND FINAL INTERPRETATION

EQA panel ID _____ Year _____					
	Participant results				
Material ID (expected results)	Test kit 1	Test kit 2	Test kit 3	Final status	Score
1 (Negative)	Non-reactive	Not done	Not done	Negative	2 of 2* or 20
2 (Positive)	Reactive	Reactive	Non-reactive	Positive	3 of 4 or 15
3 (Positive)	Reactive	Reactive	Reactive	Positive	4 of 4 or 20
4 (Negative)	Reactive	Non-reactive	Non-reactive	Inconclusive	2 of 4 or 10
5 (Positive)	Reactive	Reactive	Reactive	Positive	4 of 4 or 20
Total score					85%

Maximum score = 100 with 20 points allocated to each exercise material. Within each exercise material there are up to four answers required.

* Maximum score allocated: both possible answers correct (test kits 2 and 3 did not require answers for material 1).

SCORING METHOD FOR TEST RESULTS, FINAL INTERPRETATION AND FOLLOWING ALGORITHM

EQA panel ID _____ Year _____						
	Participant results				Score	
Material ID (expected results)	Test kit 1	Test kit2	Test kit3	Final status	Test results (80%)	Test algorithm (20%)
1 (Negative)	Non-reactive	Non-reactive	Non-reactive	Negative	16/16	0/4*
2 (Positive)	Reactive	Reactive	Non-reactive	Positive	12/16	4/4
3 (Positive)	Reactive	Reactive	Reactive	Positive	16/16	4/4
4 (Negative)	Reactive	Non-reactive	Non-reactive	Inconclusive	8/16	4/4
5 (Positive)	Reactive	Reactive	Reactive	Positive	16/16	4/4
Total score					84%	

Maximum score = 100 points with 20 points allocated to each exercise material. Within each exercise material there are up to four answers required worth 4 points each and 4 points awarded if the algorithm was followed.

* No point awarded for following the algorithm because participant continued to test in test kits 2 and 3 despite obtaining a negative result in test kit 1 for material 1.

Confidential performance evaluation by marker: _____

External quality assessment scheme – panel ID: _____

Participant ID: _____

Syphilis	HIV	HTLV	HCV	HBsAg
A	A	A	A	A

Qualification criteria:

A 100% correct results, no false positive and no false negative results.

B¹ False positive result was reported ($\leq 5\%$ of the total of determinations performed by the participant).

B² False positive result was reported ($> 5\%$ of the total of determinations performed by the participant).

C False negative result was reported.

