MEDECINS SANS FRONTIERES

MSF laboratory quality assurance manual

A practical guide for laboratory workers in resource-limited settings

Internal document
2019 edition

MSF laboratory quality assurance manual

A practical guide for laboratory workers in resource-limited settings

Internal document
2019 edition

Author
C. Kamau

Contributors
D. Beels, M. Berti, P. Chaillet, A. Chua (Coordinator), L. Flevaud, D. Gomez, M. Gueguen, S. Guiramand, C. Lastrucci, E. Piriou, E. Tran.

Reviewers
M. Henkens, J. Carter

Design and layout
E. Laissu

Published by
Médecins Sans Frontières

Médecins Sans Frontières. *MSF Laboratory quality assurance manual*. 2019 edition.
Ref. L013LABM14E-P

Foreword

This manual is intended for laboratory technologists and scientists and for the advisors or laboratory referents that support them.

The aim of this manual is to explain the minimum quality control procedures that should be implemented in all MSF supported settings. These procedures are proposed and adapted by the Laboratory Working Group for field use. The Laboratory Working Group aims to continue to explore options on quality assurance that is implementable and feasible in MSF settings. Accompanying this manual are simple and user-friendly tools aimed at making recording, monitoring and analysis of quality control results easier.

The Laboratory Working Group also aims to issue a French edition soon.

The manual is intended to be complimented by the latest editions of the MSF Laboratory Manual and the ITC Medical Catalogue, Volume 5. They are frequently cross referenced in this manual.

Despite all efforts, errors may have been overlooked in this manual. Please inform us of any errors detected. The Laboratory Working Group would also be grateful for any comments to ensure that this manual continues to evolve and remains relevant to the needs of the field.

Please address comments to:

Médecins Sans Frontières
Diagnostic Network
Plantage Middenlaan 14
1018 DD Amsterdam
Netherlands
+31 (0) 20 520 8700
e-mail: diagnostic-network@msf.org

This manual is available as a pdf document through laboratory advisors of each MSF section. Requests can also be made by sending an email to diagnostic-network@msf.org.

Table of contents

Annexes

Abbreviations

ADA	Adenosine deaminase
AFB	Acid fast bacilli
ALT	Alanine Aminotransferase
APU	Amsterdam Procurement Unit
CRP	C reactive protein
CV	Coefficient of variation
EDTA	Ethylenediaminetetraacetic acid
EQA	External Quality Assessment
ESC	European Supply Centers
FEFO	First expired, first out
FIFO	First in, first out
HB	Haemoglobin
HCT	Haematocrit
HIV	Human Immunodeficiency Virus
HRC	Highly Regulated Country
IATA	International Air Travel Association
IQC	Internal Quality Control
ITC	International Technical Coordination
IV	Intravenous
IVD	In Vitro Diagnostics
LJ	Levey-Jennings
LQAS	Lot Quality Assurance Sampling
LWG	Laboratory Working Group
MCH	Mean Corpuscular Haemoglobin
MCHC	Mean Corpuscular Haemoglobin Concentration
MCV	Mean Corpuscular Volume
MoH	Ministry of Health
MPV	Mean Platelet Volume
NTP	National Tuberculosis Programme
OC	Operational Centre
OCV	Optimal value (Levey Jennings chart)

OPD	Out Patient Department
PDW	Platelet Distribution Width
P-LCR	Platelet- Large Cell Ratio
PLT	Platelet
POC	Point of Care
QA	Quality Assurance
QC	Quality Control
QI	Quality improvement
RBC	Red Blood Cell
RCW	Red Blood Cell Distribution Width
RDT	Rapid Diagnostic Test
RDW-CV	Red cell Distribution Width -Coefficient of Variation
RDW-SD	Red cell Distribution Width -Standard Deviation
RPR	Rapid plasma reagin
SI	Système International d'Unités
TB	Tuberculosis
TSH	Thyroid stimulating hormone
SOP	Standard operating procedure
WBC	White Blood Cell
WHO	World Health Organization

Definitions

Accuracy refers to the closeness of an obtained test result to the target or true value.

Assayed controls are control materials of known value.

Bias is the deviation of the measured value from the target or true value.

Clinician is the health professional who performs the patient evaluation, requests the laboratory tests and interprets the test results for diagnosis, follow-up and monitoring of patients.

Desiccant refers to a substance that absorbs humidity from the air and is used as a drying agent.

External quality assessment refers to a system where the sample material sent by an external body to objectively assess the laboratory's performance. This is achieved as part of a proficiency testing programme or laboratory assessment scheme.

Internal quality control refers to the sample material of known value that assesses the day-to-day performance of the laboratory test system and allows the laboratory to take corrective action immediately avoiding the release of incorrect results.

Laboratory advisor or referent refers to the laboratory personnel based at the operational centre headquarters and who oversees the strategic vision for and implementation of laboratory activities within their respective operational centre.

Panic values are values outside the reference range that require immediate action by the clinician.

Precision refers to the reproducibility of a test result or the extent to which the results agree with one another.

Proficiency testing is a form of quality assessment using samples of undisclosed value provided to the laboratory by an external organising body. The results achieved by the laboratory for each sample are then compared with the target value set by the reference laboratory or the results from other laboratories. This aims to determine the accuracy of the tests conducted in the laboratory and to compare (benchmark) the performance of laboratories against each other.

Laboratory Quality assurance is the combination of measures taken to ensure the reliability and relevance of laboratory results, from the collection of the specimen to the delivery of the report to the clinician.

Quality control is an element of quality assurance intended to ensure that consistent, reproducible results are achieved on a day-to-day basis.

Quantitative tests are tests that provide a result with a number or value.

Qualitative tests are tests that provide results often reported as ‘positive’ or ‘negative’, without a value or number.

Quarantine as used in the context of laboratory instruments refers to the state of isolation of items before a decision is made about its actual use or destruction.

Rejection criteria are a set of rules that state which samples will not be accepted into the laboratory for further processing and testing.

Un assayed controls refer to control material whose value is unknown.

1. Introduction to laboratory quality assurance

Quality assurance includes all the laboratory processes that ensure the results given to a patient are reliable and can be acted on with confidence. Quality assurance is defined by how well each function of that testing chain works, from test selection to sample collection, testing and test result issuance, and results interpretation.

Objectives of quality assurance

The primary objective of quality assurance is to ensure that the patient's results reflect their true state. The confidence placed on the reliability of laboratory test results will have a positive effect on the care of patients and their safety.
The secondary objectives of quality assurance are to evaluate achievement of a laboratory, to formulate a plan for quality improvement and to comply with country regulations.

Principles of quality assurance

All quality assurance programmes should abide by the following principles:

- Quality is patient focused. Patients are the ultimate reason for quality assurance and all activities should be geared toward the benefit of the patient.
- Quality involves the individuals performing the diagnostic tasks as well as the managers and leaders of the laboratory. This ensures that all aspects are considered when designing a quality assurance programme, making it easier to achieve the desired objectives.
- Decisions are made based on facts and not anecdotes or opinions. This means that before any changes are implemented, data are reviewed and support the need for change.

Components of quality assurance

There are many components of quality assurance but in this manual, we will consider only the following aspects:

2. Test selection

2.1 Choosing which tests to implement

When setting up a new project, the medical team can refer to the MSF Diagnostic Packages (2017) [see Annex 1] to guide the selection of diagnostic tools recommended for project implementation.

The **basic or minimum recommendations** for diagnostic tests in the MSF diagnostic packages imply that these tools should always be made available for each specified programme. The **recommended or medium** and **desirable or ideal** recommendations allow for flexibility and are dependent on programme objectives and other considerations such as the nature of programme, staff capacity to perform the tests, capacity of the clinical team to request and interpret the tests appropriately, and infrastructure of the laboratory to support the activities required by the tests. The decision on whether to implement the **recommended or medium** or **desirable or ideal** laboratory capacity should be made together with the medical team, medical coordinator, and health advisor/polyvalent and the laboratory referent/advisor.

It is assumed that the staff carrying out diagnostic testing (including test interpretation and quality control) are trained and supervised on a regular basis. The development of this training and supervision capacity must be planned for each new project.

2.2 Choosing appropriate tests

The selection process of diagnostic tests and test kits consists of clearly defining the most suitable equipment and supplies for a given situation. It focuses on several factors including 1. a market review based on the operational needs in MSF field conditions 2. the assessment of the safety and performance of the test as claimed by the manufacturer and as published in independent studies.

This is done at MSF headquarters level. Based on operational field priorities and in consultation with other medical working groups, the Laboratory Working Group (LWG) defines the end-user (patient and healthcare workers) needs. The LWG oversees the market review, the assessment of the test performance through manufacturer data and literature review, the product desk assessment and the need for field testing. The product quality assessment is performed by the MSF Quality Assurance (QA) network, which is composed of the international QA coordinator for Medical Devices and In Vitro Diagnostics (IVD) and the MSF European Supply Center (ESC) QA referents.

From QA standpoint, MSF favours the sourcing of diagnostics tests that are (in order of preference):
1. WHO prequalified
2. Cleared in Highly Regulated Countries[a] (HRC), i.e. CE marked according to 98/79/EC European Directives for IVD and/or US FDA cleared

For non-WHO prequalified products, the stringency of MSF assessment depends on the product classification according to the European legislation and its relevance to MSF contexts. In some cases, the risk classification defined in highly regulated country (HRC) does not correspond to

a The International Medical Device Regulators Forum (IMDRF, previously Global Harmonization Task Force (GHTF)) founding countries: USA, Canada, Japan, Australia, EU, EFTA (Norway, Iceland, Liechtenstein and Switzerland). Current members also include Brazil, China and Russia. However, for the purpose of MSF QA policy Brazil, China, Russia and Turkey are not considered as HRCs.

MSF's reality of use. For example, the syphilis rapid diagnostic test is classified by HRCs in the least stringent / lowest risk category and permits product self-certification by manufacturers. In contrast, the quality and the performance of this product is crucial to the quality of care in the countries where MSF operates and will require more than a self-certification by manufacturers.

In the case where no WHO prequalified or cleared product corresponding to MSF specific needs is available, MSF conducts on site audits of the manufacturer which is led by external auditors with ISO 13485 as a reference. These audits are focused on assessing the product's performance in view of MSF's conditions of use and based on manufacturer's validation data.

Once the full product assessment is completed, the introduction of new tests or changes on existing tests in the MSF catalogues done by the International Technical Coordination (ITC) are submitted to the medical directors for approval. The product can be approved, rejected or exceptionally approved by the medical directors based on a risk/benefit analysis based on the LWG recommendations on performance and clinical relevance, the outcome of the QA assessment and available product alternatives.

Once approved by the medical directors, the test is added as a standard item in the relevant MSF catalogue so that field personnel can order it. The catalogues are updated on a yearly basis by the ITC. The standardization process is essential for harmonizing supplies used in the field. Each item in the ITC catalogues is described in a technical sheet comprising a definition, a list of components, technical specifications, basic instructions for use, precautions for use, storage and waste management recommendations. Having a standard list of diagnostic tests enables smoother management, simplification of ordering and a decrease in overall costs. It also allows for continuity in the approach when staff changes and simplifies training.

Please make sure you can access the latest version of the MSF catalogue either online by logging in the MSF intranet or by ordering a copy by international order. The codes are listed below:

- [L045CATM05EFP] Medical catalogue, vol. 5, laboratory, En/Fr, A4
- [L045CATM06EFP] Medical catalogue, vol. 6, TB diagnostics, En/Fr, A4
- [L045CATM08EFP] Medical catalogue, vol.8, Bacteriology laboratory, En/Fr, A4

Any item that is not in the ITC catalogue is considered a non-standard item for MSF. The ordering of these items is a separate process under each OC and will not be described here.

3. Quality complaint reporting

As part of post-market surveillance, MSF has implemented a vigilance system requiring that any problems experienced while using a test kit and other laboratory material in the field be reported to the respective laboratory advisor who will start the investigation on the nature of the problem and the possible root cause. When enough information is available, the case is referred to the QA MD referent for notification to the manufacturer. This workflow may differ among sections and the ESC QA referent or the section pharmacist may be the first one to be notified. Depending on the extent of the problem, different actions may be taken. The LWG is consulted in cases when more than one OC is impacted. The possible actions include: batch recall, quarantine, restriction of use or good practices reminder. This system also enables detection of product misuse and monitoring of proper application of MSF standard protocols, while providing continuous feedback to manufacturers on product quality.

Alternatively, the project might also be informed about batch recalls or field safety notices issued by manufacturers and be required to proceed according to the laboratory advisors' and ESC QA referents' instructions.

The same process applies when tests and supplies are bought locally in the country of use and not ordered through MSF European supply centres.

3.1 Procedure for reporting quality complaint

- Fill in the MSF medical quality complaint form [see Annex 2] together with the person responsible for the supply in the project. This could be a pharmacist, a logistician or a nurse. Give as much detail as possible in the quality complaint form and if possible include pictures of the problem.
- Forward the form to your laboratory advisor, the ESC QA referent or the section pharmacist depending on your internal procedure.
- Make a copy of this form and archive in the laboratory incident book or file.
- Inform the clinical team if the service delivery will be affected. This depends on the nature of the problem.
- Keep the diagnostic test or tool in quarantine while waiting for further instructions from your respective laboratory advisor or the ESC QA referent.
- Implement the recommendations.
- Record the entire incident in the laboratory incident book.

4. Supply management

4.1 Order Management

Ordering and maintaining adequate quantities of reagents and consumables to run a quality laboratory service is an essential aspect of quality assurance.

4.1.1 Calculating consumption

Ordering of laboratory supplies depends on the current consumption, expected workload of the laboratory, frequency of ordering, source or sources of supply, and timing of shipment or delivery (delay between ordering and receiving of the item) and overstock. All staff must keep stock records accurately so that the laboratory does not reach a situation of critical shortages of reagents or consumable items. Staff must be responsible for alerting the laboratory manager when stocks reach the level for re-ordering.

- Keep a record of which items have been ordered and received and keep track of usage over time. This is important for reagent kits and internal quality control (IQC) reagents, which may have variable shelf lives, and for preparing orders in the future.
- Historical laboratory statistics give a good picture of requirements for monthly consumption and should be used together with a forecast of medical activities to determine re-order quantities.
- Stock levels should be reviewed regularly by performing stock counts every 1-3 months, and orders placed according to the normal ordering pattern for a particular mission or operational section.
- Systems must be in place to ensure that the stock is used on a ‘first expired, first out’ (FEFO) basis.
- A stock system can be as simple as cards kept in a file box in the storage areas. Each time a consumable or reagent is withdrawn from the stock, the card is updated and signed. Store stock cards alphabetically or by ITC code or in another logical way, such as by department. Use standard MSF stock cards [ALSTSCAR4W-] specific for recording laboratory stock [see Annex 3].
- Computer records can also be kept, provided they are updated regularly and are securely backed-up.
- Before opening any reagent or kit for the first time, check the expiry dates of different lots available at project level, and adopt the” first expired first out” (FEFO) principle to avoid expiry of items. Once the box or vial is opened, mark the opening date on it. Do not use any reagents or kits beyond the expiry date.
- Conduct monthly meetings with the person in charge of supply to review laboratory stock against consumption to avoid overstocks and expiry of items.
- Participate in project stock counts at the medical warehouse. Laboratory personnel are often needed to help point out specific laboratory items that warehouse staff are unable to identify. If laboratory personnel are not present during the inventory and stock taking, there is a risk that laboratory items may be mislabelled and misplaced in a corner where they run the risk of not being used.
- Donation of laboratory items and reallocation to another MSF project. The laboratory supervisor is responsible for monitoring the stock and the expiry dates of laboratory tests, kits and reagents. In case of over-stocking, a donation list should be prepared and communicated to the medical coordinator, who will coordinate the donation. The most important things when looking at donation (within MSF or outside of MSF) is to guarantee that the receiving structure will be able to use all the stock until the expiry date. Donate only what is going to be used by the third party until the expiry date.

- Most projects work on bi-weekly or monthly orders which means that the laboratory has to store a significant amount of test kits for a prolonged period. If the laboratory cannot accommodate the storage requirements, discuss with the person in charge of supplies in your project the possibility of ordering more frequently, such as weekly, in order to store fewer test kits in the laboratory. This will also reduce the chance of exposure to high temperatures in the laboratory.
- Be careful not to base needs estimation solely on previous consumption. This may be misleading if there have been shortages or overstocking, if there are plans to expand or reduce the programme in future, or in case of seasonal peaks.

[Refer to the MSF guideline: Supply of Drugs and Medical Supplies and Management of Pharmacies, 2nd edition, 2008]

4.1.2 International orders versus local purchases

According to the MSF procurement policy, most laboratory supplies are purchased through the MSF international order process which is carried out by MSF ESC: Amsterdam Procurement Unit (APU), MSF Logistique and MSF Supply.

Local purchases may be considered under the following exceptional circumstances:
- Import restrictions
- Punctual stock ruptures
- Emergencies

Local purchases must be approved by the respective operational centre headquarters. Before any purchase, an assessment of the local suppliers needs to be carried out under the responsibility of the section pharmacists or OC medical device/IVD referent in cooperation with the laboratory advisor to check the quality of the products, storage and transportation conditions. In some countries, a database of approved products for local purchase is available and maintained up-to-date, but otherwise any local purchase requires the validation of the Medical Director who can delegate this task to the section pharmacist, OC medical device/IVD referent or laboratory advisor according to internal setup.

4.2 Reception

Items are supplied to the laboratory from either the central pharmacy, warehouse or medical store. Visually inspect the items to make sure they are the correct item. Check for any have damage that may have occurred during shipment. Make sure that none of the items have expired.

Select two to three kit boxes and check the expiry date. Open the kit boxes to check that the individual packaging has not been damaged. For RDTs, note that the components of the kits will vary depending on the RDT product or brand. For RDTs that are supplied with one bottle of buffer, ensure that the buffer does not leak and has the correct appearance. If a problem is detected, open more boxes from the same lot to identify how many boxes have been affected. If RDT kits are damaged, incomplete or expired, do not use them. Refer to Section 3.1 Procedure for reporting quality complaint.

4.3 Storage

Storage conditions recommended by the manufacturer are indicated on the packaging of the test kit by this symbol.

The technical sheet in the MSF catalogue also indicates the storage conditions.

Diagnostic tests are either stored in the medical store or the laboratory, in the refrigerator or at ambient temperature. Wherever tests are stored, proper stock management including temperature monitoring must be applied. The laboratory staff are responsible for proper storage of items inside the laboratory.

The table below indicates the most common temperature monitoring devices used in MSF and the recommendations for use.

Table 1 - Temperature monitoring devices

PCOLMONITLIF TEMP. TRACER (Logtag TRID30-7F) display, fix batt, int.sens.

How it functions:
- Shows the temperature and time.
- Records when the alarm thresholds are exceeded (1 hour below +2 °C or above +8 °C).
- Retains the duration of the breach and the maximum or minimum temperature reached, for the previous 30 days.
- Mentions “ALARM” on the screen in case of any abnormality.

How to use it:
- Ask the pharmacist or the logistician to set according the standard configuration for cold chain or room temperature.
- Check daily to see if the alert is blinking red or mentioning ‘Alarm’.
- If it is blinking red or mentioning ‘Alarms, remove and bring it immediately to the pharmacist or the logistician to download the data.
- Download and analyse the data at least once per month even when the blinking remains in green or no Alarm message is displayed.

Where to use it:
- 1 in the refrigerator
- 1 in the area with the laboratory equipment
- 1 on the shelf or cupboard with test kits
- 1 in the laboratory refrigerator, preferably in the middle next to the reagents and test kits
- 1 in the transport boxes with test kits or samples

[PCOLMONITLX] TEMPERATURE RECORDER (LogTag TRIX-8) multi-use

How it functions:
- Reads and records temperature data continuously.
- It blinks red if the temperature limit has been breached and green if not.

How to use it:
- As described above

Where to use it:
- As described above

[PCOLTHER45A] THERMOMETER alcohol (Moëller 104614) -40 °C-+50 °C

How it functions:
- Shows the temperature at any one time.

How to use it:
- Read the temperature twice a day at the hottest and coldest time of the day, such as 8 am and 3 pm.
- Record readings on a formand review the recordings at least monthly.

Where to use it:
- 1 in the refrigerator
- 1 in the laboratory room
- 1 in the refrigerator preferably in the middle next to the reagents and test kits.

[PCOLMONIFFE] FREEZING INDICATOR (Freeze-tag) electronic

How it functions:
- When an 'X' appears in the display window it implies exposure to temperatures below 0 °C for more than one hour and when a 'v' appears, it implies temperatures have been kept above 0 °C.

How to use it:
- Check the expiry date.
- Inspect once daily before using items in the cold chain.
- Use it also for transport of samples and materials and inspect while unpacking.
- This is a single use device. Once the alarm has been triggered, discard and replace with a new one in the refrigerator.

Where to use it:
- 1 in the laboratory fridge
- 1 in the transport box (samples, reagents and test kits)

Improperly stored test kits may lead to incorrect results (invalid, false positive or false negative results). Exposure to extreme temperatures (high temperatures and freezing conditions) causes the most damage both to tests and equipment. When available, MSF purchases sealed (tropicalized) versions of a test or consumable to help resist high humidity.

Troubleshooting: What to do if test kits have been stored outside the recommended temperature range

1. Report to the person responsible for storage and cold chain in your project. Also, inform the laboratory or pharmacy referent or advisor.
2. Put all the affected test kits into quarantine in the recommended storage temperature so they are not used while the investigation is ongoing. This should be done even before reporting

the problem to avoid inadvertent use during the period of communicating the problem and awaiting feedback.

3. Perform quality control checks 3 times as detailed below on a sample of the test kits.
   Example: If the temperature variation involves an ALT reagent, use the quality control material to run the tests in triplicate for all the kits affected.
4. Share these results with your laboratory advisor or referent and the person responsible for the cold chain in the project so you can determine together whether to use or discard the test kits. Further tests may be needed before a final decision can be made.
5. Work with the person responsible for storage and the cold chain to avoid similar events in the future by establishing proper storage and transport conditions of the test kits as well as systematic monitoring using the MSF standard monitoring tools. This is especially important for test kits that do not need refrigeration but should be stored below a certain temperature, such as 25 °C, 30 °C or 40 °C. This action should equally be applied from the project store to the end-user's units.

It is also possible to store some items in the refrigerator where ambient temperature is above the recommended storage temperature. For example, if a test kit can be stored between 2–30 °C and the laboratory ambient temperature is 35 °C, this test kit can be stored in the refrigerator at 2–8 °C. Always allow some time for the test kit or reagent to reach ambient temperature before using it.

While storage of test kits outside the laboratory is usually the responsibility of the pharmacist, or the supply or logistics department, quality of the test kits is the responsibility of the laboratory, therefore good communication between the departments is essential.

5. Sample management

5.1 Introduction

The management of samples is based on the 3 phases in the laboratory procedure.

- Pre-analytical phase: these are procedures which take place before the analysis of the patients' samples
- Analytical phase: these are all the steps related to performing the laboratory examinations, including the actual analytical procedure
- Post-analytical phase: these are the processes following the analytical phase including review, formatting and interpretation, authorization for release, reporting and transmission of the results, and storage of samples after the testing is done as well as the clinical interpretation of the tests.

Errors and mistakes may occur in all phases. Most errors are human errors and occur in the pre-analytical phase, followed by errors in the post-analytical phase. Following proper procedures can reduce the number of errors in these phases.

5.2 Pre-analytical phase

The laboratory is not always responsible for sample collection. For this reason, constant communication with all the departments that refer samples to the laboratory is important.

5.2.1 Sample quality

The quality of the result is greatly affected by the quality of the sample material. Failure at this stage will result in poor-quality test results despite having good-quality analytical processes. It is important to follow instructions for sample collection for the specific tests. The laboratory should provide guidelines for clinicians on the sample requirements to avoid sample rejection. It is important to follow the standard operating procedure (SOP) related to a specific test.

Key considerations that relate to sample quality:

- Use only the type of sample container recommended for the specific test.
- Process the sample within the optimum time after collection.
- Use the correct sample collection technique. For example, midstream urine collection.
- Collect the correct volume of sample.
- Collect sample at the right time. For example, fresh morning specimen of urine.
- Pay attention to other patient requirements, such as fasting before blood collection.

5.2.2 Proper request forms

A laboratory request form is sent with the sample that has been drawn or obtained from a patient. The patient's data must be completed in full and the name of the requested laboratory test should be noted. The name of the clinician who requested the test is mandatory.

Request forms are discussed in more detail in Section 6.3.

5.2.3 Labelling of samples

All samples must be given a unique identification number. Record the date and time of receipt of samples. Refer to Section 6.4. There must be a written policy to deal with incorrectly identified samples received by the laboratory. This is one of the sample rejection criteria and is discussed below.

5.2.4 Rejection criteria

These are a set of rules that define which samples will be accepted or rejected by the laboratory for further testing. These rules are set to ensure that the samples processed by the laboratory give the best possible chance of giving the true result of a patient as well as to ensure that laboratory resources are used efficiently. Specific rejection criteria are listed in each SOP in the MSF Laboratory Manual.

Some of the common rejection criteria include:
- Unidentified or unlabelled samples
- Incorrect container used
- Inadequate volume
- Improper sampling conditions, for example, the patient was not asked or forgot to fast
- Haemolysed blood
- Clotted blood for haematology
- Salivary sample for sputum AFB analysis[a]
- Sample stored for too long after collection before delivery to the laboratory
- Sample collected from an intravenous (IV) access site/tubing

If the laboratory rejects a sample, 'sample rejected' should be recorded on the request form including the reason for rejection. Return this request form to the referring clinician immediately so they are informed and have a chance to collect the sample in the correct way. The laboratory's personnel can also offer to assist with the sample collection or offer training if they are equipped to do so.

5.2.5 Sample transport

The laboratory must provide instructions for transportation of samples to the laboratory within the correct period, at the correct temperature, and what the designated preservatives are for the requested analysis to be performed. Transport must be safe for the carrier, the public and the receiving laboratory, and must adhere to national or accepted regulatory requirements. Liquid samples, including blood sample bottles and tubes, should be transported upright and secured in a screw cap container or in a rack in a transport box. Containers with liquid samples should be wrapped in absorbent paper to soak up the liquid in case of spillage.

Procedures for transporting samples

Biological samples are considered as «hazardous materials» whose transport is subject to strict regulations based on the «United Nations Recommendations on the Transport of Dangerous Goods».

The international regulation (IATA) on air transport is the most restrictive.

Regardless of the type of transport: national or international, road, rail, sea or air, any suspicious sample transported out of an epidemic context, that is carried out by MSF must comply with this regulation.

a Immunocompromised patients e.g. HIV-AIDS infected patients, might not produce good quality sputum therefore a different rejection criterion may exist in such programs.

Detailed instructions for sample transport can be found in the chapter “Procedures for transporting samples” of the Medical catalogue, vol. 5, laboratory, En/Fr, A4 [L045CATM05EFP] and Medical catalogue, vol.8, Bacteriology laboratory, En/Fr, A4 [L045CATM06EFP]. Analytical phase

5.3 Analytical phase

Careful selection of the examination procedure is important and depends on the facilities, equipment and staff available, and the number of samples for examination. SOPs must be prepared for all analytical methods and be made available at workstations.

The laboratory must have an IQC system to verify that the intended quality of results is achieved for every batch of examinations.

The most important points to pay attention to during the analytical phase are:
- Following the SOP closely to avoid inter- and intra-operator variability.
- Allow the equipment to warm up for 30 minutes after switching on before running the test.
- Run the IQC controls once daily before running any patient samples. If the IQC results fail, troubleshoot first and do not run any patient samples. If QC troubleshooting does not resolve the problem, do not run patient samples. Inform the clinician that those tests will not be available until further notice, then contact your laboratory advisor or referent.

At the end of the day, perform proper shut down procedures of all equipment. This process also includes several cleaning steps.

5.4 Post-analytical phase

A designated staff must review and authorize the release of test results. Laboratory results must be legible, without transcription mistakes, and preferably reported in the ‘International system of units’ (SI, in French: Système International d’Unités’).

The laboratory must establish procedures for notifying the requester or clinician responsible for the patient’s care when laboratory testing results fall in the range of panic values. Panic values are defined as values that fall outside the normal range to a degree that may constitute an immediate health risk to the patient or one that necessitates immediate action by the ordering physician. Panic values must be established by the laboratory supervisor, advisor or referent as part of the SOP for that test or be indicated in the laboratory service manual. The procedure must include the process of reporting urgent results, such as by telephone or walking to the ward. If a VHF radio is used, care must be taken to maintain patient confidentiality. This can be done by informing the clinician of the urgent report without giving the patient name or ward. The test should be repeated to make sure the panic result was not obtained erroneously.

Procedures must be in place for storage of samples post-examination for a specified time to enable re- examination if required, and for their eventual safe disposal.

5.5 Sample management for microscopic procedures

Good quality samples, and proper technique in spreading and staining are the foundation of quality microscopy.

Other factors which impact on the results include: quality of stains, correct functioning of the microscope and skills of the reader.

Table 2 - Recommended areas to check to ensure quality microscopy

Quality area	Actions to guarantee quality
Stains	• When possible, always use MSF validated stains at all times. If stains have to be purchased locally: - Check the local availability of the MSF validated stain. If this is not available, consider the use of international brands that are widely used such as: Merck, Biomerieux, Carlo Erba, RAL, Sigma-Aldrich. - Choose prepared stains instead of stains that require additional preparation, that is preferably not in powder form as the mixing process can be long and inefficient without proper equipment. - If buying ethanol or methanol choose one that states: 'analytical grade' or 'pure' and which indicates a water content of < 0.05%. • Prepare stains according to standard operating procedures as detailed in the MSF laboratory manual. • Check the quality of every new prepared batch of stains by staining a known positive and known negative smear or film, and reading them under the microscope. To prepare Positive and Negative smears for stain QC: 1. Identify a highly positive sample during routine laboratory work (for example a 3+ TB smear) 2. Once the sample has been processed and results issued, prepare several slides from the leftover sample. 3. Dry and store these slides unstained in a slide box labelled 'Stain QC slides' with the sample type and result written on the slide is found (preferably 2+ or 3+). Every time a fresh batch of stains is prepared, retrieve one of these slides, stain them and examine them for staining quality.
Film and Smear preparation	• Follow SOP for film or smear preparation as detailed in the MSF Laboratory manual paying attention to size and thickness of the film or smear.
Staining	• Follow the SOP for staining as detailed in the MSF Laboratory manual paying attention to timing. This is best done by using a timer for each step.
Microscope	• Use an MSF standard microscope. MICROSCOPE (PrimoStar iLED), light and fluorescence 100-240V [ELAEMICE6--]. • Other good microscopes like the Olympus CX21 or CX22 may be used. • Maintain the microscope in good condition and report when broken.
Reader skills	• Train every new staff on microscopy and register all trained persons (name, date, skills checked.).

5.6 Sample management for procedures involving semi-automated systems

Whole blood, serum, plasma and urine are the samples mostly analyzed with semi-automated systems:

- Reflotron [ELAECCHE2-- CLINICAL CHEMISTRY ANALYSER (Reflotron Plus), 115-230V]
- Humalyser 2000[ELAESPEE4-- SPECTROPHOTOMETER (Humalyzer 2000), contr.temp. 110-230V]
- Sysmex XP300[ELAEHAAE1-- HAEMATOLOGY ANALYSER (Sysmex XP 300), 115-240V, 50-60Hz]

Table 3 - Recommended actions to ensure quality for semi-automated systems

Steps in procedure	Recommended actions
Sample mixing	For anticoagulated samples, mix whole blood samples immediately after collection to ensure proper exposure to the anticoagulant and avoid clotting. Clots in the samples may interfere with results, e.g. CD4 or full blood counts. Mix whole blood again before analysis to homogenize the sample. If this is not done, there is a risk of incorrect results. Mix the sample with reagent properly before performing the test. This can be done by gently inverting the tube several times or gently rolling the tube between the hands or using a roller mixer and dispensing in the same tube several times to avoid the formation of air bubbles or foam.
Sample separation	For procedures requiring serum or plasma, samples should be separated in the recommended time frame. For serum – within 30 minutes; for plasma – up to 6 hours.
Making aliquots	Aliquoting should be done using a fresh sample before the sample is frozen, as repeated freezing and thawing of samples can damage the sample by denaturation of antibody or nucleic acid content. Note that certain types of freezers are designated 'frost free'; these should not be used for sample storage as the temperature cycling involved in keeping them free of ice accumulation can damage samples.
Clean tubes	For biochemistry, serology or molecular tests always use a new or clean tube. Inspect the tube to see that there is no visible dirt or dust, and discard if this is the case.
Good pipetting	Set the pipette to the correct volume. Eject the pipette tip after each sample. Avoid contaminating the stock reagent. **Never use your mouth to pipette**. Use the forward pipetting technique as described in the MSF laboratory manual.

5.7 Sample management for procedures involving hand held analysers

As most handheld analyzers operate by using cartridges or strips, the most important sample management aspect is to fill the cartridges properly. This means that the cartridge is filled to capacity and there are no air bubbles.

This can be accomplished by either adding blood to the cartridges or strips directly after skin puncture with an adequate flow of capillary blood, or by first collecting blood into a capillary tube and then filling the cartridges or strips with blood from the capillary tube. The latter technique is used for the Pima analyzer [ELAECD4E1-- ANALYSER CD4 (PIMA), 100-240V, 47-53Hz, 260300003] and works very well.

5.8 Storage and disposal of samples

Samples should be stored for a limited time before being disposed of. The recommended times for sample storage are specific to the analysis performed and take into account the time for clinical follow up and repeat testing if needed, the length of time when the results would still be valid in cases of re-runs. These recommendations are based on the Good Clinical Laboratory Practice Guidelines established by WHO and ISO 15189.

Table 4 - Whole blood, Serum and Plasma storage validity time at different temperatures (ref. Use of anticoagulants in diagnostic laboratory investigations & stability of blood, plasma and serum samples, World Health Organization, 2002)

	Blood	Serum/Plasma	
Analyte	Room temperature	2-8 °C	20-25 °C
Alanine aminotransferase (ALT)	47 hours	7 days	3 days
Albumin	3 weeks	5 months	2 months
Alkaline phosphatase	4 days (may cause a decrease in value)	7 days	7 days
Amylase	4 days (may cause a decrease in value)	7 days	7 days
Aspartate aminotransferase (AST)	7 days (may cause a decrease in value)	7 days	4 days
Bilirubin (Total)	Unstable	7 days	1 day
Calcium (Total)	2 days (may cause a decrease in value)	3 weeks	7 days
Chloride	1 day (may cause a decrease in value)	7 days	7 days
Cholesterol	7 days (may cause an increase in value)	7 days	7 days
Creatinine	2-3 days (may cause an increase in value)	1 month	4 hours
C reactive protein (CRP)	3 weeks (at 2-6 °C)	2 months	11 days
Glucose	Minutes	7 days	2 days
Haemoglobin	4 days	7 days (EDTA blood)	4 days (EDTA blood)
HbA1c	3 days (EDTA blood)	7 days (Haemolysate)	3 days (Haemolysate)

	Blood	Serum/Plasma	
Haematocrit	1 day or 4 days (at 4-8 °C)	4 days (EDTA blood)	
Lactate	Less than 5 minutes (unstable and may cause an increase in value)	3 days	8 hours
Lipase		3 weeks	7 days
Magnesium		7 days	7 days
Potassium	1 hour (may cause an increase in value)	6 weeks	6 weeks
Sodium	4 days (may cause a decrease in value)	2 weeks	2 weeks
TSH	7 days	3 days	1 day
Urea	1 day (may cause an increase in value)	7 days	7 days

Discard all leftover samples into the biological waste bin.

For blood slides, these can be destroyed after the QC results are received and reviewed. Discard slides in the dedicated glass container.

Please contact your laboratory advisor for questions regarding waste disposal plan for specific samples and items in the laboratory.

6. Documentation

6.1 Introduction

Documentation includes policy and operational documents needed in the laboratory for activities that are carried out. Having complete documentation means that: 'you do what is written, you write what you do, and you can prove what you have done'.

The following principles apply to all documentation generated and used in the laboratory.

- All staff working in and with the laboratory should be familiar with all the documents that are relevant to them, for example, cleaners and drivers working with the laboratory should be familiar with the laboratory safety document appropriate for their tasks.
- Information contained in various documents should be reviewed regularly and appropriate actions taken for missing or inaccurate data or as needed.
- Where manual methods are used, all data should be filled in using legible handwriting. The notebooks or ledgers that are used should also be of good quality and should not fall apart during use.
- Routine laboratory data should be stored and available according to country requirements. If no country regulations exist, data should be stored for 10 years.
- Electronically stored data should be backed up at least weekly.
- The confidentiality of patient information should always be maintained. This means having limited access and full control over who can see the recorded data. This can be achieved by restricting access to the laboratory where these books are kept and used and keeping the books in a locked cupboard at the end of the day. Each laboratory computer must have a password and all data containing patient names should also be password protected.
- Documents should always be kept up to date. The number of the current version and its date should appear at the bottom of each document.

6.2 Laboratory service

This is a document that helps to communicate the general organization of the laboratory (normal working hours, night shifts or on-call duties, organizational tree, etc.), what tests are available in the laboratory, what samples should be collected and under what conditions (container, temperature, time to analysis, etc) and how they should be transported. It also states what is expected from the laboratory in terms of turnaround time [see Annex 4].
This is also a useful document to use as a briefing tool for new medical doctors and nurses who join the project.

6.3 Laboratory request and report forms

Request form

Laboratory request forms must be correctly filled by clinicians in readable handwriting when requesting tests. Clinicians should not scribble requests on pieces of paper. [see Annex 5] These forms can be adapted to fit the particular needs of the MSF facility. The form generally should contain information to correctly identify the source of the sample (e.g. patient identification, age and gender) and the person requesting the test (name and signature of clinician). Clinical

information, including provisional diagnosis and treatment, is required to have a satisfactory and proper interpretation of the results. Proper filling of request forms is the responsibility of clinicians, but the laboratory should check that there is no missing information.

A laboratory request form is sent with the patient or with a sample that has been drawn or obtained from a patient. The patient's data must be completed in full and the name of the requested laboratory test should be noted. The signature of an authorized personnel is mandatory.

Report form

Laboratory report forms contain the results of various laboratory examinations. The report form may be combined with the request form. It is important to indicate whether results are preliminary (awaiting confirmation) or final. The laboratory technician who validates and releases the results should sign the report form.

Identification of the laboratory and laboratory technician (name and signature) issuing the report.
- Full name of patient or Patient code.
- Name of person who requested the test.
- Type of sample.
- Comments on the quality of the primary sample which could invalidate the result, such as clotted sample for haematology parameters.
- Testing method used, such as malaria blood films or malaria RDT.
- The results and units of measurement where appropriate.
- Where possible, the normal reference interval (reference range).

The following items are also good to have on the laboratory report
- Date and time of primary sample collection.
- Date and time of receipt by the laboratory.
- Date and time of reporting.

6.4 Laboratory registers

Laboratory registers are used to keep patient data and information. This data are used for the follow-up of patients, for future reference, and for evaluations of the laboratory. Registers should be kept safely as they contain the personal and confidential data of patients.

A large hard cover book is preferred for such a register.

6.4.1 Reception book

This is a book that is usually placed at the sample reception room or area of the laboratory. All samples received in the laboratory are registered here before being passed on to the relevant laboratory departments for processing. It contains the data on received samples and the requested tests following a numeric sequence related to the patient and not to the tests.

In this way all the different departments of a laboratory will have a single unique number for the same patient, and it will preserve confidentiality, keep track of all the samples and ensure all of them are analysed.

6.4.2 Main laboratory register

This is the book with all patient data. Staff members must correctly complete patient and sample information in this register book and add all the results once testing is completed. Upon arrival, all samples must be registered and given numbers, and the results of all investigations must be recorded.

Samples are only identified by their laboratory registration number in the laboratory registers, therefore, it is important to make sure there are no clerical errors. This system has the advantage of more confidentiality and less manual copying.

6.4.3 Specific test registers

These other registers, kept in hard cover books, contain all the information about various tests carried out in the laboratory.

Such tests include parasitological investigation of stool and urine, biochemical results for urine or plasma, blood films for malaria, Gram stain smears, WBC, haemoglobin, haematocrit, skin snips etc., and samples referred to other laboratories.

Vertical programmes like TB, HIV, malaria, diabetes, hypertension may have their own forms and registers. Follow the recommendations specific to these programmes. The national tuberculosis programme (NTP) often supply the Tuberculosis Laboratory Register. [see Annex 6 for a template of a TB laboratory register, if an NTP is not available].

6.5 Laboratory incident book

This book should be kept by the laboratory supervisor and should contain details about laboratory accidents and the measures taken. The accident should be reported to the person in charge and details of the following should be noted in the laboratory incident book. [see Annex 7].

Both the laboratory supervisor and the person involved in the accident should sign the statement. Some of the examples of events that should be recorded in an incident book are:

- Accidents to staff and patients
- Complaints from clinical staff
- Inappropriate behaviour
- Lost samples
- Delays in sample delivery

6.6 Standard operating procedures

All staff that have been trained for a certain procedure should read and sign a copy of the associated SOP to indicate they have fully understood the SOP and they will perform the tests in accordance with the SOP. This signed copy should be kept with the human resource or training department. The most important standard operating procedures are contained in the MSF laboratory manual.

Bench aids may be posted on the walls as reminders, but not detailed procedures.

Records of training on SOPs and other procedures should be kept systematically for every staff member. The record should contain the date of training, training method (reading SOP, presentation), signature of trainee and signature of trainer or supervisor. Training should be repeated when new versions of SOPs or other documents are issued.

6.7 Quality control workbook

This contains all the quality control tests run for a particular assay, as well as calibration records, notes on External quality assessment (EQA) results and records of any troubleshooting steps and corrective action taken.

6.8 Other documentation

- Inventory of all the equipment in the laboratory [see Annex 8]
- Staff duty roster – this would normally be posted on the wall for easy reference, for example, who is on call.
- Maintenance contract.
- Routine maintenance schedules and trouble shooting
- Contacts list of external laboratories and suppliers

- Operating manuals of equipment
- Package inserts of all tests and reagents
- Safety data sheets for all reagents

6.9 Monthly reports

At the end of every month, the laboratory supervisor should compile a monthly report of activities for the MSF management (medical team leader and/or project coordinator and medical coordinator) as well as ministry of health where relevant and the laboratory advisor or referent.

The monthly reports help to monitor laboratory activities and are useful for ensuring adequate staffing, supplies, and budget, as well as providing information on public health surveillance. A format of this report is available through your medical team leader or your laboratory advisor.

7. Quality control

7.1 Introduction

Quality control (QC) is an element of quality assurance that is intended to ensure that consistent, reproducible results are achieved on a day-to-day basis. This involves the use of quality control samples along with patient samples to identify any errors before patient results are issued.

This is comprised of internal quality control (IQC) and external quality assessment (EQA). Ideally, both elements must be available in a laboratory.

General:

1. The QC system should be set up in such a way that it encourages all laboratory workers to work towards producing consistent and reliable laboratory test results for all patients. This means that it must be feasible and incorporated into routine procedure.
2. It is essential that not only correct IQC/EQA results are registered, but that also incorrect results are documented, to understand technical challenges and how they were solved. Every (corrective) action taken after an abnormal QC-result must be documented. The laboratory will have erroneous and biased information if only the 'good' IQC and EQA results are recorded.
3. The laboratory staff decides on the corrective actions in the laboratory system.

IQC:

4. QC results should be interpreted and acted on as soon as the laboratory sees the result and in case of "out of range" results, the laboratory should stop testing, investigate and try to solve the problem before testing patient samples. The medical team should be informed in case of "out of range" QC results that cannot be solved by the laboratory team.
5. Every time a laboratory worker produces a new IQC result, he/she must evaluate the result in relation to previous IQC results. It is important to do this directly after the measurement to avoid reporting erroneous results.
6. IQC results are also intended to check if there is any tendency of an instrument towards releasing results in a certain direction, such as continuous increase or decrease of values.This would help prompt a timely intervention with corrective action.

EQA:

7. Results of EQA samples must be evaluated in a meeting with all laboratory workers to discuss any gaps with the desired results.
8. Proficiency testing (a form of EQA) should not be conducted only by the supervisor or the person deemed most competent in testing, but by every laboratory worker performing the test routinely. This is done to simulate the routine work conditions and to provide an appropriate representation of the quality of daily testing.

7.2 Scope

This chapter will focus on quality control for the following techniques:

1. Rapid diagnostic tests – malaria, syphilis, HIV, hepatitis B, hepatitis C
2. Stained microscopy slides – TB, malaria, kala azar, Gram stain
3. Semi-automated systems – Humalyzer 2000, Sysmex
4. Complex multi-analyte systems - Reflotron plus, Piccolo, WBC diff
5. Hand held analyzers - Glucometers, HemoCue, i-STAT

7.3 Organization and responsibilities

Each laboratory should appoint a responsible coordinator for quality control; usually this is the laboratory supervisor. A guide for task division is listed in the table below.

Table 5 - Overview of QC related responsibilities

Position	Responsibilities
Laboratory advisor/referent/ implementer	• Trains supervisor on QC implementation. • Provides technical and operational support. • Helps with troubleshooting.
Laboratory supervisor	• Ensures IQC is performed. May delegate day to day running to a colleague but is ultimately responsible for QC. This also involves making the necessary plans to send samples for EQA (inter- laboratory checking with another laboratory is a form of EQA) and receive back the results. • Trains colleagues on QC implementation. • Performs monthly analysis of QC reports. • Ensure QC procedures (including corrective actions) are available for all tests. • Ensure that all staff are trained. • Creates a mechanism of communication to inform staff about problems.
Laboratory technician	• Performs QC procedures according to standard operating procedures. • Performs and records day to day analysis of QC results and reports any anomalies to the laboratory supervisor.

7.4 Quality Control of Rapid Diagnostic Tests

7.4.1 Introduction

The term rapid diagnostic tests (RDT), is a qualitative or semi-quantitative in vitro-diagnostic medical device, used singly or in a small series, which involve non-automated procedures and have been designed to give a fast result. RDTs are suitable for preliminary or emergency medical screening and for use in medical facilities with limited resources. Generally, the time needed to perform the test is between 10 minutes and 2 hours, and results can be given to the patient on the same day. While rapid tests are developed to be simple to use and can be performed by trained, non-laboratory staff, they still need to be performed with care, and with careful adherence to testing procedure.

7.4.2 Scope

This section refers to the quality control of all tests whose MSF code starts with SSDT in the ITC Catalogue, Volume 5.

7.4.3 QC for RDTs supplied with commercial controls

Most rapid tests used in MSF are supplied without internal quality control vials except the Stat-Pak HIV test. An internal control line is instead included in the strip or cassette. The control line is a procedural control and measures how well the mechanics of the test are working (i.e.; the

integrity of the antibody-dye conjugate, and the flow of sample). This does not function as an internal quality control where it confirms the ability of the test to detect the analyte or target.

Some tests like RPR (rapid plasma reagin) are supplied with a set of control vials. Make sure to check the manufacturer's instructions on how to interpret different intensities of the positive line. In this case, run the controls once a week and/or each time a lot reagent number changes according to manufacturer's instructions. If the test gives the expected result for both the positive and negative control, then the test kit is safe to use. Record the results and proceed to use the test.

If the kit does not pass the control test, follow the troubleshooting plan below (Section 7.4.4).

> Control materials should ONLY be used for the test kit for which they are supplied.

7.4.4 Troubleshooting: What to do when a test kit does not pass QC

A quality control sample is said to have "passed" if it gives the expected results, that is, if the positive control gives a positive result and the negative control gives a negative result.

If this does not happen, the following steps should be followed.

1. Repeat the QC using a different test strip or cassette from the same test kit. Be careful to follow the procedure strictly.
2. If the test still fails, repeat using a test from a different test kit of the same batch.
3. If this still fails, record the results and contact your medical team leader and/or laboratory advisor or referent for further action and stop the clinical testing of patients' samples with this batch.

7.4.5 Reporting and documentation

The reporting format below shows the pertinent information to record after performing quality control for an RDT [see Annex 9].

Table 6 - Example of an internal quality control recording for RDTs

MSF CODE:

MSF DESCRIPTION:

Date	Batch number test kit	Batch number of control reagent	Negative control	Positive control	Conclusion control samples	Remedial action	Run by
6-9-2018	C3029KFR	D12540	Negative	Positive	Pass	None	Jane Doe
13-9-2018	C3029KFR		Negative	Negative	Fail	• Run the control again. Same result. • Informed supervisor. • Changed batch of test kits.	
15-9-2018	H9203RFK		Negative	Positive	Pass	None	John Doe

7.4.6 External quality assessment of rapid diagnostic tests

There is currently no EQA programme that MSF subscribes to for RDTs. Laboratories are encouraged to participate in any programme that may be offered by a reliable organization nationally or regionally (verify this with your laboratory advisor). These options are generally offered through the ministry of health or a partner of the ministry of health.

7.5 QC for stained microscopy slides: cross-checking procedure

7.5.1 Scope

This section covers the QC procedures for stained slides that are used for diagnosis. Follow-up slides are not included because the positivity rate tends to be low which would require to increase the number of slides the laboratory needs to examine. This would increase the workload and costs to the laboratory and might be counterproductive to the purpose of QC.

The slides prepared for the diagnosis of malaria, TB, kala-azar and bacteria (Gram stain) are included in the QC. Manual differential counts have been purposely left out to keep the QC workload of the laboratory low.

7.5.2 Key aspects of cross-checking of stained slides

In order to conduct the cross checking procedure of stained slides, 3 different readers are needed.

- 1st reader - This is the person who first reads the slide for diagnostic purposes (routine laboratory testing). The result of this reading is recorded in the laboratory register and in the patient request form.
- 2nd reader - this person reads the slides for QC purposes. It is preferable that the second reader is external to the laboratory, such as another MSF project, a reliable individual from a Ministry of Health (MoH) run laboratory or a private laboratory. Slides would then be sent to this person/ laboratory for the 2nd reading. If this is not possible operationally or logistically to organize this, a second reader can be appointed from the same MSF laboratory as long as the individual is blinded to the results of the first reader. In principle the 2nd reader will spend more time on each slide and is more experienced, as compared to the routine reading, in order to get results as close as possible to optimal or true result. The 2nd reader also provides comments on the quality of the smear or film, and the staining of each slide.
- 3rd reader - This is a skilled microscopist who will serve as a tie-breaker in case there are discrepancies between the 1st and 2nd reading. This person can either be from the same laboratory of the 1st or 2nd reader, or another laboratory altogether.

The most important aspects for cross-checking of slides are:

- Blinded cross-checking: the cross checker does not know the original results.
- The cross-checker is a trained person and has sufficient knowledge and skills, and is currently in the routine practice of reading slides to perform the cross-check.
- The results of the cross-checking procedure are issued in a timely manner, preferably within four weeks. This allows the laboratory to take appropriate action within a reasonable timeframe.

7.5.3 Introduction to LQAS

There are various approaches to perform the cross checking of stained slides. MSF has decided to replace previous traditional empirical approaches such as re-checking all positives and sampling 10% of negative slides and to instead use the Lot Quality Assurance Sampling methodology (LQAS). LQAS has been adapted from the document External Quality Assessment for AFB Smear Microscopy (IUATLD, WHO, CDC, KNCV).

LQAS is a tool for sample selection that was developed for the quality control of industrial production. It is designed to give the minimum sampling size required for re-checking to give a statistically significant analysis with a 95% confidence limit. From our perspective, it is important

to balance the number of samples to be cross-checked and the additional workload it requires from the laboratory. Using the LQAS would take this into consideration and still have a statistically valid result from the cross-checking process.

For ease of use in MSF contexts, an Excel based tool has been developed based on LQAS principles to assist in calculating how many slides to cross-check in each laboratory each month and how to interpret the results [see Annex 10 in the USB/CD version].

It is recommended that the tool be used at the beginning of each year to determine the number of slides to cross-check and the thresholds for when to take action.

Definitions to help guide the use of the tool:

- **False negative** – results reported as negative by the first reader (routine laboratory testing) but reported as positive by the second reader.
- **False positive** – results reported as positive by the first reader (routine laboratory testing) but reported as negative by the second reader.
- **Critical value** – a number used to determine alert and action thresholds.
- **Alert** – an expected error that requires no action. Even the best laboratory will have a few errors once in a while so the LQAS tool allows for such errors.
- **Action** – an investigation needs to be done because the number of errors exceeds the number that is allowed or expected.

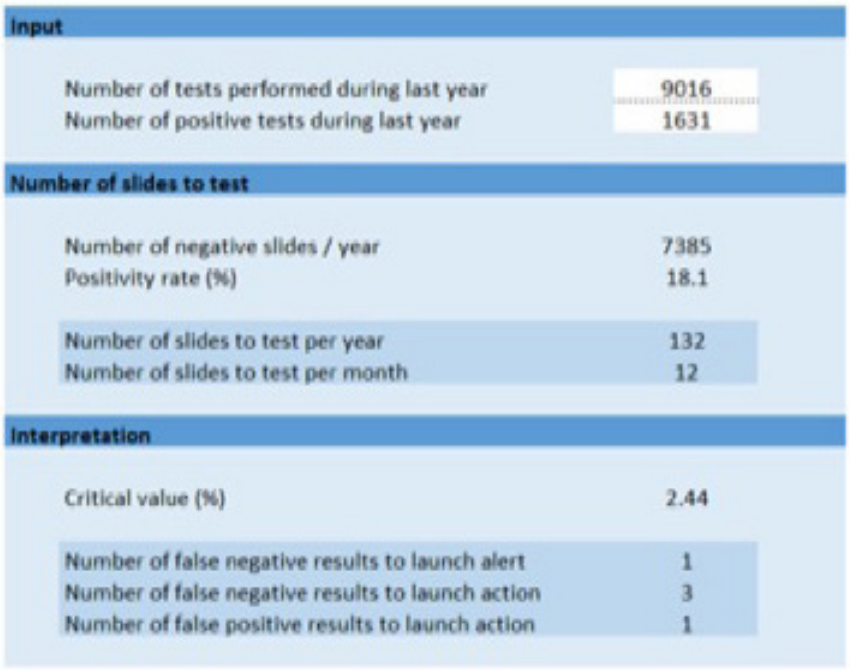
7.5.4 Use of the LQAS Excel tool

Setting the targets for the cross-checking procedure

This process is conducted at the beginning of every year in each laboratory. Collect data from the previous year showing the total number of stained slides that were examined and the number of negative results. Enter this information into the LQAS tool and take note of the number of slides to examine monthly as well as the alert and action thresholds.

To illustrate in this example for laboratory X: In 2017, the laboratory examined 9,016 diagnostic TB slides and 7,385 of them were negative. At the beginning of 2018, the laboratory supervisor enters this data into the LQAS tool as shown below and the tool generates the proposed number of slides to test per year and month as well as the critical number to which an alert and action will be launched.

Figure 1 - Output of the LQAS calculation tool, laboratory X, TB slides.



Input	
Number of tests performed during last year	9016
Number of positive tests during last year	1631
Number of slides to test	
Number of negative slides / year	7385
Positivity rate (%)	18.1
Number of slides to test per year	132
Number of slides to test per month	12
Interpretation	
Critical value (%)	2.44
Number of false negative results to launch alert	1
Number of false negative results to launch action	3
Number of false positive results to launch action	1

Based on the example above, the laboratory supervisor will plan for the following:
1. Twelve TB slides will be selected every month for crosschecking.
2. If the results of the cross checking reveal 1 false negative, it should raise an alert but no need for action.
3. If there are either three false negatives or one false positive result, then the laboratory supervisor will need to" launch an action. The laboratory supervisor will need to generate a proposed plan using the LQAS tool for each type of stained slides examined in the laboratory.

Conducting the cross-checking procedure

Follow the monthly QC procedures described below.

- Store all diagnostic slides examined per month in a box in numerical order and based on the date they were examined. Do not separate negative from positive slides.
- At the end of the month, select the number of slides as indicated in your LQAS tool by dividing the total number of slides examined that month by the number of slides to cross check per month.

  For example: the LQAS calculation states to cross check 12 slides per month. Assume in that month they read 245 slides. Divide 245/12= 20.41. The laboratory supervisor should then select every 20th slide.
  Note that there are other methods to select slides for cross-checking, but from MSF experience, the use of a physical slide box for selection is more feasible and as robust.
- Place the selected slides in a separate slide box and label the box as QC slides including the month.
- Record the number of each slide on 2 QC sheets as shown in red, as an example, below. Do not record any results on the sheet or on the slides. Send one sheet to the 2nd reader and keep one sheet for yourself [see Annex 11].

Table 7 - An example of the form which has been filled (in red) accompanying the QC slides.

HIGHGATE LABORATORY				
TUBERCULOSIS SLIDES				
JANUARY 2017				
Slide number	**Reader 1**	**Reader 2**		
		Results	**Quality of smear**	**Quality of staining**
CK225-15				
CK230-15				
CK235-15				
CK240- 15				
CK245-15				
CK250-15				
CK255-15				
CK260-15				
CK265-15				
CK270-15				
CK275-15				
CK280-15				

- Pack the slides in a slide box and send them to the 2nd reader. Ensure there are enough packing materials, so the slides do not break during transportation. Include plenty of cotton gauze inside the slide box and bubble wrap on the outside of the box. Slides should be sent as ordinary mail and not as dangerous goods.
- Follow up with the 2nd reader to make sure they have received the slides.
- Follow up to make sure you receive the results within 4 weeks.
- Record the number of false positive and false negative results.
- Check in the LQAS tool to see how many errors are allowed before an 'alert' or 'action' needs to be launched. If any of these thresholds have been crossed, follow the troubleshooting guide as described below.
- Make an analysis of the report and take the corrective actions, if any.
- Keep a record of the analysis.

Table 8 - Example QC results - Tuberculosis QC results, January 2018, Lab X.

HIGHGATE LABORATORY				
TB SLIDES				
JANUARY 2018				
Slide number	**Reader 1**	**Reader 2**		
		Results	**Quality of smear**	**Quality of staining**
CK225-15	Negative	Positive 3AFB seen	Too thick	Phenol crystal deposits
CK230-15	Positive 3+	Positive 3+	Good	Good
CK235-15	Negative	Negative	Too thick	Good
CK240- 15	Positive 9AFB seen	Positive 2AFB seen	Too thick	Plenty of artefacts
CK245-15	Negative	Negative	Good	Good
CK250-15	Negative	Negative	Good	Good
CK255-15	Negative	Negative	Good	Good
CK260-15	Positive 2+	Positive 3+	Good	Good
CK265-15	Positive 4AFB seen	Positive 5AFB seen	Good	Good
CK270-15	Negative	Negative	Good	Good
CK275-15	Positive 1+	Positive 1+	Good	Good
CK280-15	Positive 1+	Positive 1+	Good	Good

Fill in a 2x2 table as follows:

	Reader 2	
Reader 1	**Positive**	**Negative**
Positive	A	B
Negative	C	D

Where: A = Number of slides read as positive by both readers i.e. True positives.

B = Number of slides read as positive by the 1st reader and Negative by the 2nd reader – false positives

C = Number of slides read as negative by the 1st reader and positive by the 2nd reader – false negatives

D = Number of slides read as Negative by both readers – True negatives.

The 2x2 table for the Laboratory X results would look like this:

	Reader 2	
Reader 1	**Positive**	**Negative**
Positive	6	0
Negative	1	5

Result:
Number of errors: 1 false negative.
Based on the interpretation generated by LQAS tool for laboratory X for this TB staining procedure, the result of this QC would generate an 'alert'.

7.5.5 Troubleshooting

What to do when you have reached the **alert** threshold

The following actions should be taken by the supervisor when an alert threshold has been reached:

1. Communicate with the laboratory staff that the result of the QC resulted in an alert.
2. Remind the laboratory staff to follow the SOPs and conduct retraining. Report any problems if noted.
3. File the results of the QC exercise in the monthly register.
4. Inform the treating clinician or doctor about the false negative result, in order to trace and follow up with the patient.

What to do when you have reached the **action** threshold

1. A 3rd reader (tie-breaker) needs to review the slide(s) that showed discordant results between reader 1 and reader 2. If the review of the slide shows that the first reader was correct, no further action is required.
2. If the results show that the first reader was wrong, proceed to investigate what the problem was. Table 9 shows some common errors, their causes and proposed corrective actions.
3. Record the exact error that was made and describe the corrective actions taken. Follow the outcome on future QC results. The results of the QC cross-checks must be made available for all staff members and discussed with everyone involved.
4. If you cannot identify the problem to take the right corrective action, contact your laboratory advisor or referent for support.
5. Inform the clinician or doctor of the false negative result so they can trace and follow up the patient.

Table 9 - Troubleshooting guide for slides QC

Problem area	Causes and action
Slide with low burden of organisms (low parasite or bacteria load) are read as negative	• High workload – laboratory staff have insufficient time to thoroughly examine the slides and thereby miss weak positive slides. Action: As this is not a training issue further training will be ineffective. The primary cause of the problem is laboratory workload and/or excessive clinical referral – correction is therefore a management issue. Discuss with your medical team leader. • Poor equipment – the quality of microscopy work is directly related to the quality state and maintenance of the microscope. This again is a management issue and not a training issue – additional training will not be effective. Action: Discuss with your medical team leader the provision of proper equipment. • Poor slide preparation and/or staining – this can both be a training issue and/or a management issue. [An example of a management issue - Giemsa staining requires good pH control. If the laboratory does not measure and control the pH then no amount of training will rectify the problem.] • Overconfidence: staff can become overconfident of their skills and believe that they can report a slide negative after a very short period of slide examination. This is a management issue to correct with the staff member. • Staff turnover – for example, when a new staff has recently joined and has not received enough training on the subject. In this case the laboratory supervisor should train the new staff on how to perform the examination followed by supervision of the new staff the first few times he/she performs the test. The staff should only be allowed to work independently once sufficient training has been provided and the staff member is deemed competent to perform the test.
Slide with high burden of organisms (high parasite or bacteria load) are read as negative – high false negative (*hfn*)	This is indicative of a more serious problem compared to the previous problem . An occasional *hfn* is caused by either a straightforward reading error (simply didn't read the slide properly) or a clerical error. Repeated *hfn* results require immediate investigation. They are more likely to be due either to a poor microscope and/or poor preparation and/or staining rather than deficient reading skills. As such, the primary remedial action should be directed to the improvement of the quality of the equipment and preparation and staining rather than training of staff to improve reading skills.

Problem area	Causes and action
A negative slide is read as positive	This is more often encountered in reading of malaria films and less of a problem with TB and Kala Azar. This is very often a non-technical problem, although cross-contamination must be considered for AFB slides. The presence of artefacts in the slide could be mistaken for AFB bacilli. For malaria slides a primary cause of the problem is that many laboratory technicians consider that it is 'safer' to call a slide 'weak positive' than negative. [The reason for being on the 'safe' side is the assumption that the patient would not have been referred for testing unless there were clinical symptoms suggestive of malaria and that overtreatment with anti-malarial drugs is deemed more acceptable than the risk of being wrong.] The first step is to check that the slides are readable, that is ensure that staining is of good quality and there is absence of excessive debris such as stain precipitate or artefacts from water sourced from the river, and that artefacts are not incorrectly read as positive organism. If the slides are readable, then this problem has to be primarily resolved at the slide reading stage. • Provide refresher training on slide reading. • Assist staff to develop confidence in their slide reading skills. • Emphasize that intentionally reporting a false weak positive can do more harm to the patient. The patient will be wrongly over treated with anti-malarial drugs and will not receive further investigation and subsequent treatment for the true cause of their illness. • Ensure slides are not re-used for any other staining procedure.
Quantitation error	When slides are adequately prepared, quantitation errors are generally a staff training issue. Often laboratory technicians may have not been adequately trained in the method of quantitation used by the laboratory. This can be solved with training.
Species identification errors	When slides are adequately prepared, species misidentification can be either related to laboratory protocols or reading skills. Many laboratories do not routinely prepare thin films which makes it difficult for the reader to accurately identify species. This specific reader skill is dependent on a high level of training.

All investigations should be deemed serious however not all investigations result in a serious offence.

Sample illustration of Corrective Action for Laboratory X: In the month of February, the QC results of TB slides showed one false positive result. This requires an action to be launched. The following were the investigations that were taken in Laboratory X.

Table 10 - Example of corrective actions for QC- Laboratory X

LABORATORY X						
TUBERCULOSIS SLIDES						
FEBRUARY 2017						
Slide number	**Reader 1 Routine results**	**Reader 2 - Cross checker**			**Investigation done**	**Corrective action taken**
		Results	**Quality of smear**	**Quality of staining**		
K240- 15	Positive	Negative	Too thick	Plenty of artefacts	Slide reviewed by 3rd reader. Confirmed as negative	• quality of stain checked – good • Staining procedure reviewed – the filtering step was not always done. • SOP for staining procedure reviewed with staff. • Staining procedure supervised by laboratory supervisor in April. • Slides re-checked randomly. • Stains have improved.

7.5.6 Reporting

A blank template for the reporting of QC of microscopy slides is provided in Annex 11.

Store all the reports per month in your QC folder.

Include the performance in the monthly laboratory report that you submit every month either to your medical coordinator or laboratory advisor.

7.6 Quality control of Semi – automated systems

7.6.1 Introduction

Quality control procedures are required to detect and minimize errors in the performance of tests and to keep precision and accuracy errors to a minimum. When performing quality control for (semi-) automated analysers, knowledge of the accuracy and precision of a method is important to keep these parameters controlled.

Figure 2 - Diagrammatic representation of accuracy and precision

High accuracy High precision	Low accuracy High precision	High accuracy Low precision	Low accuracy Low precision

ACCURACY is defined by the proximity between an obtained value and the target value (true value). Errors of inaccuracy are often constant and regular. The difference between all obtained values and target value are similar.

PRECISION measures reproducibility. Imprecision errors are often irregular and random. The differences between obtained values and target value are variable.

Factors that can affect accuracy

- Incorrect calibration of a test method or equipment.
- Tests read at the incorrect wavelength or the wrong filter was used.
- Incorrect setting of the automatic pipette.
- Errors in calculation, such as an incorrect factor was used.
- Use of poor quality reagents, standards or controls.
- No recalibration was done after a change of reagent lot or batch.
- Incorrect maintenance of the analyser.
- Incorrect measuring of temperature, such as for enzymatic tests.

Factors that can affect precision

- Incorrect and variable pipetting and dispensing.
- Inadequate mixing of sample with reagents.
- Inconsistent, suboptimal and/or incorrect incubation of samples, such as variable temperature and duration.
- Inadequate cleaning or improperly dried items such as glassware or plastic ware.
- Equipment malfunction.
- Incomplete removal of interfering substances.

Good quality laboratory practice for clinical chemistry begins with the testing of normal and abnormal controls for each test at least daily to monitor the quality of the analytical process. Testing on patient clinical samples should only be carried out when the instrument has passed the testing with normal and abnormal controls.

It is not enough to use the manufacturer's validation report for new analysers or methods, or to use the approval (reference) ranges for QC reagents. These ranges are too wide and do not reflect the specific situation for your laboratory (including type of instrument, temperature, etc). For this reason, a Levey-Jennings chart should be established by each laboratory for every test on every analyser and be used to interpret internal QC (IQC) results.

7.6.2 Scope

This section will address the quality control procedures for the following analysers.

- Humalyzer 2000 and other spectrophotometers
- Reflotron plus
- Sysmex KX21N and XP300 and other automated haematology analysers
- i-STAT hand-held analyser ***only*** when it is used inside the laboratory.

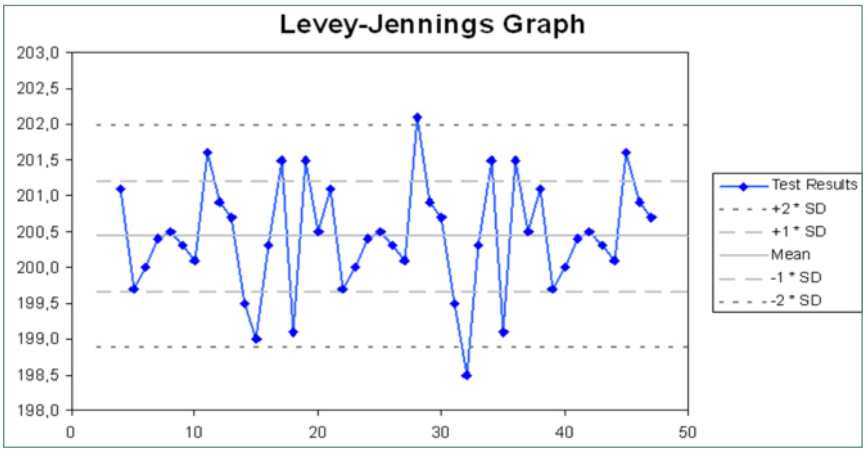
7.6.3 Use of Levey Jennings (LJ) chart

A Levey-Jennings chart is used to graph successive quality control data and gives a visual indication of whether a laboratory test is working well. It is based on two indicators, the mean and standard deviation (SD).

Construction of an LJ chart

The first step is to create a Levey Jennings chart, using optimal values (OCV) for mean and SD in perfect conditions by repeating the normal or abnormal control for a given parameter 20 times in one sitting. This chart is used to calculate and set the decision limits for accepting subsequent QC results as valid or invalid. A graph is constructed with the date plotted on the x-axis and the mean plotted on one side of the y-axis and one (1SD), two (2SD) and three (3SD) standard deviations plotted on the other side of the y-axis. Every time a control test is performed, a mark is made indicating how far the actual result was from the mean (the expected value for the control).

Figure 3 - Levey-Jennings chart sample (with results of daily QC plotted against the chart)
(Taken from :https://en.wikipedia.org/wiki/Laboratory_quality_control#/media/File:Levy-Jennings_SampleChart.png)



As a second step, actual values are added to the first set of values which reflect the different daily conditions including temperature and user. This will be done by using control values obtained during the previous 20 consecutive working days, which are then used to construct an LJ that closely reflects the real work situation. The final LJ decision limits are based on these 2 steps. Patient results can be issued during this time provided the QC results for the day have passed.

Table 11 - Summary of LJ chart basics

Reason for setting up an LJ chart for each test	• To make it possible to accept or reject the most recent results of quality control samples, based on the decision limits in the LJ chart and thereafter to accept or reject the actual patient results of the particular run if it falls within or beyond the decision limits of the LJ chart. • To test the condition of the analyser in the laboratory.
When to prepare a new LJ chart	• When you have validated a new analyser. • After major repair of an existing items of equipment. • When starting a new test or method. • When you receive a new batch of reagents or controls.
Who can set up the LJ chart	• Any technician who is responsible for performing biochemical tests in the laboratory.

Procedure to set up and use of the LJ chart	• Set up a LJ chart per test or method and per quality control level. • Establish the decision limits: mean ±1 standard deviation (SD), ±2SD and ±3SD. • Plot the preliminary LJ chart using the established decision limits • Use the LJ chart to plot the daily QC tests. • Interpret each new QC result in the LJ chart using Westgard rules. • After 20 daily controls, set up a new LJ chart including all the 40 controls. • Establish the new decision limits (mean, ±1SD, ±2SD, ±3SD). • Plot the definitive LJ chart and use it instead of the previous one.
Where to fill and store the QC results in the LJ charts	• In the laboratory where the analyser is located.

Use of the LJ Chart

Performing IQC and plotting the results on the LJ chart should be done on a daily basis.
Evaluation of the results should also be done immediately after plotting into the LJ chart. Evaluation and analysis are based on the Westgard rules.

Westgard Rules

The Westgard Rules are a set of rules that are the basis for evaluating the results of the QC runs. They are used to evaluate the data plotted in the LJ chart on whether the results of the QC run can be accepted or rejected. Depending on the rule, it can also detect whether the QC results are indicative of random or systematic error, which warrants further action.

The Westgard rules are written in short hand notation e.g. N_1

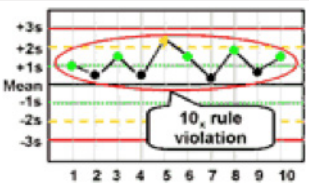
N represents the number of consecutive QC results to be evaluated

1 represents the statistical limit for evaluating the control observations

Thus 1_{3S} means that 1 control observation is unacceptable and has exceeded the ±3 standard deviation control limits.

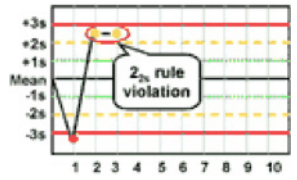
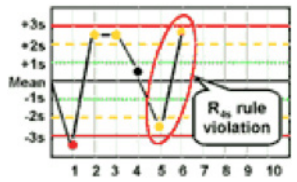
There are two types of Westgard rules: decision rules and warning rules.

- Warning rules
  When a warning rule is violated the new QC result can be accepted, but the analytical system has to be evaluated.

The 1_{2S} rule is a **warning rule**. This rule is a warning rule to trigger careful inspection of the analytical system. A warning is triggered when a one control measurement exceeds the mean +/-2SD.	
The 4_{1S} rule is a **warning rule** and requires inspection of the method/analyser. This rule is violated when 4 consecutive control measurements exceed the same mean +1SD or the same mean -1SD control limit.	
The 10_X rule is a **warning rule** and requires inspection of the method/analyser. The rule is violated when 10 consecutive control measurements fall on one side of the mean.	

(Reprinted with permission Westgard QC, Inc.)

- Decision rules
  When a decision rule is violated the new QC, result has to be rejected. Rejection means no patient results are issued before the problem is investigated and corrected.

The 1_{3S} rule is a **decision rule**. A run is rejected when a single control measurement exceeds the mean +/-3SD control limit.	
The 2_{2S} rule is a **decision rule**. It requires rejecting the run when 2 consecutive control measurements exceed the same mean +2SD or the same mean -2SD control limit.	
The R_{4S} rule is a **decision rule**. It requires to reject the run when in one Run with 2 QC-result (e.g. one QC-result from Serodos-normal and one QC-result from Serodos-path.) differ at least 4SD. The LJ-charts of both QC-levels have to be observed for this rule.	

(Reprinted with permission Westgard QC, Inc.)

7.6.4 Quality control procedures

Setting up Levey-Jennings charts

This procedure should be followed for every analyser that does not have a built in Levey-Jennings programme.

In MSF, these include the following instruments: Humalyser 2000 and Reflotron.

Step 1: Establishing the decision limits

Items needed

- Equipment: biochemistry analyser, automatic pipettes, timer
- Reagents: IQC material (Serodos level 1 and 2 or Precinorm and Precipath), test reagents (ALT, Urea, etc.)
- Stationery: Graph paper, note book, pencil, ruler, a computer with Excel, MSF LJ tool (contact your laboratory advisor for the excel file)
- Time: Allow 2 hours per LJ chart
- Staff: A laboratory technician with good skills in biochemistry. This can be the laboratory supervisor, the person most familiar with biochemistry or the QC manager.

Procedure

1. Switch on the analyser and allow it to reach ambient temperature for about 30 minutes.
2. At the same time, remove the test reagents from the refrigerator and allow them to reach ambient temperature – about 30 minutes.
3. Prepare your quality control material by following the manufacturer's instructions. Pay attention to the following:
   - Open the vial carefully to avoid any loss of material.
   - Use only distilled water and not water for injection to reconstitute the control.
   - Dispense the distilled water using an automated pipette. Do not use a syringe.
   - Dissolve the control by inverting the vial 10 times then leave at ambient temperature for 30 minutes to dissolve completely before using.
   - Do not shake or create foam as this interferes with complete dissolving of the reagents.

4. Once your equipment and reagents are ready, perform 20 measurements in one run per test for each control level: normal and abnormal. Handle the QC material in the same way as a patient's sample.
5. Record the results on a piece of paper or in a register.
6. Compare the results you obtained with the manufacturer's ranges in the instructions for use of the QC materials. If just one value is outside the given range, discard the one value and perform another one. If more than two values are outside the manufacturer's reference range, stop setting up the LJ chart and follow the procedures listed under 'troubleshooting' below.
7. Calculate the mean, standard deviation (SD) and coefficient of variation (CV) of the 20 values for each quality control level for each test or method, using the MSF provided Excel-based LJ tool.
8. Check whether the CV is within acceptable limits for the analyte of interest. Table below gives maximum optimal values of CVs for standard analytes used by MSF. If the CV is outside this range, follow the procedure below on troubleshooting.

Table 12 - Optimal CVs for biochemical analytes

Test	Maximum optimal CV%
Albumin	5 %
Alkaline phosphatase	10 %
Aspartate aminotransferase	10 %
Alanine aminotransferase	10 %
Bilirubin (total)	12 %
Creatinine	10 %
Glucose	7 %
Total protein	5 %
Amylase	5%
Urea	8%
Calcium	6 %
Potassium	5 %
Sodium	2%
Total Cholesterol	10%
LDL cholesterol	10%
HDL cholesterol	10%
Uric acid	10%
Triglycerides	10%
TSH	10%
ADA	10%
CRP	10%

Table 13 - Optimal CVs for haematological tests

Test	Maximum Optimal CV %
HB	1.43
Haematocrit	1.35
RBC	1.6
MCV	0.7
MCH	0.7
MCHC	1.06
RDW	1.8
WBC	5.73
Neutrophils	8.55
Eosinophils	10.5
Basophils	14.0
Lymphocytes	5.10
Monocytes	8.9
Platelets	4.6
MPV	2.15

Step 2: Print the LJ chart

Print the initial LJ chart.

Alternatively, you can draw an LJ chart on graph paper as follows:
1. Lay the graph paper on a flat surface with the long side facing you.
2. Label the graph with the name of the analyte and the level of control, for example “ALT Serodos normal” at the top.
3. Write the number of days 1-31 on the X-axis.
4. Using a ruler and pencil, draw a line in the centre of the paper.
5. Draw on the Y-axis a concentration scale of the analyte. Choose the concentration range so that it covers the concentration range from -4SD to +4SD.
6. Draw lines at the concentrations of +3SD, +2SD, +1SD, -1SD, -2SD and -3SD.

Step 3: Plot the LJ chart

For the next 20 days, run controls daily and enter the values on the LJ chart you printed or prepared. Enter these data on the MSF provided Excel-based LJ tool so that in total you have 40 values. Each laboratory staff who routinely runs chemistry samples from patients is in charge of this operation.

Step 4: Set up final LJ chart

Using the 40 values now obtained, recalculate the decision limits using the MSF LJ tool. Use this data now as your permanent LJ chart until the lot of the controls changes or major repairs are carried out on the equipment.

Run the controls daily and plot them on this chart.

Ability to plot the graph on the computer has been omitted deliberately as previous experience has shown that data are then filled in only at the end of the month which is not correct. An example of a filled in LJ chart is shown below for visualisation of how it should look.

Interpretation of the LJ chart

Each new result of a QC sample must be interpreted before the results of samples of that run are reported. The result of the QC sample must be plotted in the LJ chart and must be interpreted.

The interpretation should be done using the Westgard rules [see above].

In the past, the +/- 2SD of the mean values were used as acceptable limits. This is a simple method but has the disadvantage that more QC results are rejected than necessary. The reason is that statistically about 5% of the QC-results will have a result outside the +/- 2 SD-limits. To avoid false rejections and repeat sampling of otherwise acceptable QC results the Westgard rules are used to interpret the QC results.

7.6.5 Troubleshooting

What to do when the result of a control sample violates one of the decisions of the Westgard rules

1. Note the value of the control sample on the LJ chart. It is important that both 'pass' and 'fail' results are noted to enable proper analysis. Preferably use 2 different colours of pen to mark and differentiate the pass from the fail results.
   Repeat the control sample only once. Do not continue measuring the control serum repeatedly and hope that one of the consecutive values will not violate the Westgard rule. Because after many attempts the control values will fall statistically within the acceptable range but likely incorrect results will be issued for routinely measured samples as they are only measured once and for which the true or target values are unknown.
2. If the second result of the control sample does not violate the Westgard rule, note it on the LJ chart and start running patient samples for the day and consider your QC to have passed but keep track of the fail results. This means that you will have 2 values noted on the same day. Make an entry into the QC register what happened on that day.
3. If the second result also violates the Westgard rule, follow this step by step procedure to investigate the cause of the fault. Make sure to record in the QC register all steps that were taken and the outcome for further analysis.
   a. Check that the equipment was allowed to warm up.
   b. Check the reagents were allowed to reach ambient temperature.
   c. Check that the pipettes are set to the right measurement.
   d. Check that the programme of the test is still correct (refer to MSF laboratory manual chapter 9).
   e. Check that the tubes in use are clean.
   f. Check the light source and light filter of the analyser.
   g. Check the batch-numbers and shelf-lives of the reagents. A new batch of reagents can give a shift in the results of the QC samples. Set up new LJ-charts in the same way as for new QC sample batches.
   h. Check the instrument maintenance.
   i. Check the incubation temperature of the analyzer (for enzymes only).
   j. Check the temperature of the room for the non-enzymatic reactions.
   k. Check the sampling system.
   l. Check the preparation of QC materials.
   m. Check the calibration of the method.
4. If all these are acceptable, run a cleaning run on the equipment if possible.

5. Prepare a fresh sample using the same test kit and QC reagent as before.
6. If the control still violates an essential Westgard rule, restart the equipment.
7. Check the cold chain monitoring where you store the test kits and controls. Is the freeze tag marked 'X', or is the LogTag alarmed? Both these are signs that something went wrong with the stored kits. If yes, inform the person in charge of the cold chain and request fresh reagents from the medical store or warehouse.
8. If the cold chain has been maintained, prepare a fresh test kit.
9. Run the control again being careful to strictly follow the SOP.
10. If the control still falls outside± 2SD, contact your laboratory advisor. Communicate with the medical team that you will not be able to run chemistry tests for that day because you have a problem with the equipment.
11. If backup equipment is available you can start to use it after running controls. Other back up options could be referral to an external laboratory which could be a nearby MSF project or a previously assessed MoH or private laboratory, if available.

7.6.6 External Quality Assessment (EQA) Programme

As part of quality assurance, every laboratory is required to participate in an EQA programme for biochemistry. This usually involves receiving samples of undisclosed value from an external organization, analyzing them in the laboratory and sending the results back. The results are analyzed comparing the results of your laboratory against those or all other participating laboratories (benchmarking) and against the target value for the sample.

Reasons for enrolling in this system include:
- To get insight into the performance of your laboratory in relation to the performance of the other participating laboratories.
- To get information of the structural differences between the measured patient results and the real patient results (biases of the methods).
- For laboratories seeking accreditation, enrolment to EQA is a requirement.

There are many EQA programmes available. MSF currently uses the EQA programme from a collaboration between BIOLABO, which manufactures the reagents, and ASQUALAB (Assurance Qualité des Laboratoires de Biologie Medicale) which performs the statistical analysis of results. This is done by calculating the mean of all the laboratories per analyte and comparing it with the ASQUALAB target value. Each participating laboratory is then compared against the mean of all the laboratories. This EQA programme has about 700 participating medical laboratories, mainly located in France.

The details of this EQA programme can be found in Annex 12.

Please contact your laboratory advisor for details on how to enrol into this or any other EQA programme.

7.7 Haematology

The standard haematology analyser used in MSF laboratories is the Sysmex. We currently have two models in use: KX21N [ELAEHAAE11-] and the XP300 [ELAEHAAE1--] which is the newer version. The same QC procedure can be followed for both models. Expect minor differences in the referenced page of the respective manuals noted in this section.

Haematology controls

Sysmex supplies Eightcheck 3WP controls for use with their analysers. Only these controls should be used. The parameters which are included in the control are: WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, RDW-SD, RDW-CV, MPV, P-LCR and PDW.

There are 3 levels of controls available: Normal, High and Low. You need a minimum of two levels of controls: a normal and a pathological control (either low or high).

In programmes where the population is more prone to anaemia or blood transfusion, it would be more appropriate to use normal and low controls, whereas if the population is primarily paediatric, it would be better to choose normal and high controls.

Short shelf life: The controls comprise stabilised blood which cannot be stored for long periods. For this reason, the shelf life of the controls is 3 months only. This means that the supply of this reagent should be arranged in advance and in an organized way, such as placing an annual order and getting it delivered every 3 months rather than placing an order every 3 months. An example of the order schedule is given below.

Once opened, a vial can only be used for 7 days after which it must be discarded. This is one of the reasons why MSF supplies the 1.5ml vial instead of the 4.5ml vial.

Figure 4 - Sample shipment schedule for Eightcheck controls

sysmex
Sysmex Europe GmbH

Control Blood Order & Shipping Schedule 2017/2018

Product: Eightcheck-3WP

Lot No.	Order cut-off date	Shipping date	Lot Expiry date
6260	13-05-2016	26-09-2016	24-12-2016
6344	05-08-2016	19-12-2016	18-03-2017
7062	28-10-2016	13-03-2017	10-06-2017
7146	13-01-2017	05-06-2017	02-09-2017
7230	14-04-2017	29-08-2017	25-11-2017
7314	07-07-2017	20-11-2017	17-02-2018
8033	29-09-2017	12-02-2018	12-05-2018

For those sections or supply centres not supplying Eightcheck, an alternative (less desirable but more feasible) way of performing quality control for automated haematology analysers is described below.

For example:

- Keeping and recording the results of two or three blood samples from the previous day that gave “particular results” like low or high Hb, and/or WBC and comparing the results with the results of the day before.
- Comparing the results of the same patient obtained the same day or during different days.
- Comparing the results of some samples with a backup instrument (if available), or manually, or using different system, for example:
  - Red cell parameters: HemoCue for hemoglobin or Hematocrit centrifuge for hematocrit
  - White cells: manual count

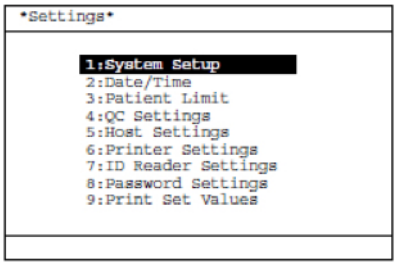
Remember that the results given by two different systems are generally not exactly the same, but it is good to note that, if one of the two is generally higher, you should expect the same difference with the controls.

Cold chain requirement: Another aspect to note is that, as they are fresh blood, the controls are denatured by freezing and therefore care must be taken during transportation. Very strict compliance to the cold chain protocol is required, including the use of pre-conditioned ice-packs. Controls must always be transported and kept in a cold chain (2-80C) with temperature monitoring devices installed. These controls can withstand temperatures above 80C quite well for short periods.

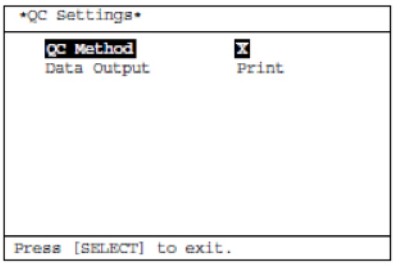
7.7.1 QC setting

The information below is contained in the 'Instrument set up' part of the manual. This is the first step before starting to do any QC, which is to select the QC method you want to use from the two available. We recommend to use the Levey-Jennings method.

1. Press the 'select' key on the analysis menu.
2. Use the cursor to move to select '6: Settings'.
3. Press 'enter'. The settings menu appears as below:



4. Use the cursor to select '4:QC Settings'.
5. Press the 'Enter' key. The current setting status is displayed. If you have a password, it might be required here.



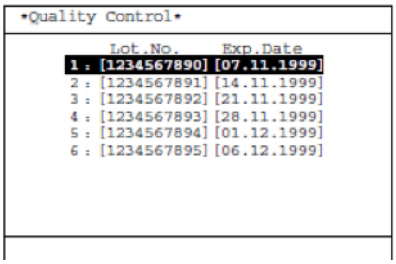
6. Select 'QC Method'. Choose the L-J control method. Press 'Enter'. The screen goes back to the 'QC Settings' screen.
7. Select the 'Data output' setting. Select 'Print'. Press 'Enter'.
8. When the settings are complete, press 'Select'. The change confirmation message appears. Press 'Set' to confirm followed by 'Enter' to execute the selected process.

7.7.2 QC Analysis

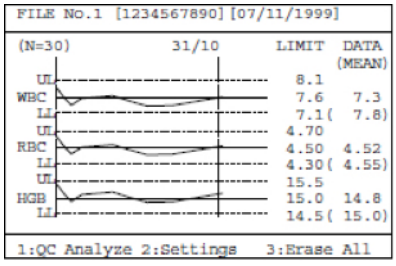
The analyser has a quality control programme which we recommend to use. Detailed information on how to use the QC programme is in the user manual. A summary version is provided here:

When you receive a new batch of controls

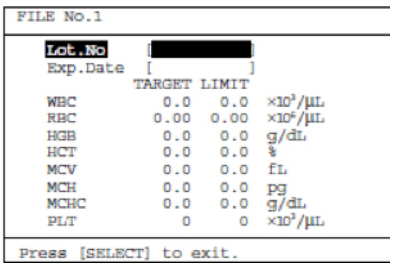
1. ▼▲ Press the 'Select' key when the analyser is in the ready status and use the keys to move the cursor to select 'Quality control'. Press enter. The QC file list appears.



2. Select any QC file on the list.

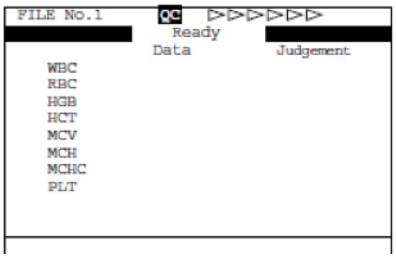


3. Erase all: To start a new QC, you have to erase the previous data.
4. Press '3' to select 'Erase all'. The 'Erase all' confirmation message will appear.
5. ◄► Use these keys to select 'Yes'.
6. Then select 'Execute" and press 'Enter' to execute the selected process.
7. Set the target values.
8. Select the QC file as described in 1 above.
9. Press '2' to select the settings. This QC file will appear.



10. Use ▼▲ to select Lot. No, Exp date and control parameter. Enter the values using the numeric keys. These can be found in the insert of your controls.
11. Use ◄► and select the target or limit in the control parameter. Enter the values using the numeric key. Press 'Enter' for the cursor to move to the next item. These can be found in the insert of your controls. There are 22 parameters which cannot all be listed on the same screen therefore use ▼▲ to move to the next screen and access the other parameters.

12. When all the values have been entered, press the ‘Select’ key. The setting confirmation message appears. Select ‘Set’.
13. Press ‘Enter’ to execute the selected process. A QC chart will be drawn only if the target and limit values are both entered correctly.
14. Execute the L-J control.
15. Remove the control vial from the refrigerator and allow to reach ambient temperature for at least 30 minutes. Do not put the vial containing the control on the roller mixer as this can cause cell lysis.
16. Display the QC chart screen as described in 1 above.
17. Press ‘1’ to select ‘1: QC analyze’. The L-J Control analysis screen appears.



18. Confirm that ‘Ready’ is displayed for QC analysis.
19. Mix the control sample by inverting the vial 10 times. Do not put the vial containing the control on the roller mixer as this can cause cell lysis.
20. Read the vial as you would a patient sample.

Results

1. The result of the analysis will be shown in 3 screens as follows:

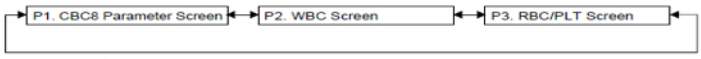
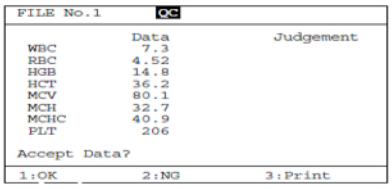
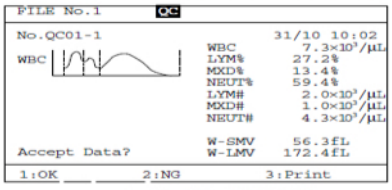


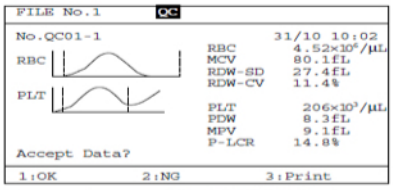
Figure 5-2-28: Page Selection in QC Analysis Result Screen



P1. CBC8 Parameter Screen

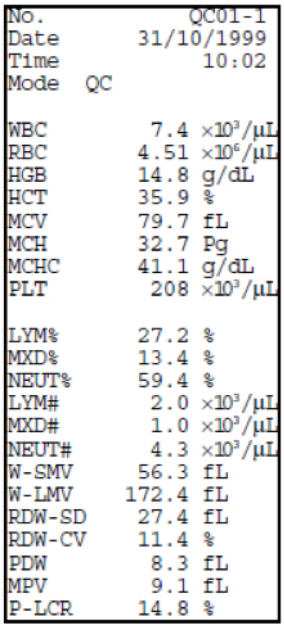


P2. WBC Screen



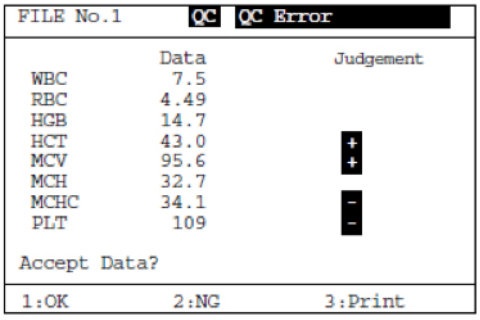
P3. RBC/PLT Screen

2. If the data are acceptable, press ‘1’ to confirm. Press ‘2’ to reject and ‘3’ to print.
   A sample print out is shown below:



No.	QC01-1	
Date	31/10/1999	
Time	10:02	
Mode	QC	
WBC	7.4	×10³/µL
RBC	4.51	×10⁶/µL
HGB	14.8	g/dL
HCT	35.9	%
MCV	79.7	fL
MCH	32.7	Pg
MCHC	41.1	g/dL
PLT	208	×10³/µL
LYM%	27.2	%
MXD%	13.4	%
NEUT%	59.4	%
LYM#	2.0	×10³/µL
MXD#	1.0	×10³/µL
NEUT#	4.3	×10³/µL
W-SMV	56.3	fL
W-LMV	172.4	fL
RDW-SD	27.4	fL
RDW-CV	11.4	%
PDW	8.3	fL
MPV	9.1	fL
P-LCR	14.8	%

3. For those values that fell beyond the control limits, a ‘+’ or ‘-‘ is shown under the judgement column as below:



FILE No.1 QC QC Error

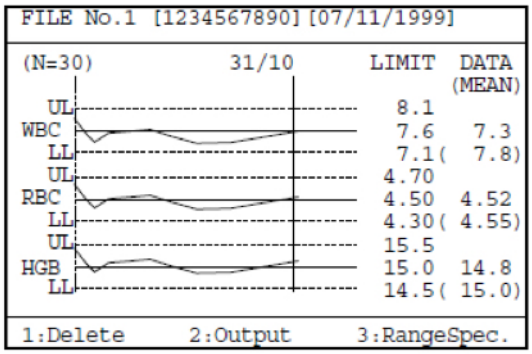
	Data	Judgement
WBC	7.5	
RBC	4.49	
HGB	14.7	
HCT	43.0	+
MCV	95.6	+
MCH	32.7	
MCHC	34.1	-
PLT	109	-

Accept Data?

1:OK 2:NG 3:Print

If this appears, press ‘2’ to reject. Run the control again after proper mixing. If this screen still appears, follow the troubleshooting guide below.

Analyse results



FILE No.1 [1234567890] [07/11/1999]

		LIMIT	DATA (MEAN)
(N=30)	31/10		
	UL	8.1	
WBC		7.6	7.3
	LL	7.1	(7.8)
	UL	4.70	
RBC		4.50	4.52
	LL	4.30	(4.55)
	UL	15.5	
HGB		15.0	14.8
	LL	14.5	(15.0)

1:Delete 2:Output 3:RangeSpec.

Explanation of the data:

The data are displayed in a standard LJ chart model with the mean as the bold line and the ± 3SD being the upper and lower limits respectively. These are the values calculated by the instrument according to what you entered from the control box insert.

The left column identifies the test (WBC for White blood cells, RBC for Red blood cells and HGB for Haemoglobin, as well as the limits (UL for Upper Limit and LL for Lower Limit).

- the +3SD (Upper Limit) for the respective tests, in this case 8.1 (WBC), 4.70 (RBC) and 15.5 (HGB)
- the mean value, in this case 7.6 (WBC) , 4.50 (RBC) and 15.0 (HGB)
- the -3SD (Lower Limit), in this case 7.1 (WBC), 4.30 (RBC) and 14.5 (HGB)

In the right column, DATA is the value (not in parenthesis) for the mean of the control measured for that day (in this case, 7.3 (for WBC), 4.52 (for RBC) and 14.8 (for HGB). In case there is a repeat measurement of the control, the value will reflect the mean between the values obtained from the repeat measurements.

(MEAN) is the second value (in parenthesis), and is the mean value of DATA calculated during the last 30 days.

The chart displays the last 30 readings and allows us only to check that the control value of the day does not fall outside the ±3SD lines.

In the event a bias is noticed, follow the troubleshooting guide below.

For applying the Westgard rules, draw the Levey-Jennings chart by yourself as explained above, using the data in the instrument.

1. Press ‘Select’ in QC screen chart. The QC file list returns.
2. Press the ‘Select’ key again to return to the analysis key.
3. The analyser can now be used for patient samples.

In the event a bias is noticed, follow the troubleshooting guide below.

7.7.3 Troubleshooting

Table 14 - Troubleshooting guide for semi-automated systems

Main causes	Actions
Insufficient mixing of control sample	Allow the control to come to ambient temperature before use. Mix the control by inverting it at least 10 times. Do not use the roller mixer as this may cause cell lysis.
Improper aspiration of control material	Only remove the control samples from the probe after the buzzer sounds two times ‘beep, beep’ and the word ‘analyzing’ is displayed on the L-J control screen.
Expired control material	Control material will deteriorate after expiry and will not read within the expected range. Please note that ‘expiry’ also means one week after opening. The platelet value is usually the first to deteriorate in the control and is your best indicator that the problem you are having is an expired QC vial. Use a new control vial from the same batch.

Main causes	Actions
Control frozen	Freezing of the sample will cause lysis. Check if the Freeze tag has alarmed or if the temperature fell below 00C on the data logger.
Instrument failure	If the causes mentioned above have been excluded, the instrument may be due for maintenance. Run a cleaning cycle once using 'cell clean' and repeat the measurement. If the results are still out of range, contact the person in charge of biomedical devices for that day. Let the doctors and nurses know you will be reverting to a manual method that day and to limit requests to urgent ones depending on laboratory capacity. The measuring chambers are different for each parameter, so, for example, the chamber for Hb may be faulty (spectrophotometry) but not the other chamber that measure red cells, white cells and platelets. It means that there is the possibility that you will be able to provide one of the parameters, but not all of them.

In case the stabilized blood controls are not available, the calibration of the red cell indices can be checked by testing a normal clinical sample (from a healthy individual) using a hematocrit centrifuge or on a haemoglobinometer (by spectrophotometry preferably HemoCue to ELAEHAEE3-- HAEMOGLOBIN PHOTOMETER (HemoCue Hb 301) tropicalized.

If manual microscopy is reliable, white blood cell count and differential from a healthy individual can be used to compare with the results given by the counter.

The analyser can now be used for patients' samples.

Beware that MCHC on clinical samples cannot exceed 38 g/dL. Hyperchromia does not exist in EDTA blood that has been correctly anticoagulated immediately after blood drawing. In case MCHC is > 38 g/dL, Hb spectrophotometer and red blood cell potentiometer calibrations are needed.

7.8 Quality control of hand held analysers

7.8.1 Introduction

Hand held analysers, also known as point of care (POC) analysers, refer to the small sized, easy to use equipment. They can be used outside the laboratory by medical professionals, often at the patient's bedside. These users, therefore, might not be as familiar with laboratory quality control procedures as laboratory staff.

We propose a more practical approach to quality control for these devices as described in this section.

It is very important that the laboratory supervisor takes the responsibility for all testing carried out in the project, both in the main laboratory and in the remote outreach sites by organising periodic visits to check the reliability of testing procedures and helping to troubleshoot procedures.

Table 15 - List of handheld analysers used in MSF

Equipment	Equipment check Available	Internal control solutions available
ELAECCHE1-- iSTAT (when it is used at the bedside of the patient)	Yes. Electronic simulator.	Yes. Low, normal and high per cartridge.
NycoCard II Reader	No	Yes. Positive and negative controls.
ELAEGLUE2-- Nova Statstrip Xpress	No	Yes. Low, Normal and High
Nova StatSensor® Creat	No	Yes. Low, Normal and High
ELAELACE2-- Accutrend® Plus	No	Yes. Low and High
ELAEHAEE3—HemoCue 201/301	No	Yes. Low, normal and high
ELAECD4E1—Pima CD4 analyser	Yes. Check cartridge	No
ELAECCHE8— HemoCue 501 HBA1c	Yes. Daily and monthly check cartridges	Commercially available but the shelf life is too short for MSF to be able to supply it.

NOTE: The procedure described here can be applied to the i-STAT only if the instrument is used always outside the laboratory (at patients' bedside). If it is used in the laboratory, an LJ chart needs to be prepared, as described in the previous section.

7.8.2 QC Procedures

When controls are supplied for the analyser

Run the control sample following the same procedure as for a patient sample daily and compare the results in the product insert sheet.

When no controls are supplied for the analyser

In the case no controls are supplied by the supplier, there will usually be a "machine check" or control cartridge available that should be run once daily (e.g. Check Cartridge Pima) unless the manufacturer recommends to do it more often. Results of the check must be recorded in the quality control record (see below).

7.8.3 Reporting

An example of a reporting format is shown in Table 16. This shows the information that is important to record after doing a control for a POC A blank format is provided at the end of the manual, but the information can also be noted down in the patient register on the day the control is performed. It is important to trace back control results if there is a doubt about the patient's results.

Troubleshooting: What to do when a test kit does not pass QC?

1. Repeat the QC using a different test strip or cartridge cuvette. Be careful to follow the procedure strictly.
2. If the test still fails, repeat using a strip from a different batch.
3. If the test still fails, repeat using a control sample from a different batch.
4. If this still fails, then contact your medical team leader and/or laboratory advisor or referent for further action.

Table 16 - Sample of a reporting format for hand held analysers

MSF CODE:	**MSF DESCRIPTION:**
ELAEGLUT211	(glucometer Nova StatStrip) CONTROL SOL. low, 4ml vial 46947
ELAEGLUT212	(glucometer Nova StatStrip) CONTROL SOL. normal 4ml vial46949
ELAEGLUT213	(glucometer Nova StatStrip) CONTROL SOL. high, 4ml vial 46948

Date	**Batch number of strip or cartridge**	**Control Batch number**	**Check cartridge/ strip**	**Low Control 2-4 mmol/L**	**Normal Control 6-9 mmol/L**	**High Control 15-25 mmol/L**	**Conclusion control samples**	**Action taken**	**Run by**
6-9-2015	D4130LGS	E23651	–	3mmol/L	8mmol/L	20mmo/L	Pass	None	Jane Doe
13-9-2015	D4130LGS	E23651	–	4mmol/L	10mmol/L	26mmol/L	Fail	• Run the control again. Same result. • Informed supervisor. • Changed batch of controls • Results now within range	John Doe

Some of the common errors made by users of hand held analysers:

Sample collection
- Not wiping away the disinfectant or allowing to it air-dry pre-puncture results in dilution of the blood.
- Too much squeezing of the finger to yield a sample results in mixing of the sample with tissue fluid.
- Use of blood sample from the IV-line result in mixing of the sample with IV fluid.

Procedure
- Not running the controls.
- Improper filling of the cartridge or strip.
- Improper insertion of the cartridge or strip into the analyser.
- Inadequate cleaning.

To address this, the laboratory supervisor should:
- Train each (new) person using the analyser using the standard operating procedures.
- Supervise all people using the analyser regularly using the supervisor's checklist (refer to the MSF Laboratory manual, Annexes – Supervision checklists.
- Ensure that quality control tests are run daily.

Not running the controls does not lead to errors, it means that you cannot guarantee the quality (accuracy and precision) of your results.

8. Quality improvement

8.1 Introduction

Quality improvement (QI) is a formal approach to the analysis of performance and systematic efforts to improve it.

8.2 Problem list

The first step to continuous quality improvement is to list down the problems the laboratory is currently facing, and the non-conformities faced. These problems can be gathered from the following places:

- Interpretation of quality control results
- Reviewing the incident report book
- Review of the equipment maintenance log
- Feedback received from the users of the laboratory – clinical team, patients, supply department
- Feedback from laboratory staff
- Observations made by the laboratory supervisor
- Evaluating some of the corrective actions that have been tried before but have not worked

For each of the main problems identified, make a detailed plan: what went wrong, how likely it is to go wrong again in the future, consequences if it goes wrong, preventative actions, control steps and corrective actions that can be implemented. Involve the laboratory staff as well as your medical team leader or laboratory referent in coming up with ideas for improvement. If there are many things that need to be addressed, a list of priorities should be made.

8.3 Making an improvement plan

Small changes to operations are made daily, often without lengthy or formal planning, to make processes work better. There is no need to document these sorts of activities in a quality management plan as they would increase the workload quite heavily. The plan should focus on major quality improvement activities that extend over longer periods of time.

- Priority 1: Activities that cause risk to patients or staff
- Priority 2: Activities that can be improved with little or no resources (money, time, staff)
- Priority 3: Activities that make the laboratory work more efficiently

With the analysis you made, the input from staff and the prioritisation, prepare an improvement plan document.

The actions should be the adaptation of SOPs for the procedures in which the preventive and corrective actions and control steps are implemented, and the tutoring of staff members in implementing the actions and controls (explaining why and how the actions and controls are implemented).

Information that should be contained in the plan include:

- Problem to be addressed
- How it is going to be addressed
- People involved
- Expected time scale
- Expected cost

8.4 Communication

Share the improvement plan document with the staff. This is best done first as a group and then more in detail with the staff that are specifically involved.

8.5 Implementation

Start to carry out the activities as listed in your plan. Keep the staff updated by adding the progress report as part of the laboratory weekly meetings.

Seek help from the medical team leader or your laboratory advisor or referent if you are facing challenges.

8.6 Documentation

Evidence of plan implementation includes meetings and minutes of the quality committee, the results of on-going measurements, and any documentation related to complaint investigation, problems, and adverse events. These records, along with the plan itself, should be available to MSF laboratory advisors carrying out project visits, as well as external inspectors.

8.7 Continuity of improvement

By nature, quality improvement is a continuous process and therefore these steps will have to be followed continuously for the entire duration of a laboratory's operation.

Figure 5 - Quality improvement process

9. References

MSF guideline: Supply of Drugs and Medical Supplies and Management of Pharmacies, 2nd edition, 2008.

MSF Laboratory manual, 2016.

WHO Guidance on Regulations for the Transport of Infectious Substances 2013-2014.

WHO SEARO Laboratory quality standards and their implementation.

WHO Guide for the Stepwise Laboratory Improvement Process Towards Accreditation in the African Region, 2010.

WHO how malaria RDT's work, 2015.

WHO guide on Use of anticoagulants in diagnostic laboratory investigations 2002.

IFCC, Fundamentals for External Quality Assessment, J.Y. et al. Verification of hematology analysers. Int. J. of Hematology, 2016.

Interpretation of EQA results, WEQAS 2018.

External Quality Assessment for AFB Smear Microscopy, PHIL, CDC, IUATLD, KNCV, RIT, WHO.

District Laboratory practice in tropical countries, Monica Cheesbrough, 2nd edition, Part 2.

Biological Variation of Laboratory Analytes Based on the 1999–2002 National Health and Nutrition Examination Survey, US CDC, 2010.

Desirable Biological Variation Database specifications, Westgard database, 2014.

Sample storage guideline, Royal Collage of Pathologists (RCPATH), UK.

Factors affecting quality of laboratory services in public and private health facilities in Addis Ababa, Ethiopia, Electronic journal of the IFCC (eJIFCC), 2017.

Annexes

Annex 1. Diagnostic packages for MSF programs

MSF Diagnostic Network in consultation with the diagnostic package team - August 2017

1. Background

With each new project opening, the implementation of diagnostic tools is discussed in great detail. Often this is a time consuming and non-standardised process.

In order to guide this process more efficiently the MSF Diagnostic Network (Laboratory and Diagnostic Imaging Working Groups) has consulted health and medical advisors from all MSF opera-tional sections to define diagnostic packages per level of healthcare. The diagnostic packages use diagnostic tools which are approved as standard items for use in MSF by the Medical Directors (MSF Catalogue, Volume 5: Laboratory equipment and reagents and MSF Catalogue, Volume 2B Medical equipment: Chapter 3 - Diagnostic Imaging equipment).

It is assumed that staff carrying out diagnostic testing (incl. test interpretation) is trained and supervised on a regular basis. This training and supervision capacity must be planned for in each program. When moving from one diagnostic package to another, e.g. from basic to recommended, the experience of the staff available needs to be taken into consideration and if necessary additional training and supervision be provided.

In addition, implementing diagnostic tests includes implementing quality control; the detailed procedures can be found in the MSF Laboratory Manual (2016) and the MSF X-ray Manual (2014) and MSF X-ray equipment user maintenance SOPs (2016).

The diagnostic packages consist of three different approaches in order to allow for flexibility depending on program aims, but also to ensure that basic standard services are coherently implemented across MSF projects.

- Basic diagnostic package: the minimum diagnostic package that should be available (according to level of health care) in MSF programs.
- Recommended diagnostic package: the medium level of diagnostic package.
- Desirable diagnostic package: the ideal diagnostic package.

We developed these three diagnostic packages for the following MSF program types, with the following human resource assumptions:

- Basic health care centre or mobile clinic with no laboratory services.
  - Nurses and/or clinical officers/MDs carry out diagnostic testing.
  - No specialized laboratory staff is routinely present.
- Primary health care clinic with a small laboratory.
  - National laboratory staff (junior and/or senior laboratory technician) is present.
- Hospital with a general in-patient and out-patient department.
  - Senior laboratory technician is present (national or expat).
  - Radiographer / X-ray technologist present.

In addition recommendations are given for the following more specialised program services (also called add-ons):

- Malnutrition
- Maternal and/or child health care (obstetrics/ANC/neonatal care)
- Surgery incl. visceral, orthopaedics, obs/gyn and trauma
- Multi-drug resistant tuberculosis (MDR-TB)
- Neglected tropical diseases: Chagas, kala azar, sleeping sickness and snake bites

The diagnostic recommendations for HIV and non-communicable diseases (hypertension/ cardiovascular disease, diabetes types 1 and 2, asthma/COPD, epilepsy, thyroid disease) are incorporated in the standard packages.

Note: The diagnostic packages do not always provide information on which concrete diagnostic tool should be used. This choice highly depends on the workload, staff capacity, registration in country etc. Thus, the selection of the concrete tool may still need to be discussed with the specialised advisors (e.g. laboratory advisor or imaging adviser) of each section. For example: if glu-cose is recommended this document may not provide the information on which glucose analyser should be used (e.g. handheld analyser or a laboratory based clinical chemistry analyser).

Implementation

The diagnostic package should be reviewed with medical advisors, MedCos, laboratory and imaging advisors of all current programs. All programs should at least have the basic requirements met. If more is required a gradual increase in the service should be planned.

When opening new programs or entering an existing Ministry of Health facility, it should be discussed with the respective advisors which package (or part of packages) will be implemented in the program in the long run.
This should be done once a service assessment of the facility has been done. This information should then be used to guide decision making for what services / packages are required.

The aim is to make resources available to have at least the basic package implemented; this is the responsibility of the medical advisors together with the ops team. Moving towards the rec-ommended or desirable package(s) depends on the program's strategy, aim, capacity and re-sources available.

Special note on ultrasound implementation: when making ultrasound available in MSF programs, next to the purchase of the machine and accessories, a training and implementation plan must be made. Ultrasound competencies are not acquired easily. Thus, it requires a staged implementation / training process to integrate ultrasound exams into routine clinical practice.
How US skills can be integrated in clinical pathways / diagnostic algorithms and how results are then clinically utilized must be considered. This involves training, re-training and supervision / quality assessment which must be made available to respective staff before they can carry out ultrasound independently.
In order to facilitate ultrasound implementation, MSF will hire ultrasound specialists to facilitate training and re-trainings.

Contact us if you have any questions: diagnostic-network@msf.org and/or the laboratory and im-aging advisor of your OC.

2. Diagnostic packages per level of health care

2.1 Diagnostic package – Primary health care centre / mobile clinic

BASIC HEALTH CARE CENTER / MOBILE CLINIC NOTES: THE DEFINITION OF MOBILE CLINIC IS A CLINIC WITHOUT ANY FURTHER SPECIALISATION BUT INCLUDES ANC. NURSES AND/OR CLINICAL OFFICERS/MEDICAL DOCTORS CARRY OUT DIAGNOSTIC TESTING. NO SPECIALIZED LABORATORY STAFF IS ROUTINELY PRESENT.					
DX AREA		**BASIC/ MINIMUM**	**RECOMMENDED/ MEDIUM**	**DESIRABLE/ IDEAL**	**NOTES**
HAEMATOLOGY	Anaemia: Hb, Hct red cell indices	Hb (POC)	Hb (POC)	Hb (POC)	To identify patients in need of transfusion.
	Infection: WBC count, differentiation	No	No	No	
	Coagulation: Thrombocytes	No	No	No	
BLOOD TRANSFUSION	Direct transfusion	No	No	No	
	Blood bank	No	No	No	
PARASITOLOGY	Malaria: RDT, smear	RDT	RDT	RDT	
	Microfilariae: Skin snip oncho, blood examination	No	No	No	
	Genito-urinary tract: Trichomonas vag., schisto	No	No	No	
	Intestinal tract: microscopy, Kato-Katz	No	No	No	
BACTERIOLOGY	General: gram	No	No	No	
	Meningitis: Pastorex, Pandy, CSF white cell count, CSF chemistry, TI for transport	No	No	No	Patient should be referred to hospital or nearest healthcare centre for a safe LP treatment. Pastorex should only be used for outbreak investigation and not for individual patient diagnosis. The hospital lab can carry out other investigations.
	UTI: dipstick, sediment	Dipstick	Dipstick	Dipstick	
	STI: Neis. gram, Syph RDT, Syph RPR	No	Syph RDT	Syph RDT	According to ANC guidelines.
	Cholera: RDT, Cary-Blair	No	No	No	Patient would be referred and treated on the basis of clinical symptoms.
	TB: ZN, bleach, Auramine, Xpert, culture	No	Sputum collection	Sputum collection and smear preparation including fixation	If referral possibilities are available.
	EPTB: Rivalta, ADA	No	No	No	Suspected patients for EPTB should be referred.
VIROLOGY	HIV: RDTs, EID, CD4, VL	No	RDT	RDT	Compulsory as minimum in programs with ANC (see additional maternal). 3 RDTs are required to build a Dx algorithm.
	Hepatitis; HBV RDT, HCV RDT, HEV RDT	No	No	No	As medium in programs with ANC (see additional maternal).

BASIC HEALTH CARE CENTER / MOBILE CLINIC NOTES: THE DEFINITION OF MOBILE CLINIC IS A CLINIC WITHOUT ANY FURTHER SPECIALISATION BUT INCLUDES ANC. NURSES AND/OR CLINICAL OFFICERS/MEDICAL DOCTORS CARRY OUT DIAGNOSTIC TESTING. NO SPECIALIZED LABORATORY STAFF IS ROUTINELY PRESENT.					
DX AREA		**BASIC/ MINIMUM**	**RECOMMENDED/ MEDIUM**	**DESIRABLE/ IDEAL**	**NOTES**
	Dengue: RDT	No	No	No	Current dengue RDT use is for investigation of suspected outbreak only and expat health.
MYCOLOGY	General : KOH, gram	No	No	No	
	HIV related: Cryp RDT	No	No	No	
CLINICAL CHEMISTRY	Lab based: Humalyzer test, Reflotron, Piccolo	No	No	No	
	PoC: iSTAT, Piccolo, crea, glucose, lactate	Glucose (glucometer)	Glucose (glucometer)	Glucose (glucometer), creatinine (handheld analyser)	Detection of hypo- and hyperglycaemia. Creatinine for NCDs. iSTAT heavily discouraged for operative purposes in this kind of settings.
	Coagulation: PT/ INR, PTT, D-Dimer	No	No	No	
	Urine: dipstick	Yes	Yes	Yes	
	Pregnancy: dipstick	Yes	Yes	Yes	
	ELISA: TSH	No	No	No	
	HbA1c	No	No	Yes	Only if diabetes patients are seen regularly
SPECILAIZED DX NTD	Kala azar: RDT, microscopy, DAT	RDT	RDT	RDT	In endemic areas. In vertical programs other tests to be added
	HAT: CATT, CATT dilution, microscopy, Woo, mAECT, CSF exam	CATT and CATT dilution	CATT and CATT dilution	CATT and CATT dilution	Maybe replaced with RDTs later. In endemic areas. In vertical programs other tests to be added.
	Chagas: RDT, IHA, ELISA	RDT	RDT	RDT	In endemic areas. In vertical programs other tests to be added.
IMAGING	X-ray	No	No	No	
	Ultrasound	No	No	Yes	BHC - Ultrasound for ANC and AST would be beneficial.
	C-arm	No	No	No	Not required / appropriate.
OTHER DX EQUIPMENT	BP cuff	Yes	Yes	Yes	
	Stethoscope	Yes	Yes	Yes	
	Thermometer	Yes	Yes	Yes	
	Otoscope	Yes	Yes	Yes	
	Ophthalmoscope	No	Yes	Yes	
	Pulse oximeter	No	Yes	Yes	
	ECG	No	No	No	
	Foetal heart doppler	No	Yes	Yes	As rest of ANC
	Audiometer	No	No	No	
	Monofilament	No	No	Yes	If diabetes patients seen regularly.
	Peak flow meter	No	Yes	Yes	If asthma patients seen regularly.

2.2 Diagnostic package – Primary health care clinic with small laboratory

PRIMARY HEALTH CARE CLINIC WITH SMALL LABORATORY NOTES: THE LABORATORY STAFF PRESENT IS NATIONAL STAFF (JUNIOR AND/OR SENIOR). MICROSCOPE IS PRESENT JUST IN THE RECOMMENDED AND DESIRABLE PACKAGE, NOT IN THE BASIC PACKAGE.					
DX AREA		**BASIC/ MINIMUM**	**RECOMMENDED/ MEDIUM**	**DESIRABLE/ IDEAL**	**NOTES**
HAEMATOLOGY	Anaemia: Hb, Hct red cell indices	Hb (POC)	Hb (POC)	Hb (POC)	
	Infection: WBC count, differentiation	No	No	No	Very subjective examinations. Assumed lab staff not well enough trained to sustain quality and reliable examinations.
	Emmel test	No	Yes	Yes	
	Coagulation: Thrombocytes	No	No	No	
BLOOD TRANSFUSION	Direct transfusion	No	No	No	
	Blood grouping	Yes	Yes	Yes	ANC
	Blood bank	No	No	No	
PARASITOLOGY	Malaria: RDT, smear	RDT	RDT	RDT and microscopy	Only if very good microscopist
	Microfilariae: Skin snip oncho, blood examination	No	No	Yes	Where endemic/ if geographically relevant.
	Genito-urinary tract: Trichomonas vag., schisto	No	No	Schisto	Context dependent
	Intestinal tract: microscopy, Kato-Katz	No	Stool microscopy	Stool microscopy	Context dependent
BACTERIOLOGY	General: gram	No	No	Yes	Gram for meningitis
	Meningitis: Pastorex, Pandy, CSF white cell count, CSF chemistry, TI for transport	No	No	Yes for TI, Pandy, CSF white cell count and chemistry (no Pastorex)	If lab staff sufficiently trained and equipment available. Glucose requires a spectrophotometer so only applicable in this condition.
	UTI: dipstick, sediment	Dipstick	Dipstick	Dipstick	
	STI: Neis. gram, Syph RDT, Syph RPR	Syph RDT	Syph RDT, RPR	Syph RDT, RPR	
	Cholera: RDT, Cary-Blair	No	No	No	
	TB: ZN, bleach, Auramine, Xpert, culture	Sputum collection	Sputum collection and smear preparation including fixation	Complete ZN or Auramine	Xpert for specialized program.
	EPTB: Rivalta, ADA	No	No	No	
VIROLOGY	HIV: RDTs, EID, CD4, VL	RDT	RDT, CD4 and sample collection for EID and VL	RDT, CD4 and sample collection for EID and VL	CD4 only in programs with high HIV case load. [Potentially portable Xpert (OMNI) available in the future for EID/ VL.].
	Hepatitis; HBV RDT, HCV RDT, HEV RDT	No	HbsAg, HCV RDT	HbsAg, HCV RDT	HCV RDT according to prevalence
	Dengue: RDT	No	No	No	Current dengue RDT use is for investigation of suspected outbreak only and expat health.

PRIMARY HEALTH CARE CLINIC WITH SMALL LABORATORY NOTES: THE LABORATORY STAFF PRESENT IS NATIONAL STAFF (JUNIOR AND/OR SENIOR). MICROSCOPE IS PRESENT JUST IN THE RECOMMENDED AND DESIRABLE PACKAGE, NOT IN THE BASIC PACKAGE.					
DX AREA		**BASIC/ MINIMUM**	**RECOMMENDED/ MEDIUM**	**DESIRABLE/ IDEAL**	**NOTES**
MYCOLOGY	General : KOH, gram	No	No	No	
	HIV related: Cryp RDT	No	Yes, CrAg in blood	Yes, CrAg and Indian Ink also in CSF	
CLINICAL CHEMISTRY	Poc or small benchtop analysers: Reflotron, Piccolo & PoC analysers	No	No	Reflotron and Piccolo possible. For NCDs: ALT, cholesterol, potassium	Access to chemistry depending on context. No larger chemistry analysers e.g. Humalyzer. Note: Reflotron strips will still be supplied in coming years. Currently Piccolo only alternative. Market review ongoing.
	PoC: iSTAT, Piccolo, crea, glucose, lactate	Glucose (glucometer)	Glucose (glucometer), creatinine (handheld analyser)	Glucose (glucometer), creatinine (handheld analyser)	
	Coagulation: PT/ INR, PTT, D-Dimer	No	No	PT/INR for NCDs	
	Urine: dipstick	Yes	Yes	Yes	
	Pregnancy: dipstick	Yes	Yes	Yes	
	ELISA: TSH	No	No	No	
	HbA1c	No	Yes	Yes	Only if diabetes patients are seen regularly
SPECILAIZED DX NTD	Kala azar: RDT, microscopy, DAT	RDT	RDT	RDT	In endemic areas. In vertical programs other tests to be added.
	HAT: CATT, CATT dilution, micros-copy, Woo, mAECT, CSF exam	CATT and CATT dilution	CATT and CATT dilution	CATT and CATT dilution	Maybe replaced with RDTs later. In endemic areas. In vertical programs other tests to be added.
	Chagas: RDT, IHA, ELISA	RDT	RDT	RDT	In endemic areas. In vertical programs other tests to be added.
IMAGING	X-ray	No	No	No	Not required for small BHC
	Ultrasound	No	Yes	Yes	US for range of conditions (ANC, FAST) and assist referral. Priority to be given to hospital programs; once US is established at hospital level expansion to lower clinical level.
	C-arm	No	No	No	Not required for small BHC
OTHER DX EQUIPMENT	BP cuff	Yes	Yes	Yes	
	Stethoscope	Yes	Yes	Yes	
	Thermometer	Yes	Yes	Yes	
	Otoscope	Yes	Yes	Yes	
	Ophthalmoscope	Yes	Yes	Yes	
	Pulse oximeter	Yes	Yes	Yes	
	ECG	No	No	Yes	For AMI and *drugs side;effects
	Fetal heart doppler	Yes	Yes	Yes	As rest of ANC
	Audiometer	No	No	No	
	Monofilament	No	No	Yes	If diabetes patients seen regularly.
	Peak flow meter	No	Yes	Yes	If asthma patients seen regularly.
	Spirometry	No	No	Yes	If asthma/COPD patients seen regularly.

2.3 Diagnostic package – Hospital

HOSPITAL WITH GENERAL IN-PATIENT AND OUT-PATIENT DEPARTMENT NOTES: HOSPITAL DEFINITION: IPD INCLUDES MEDICAL DOCTORS. SENIOR LABORATORY TECHNICIAN IS PRESENT (NATIONAL OR EXPAT). RADIOGRAPHER(S) (NATIONAL) ARE PRESENT IF AN X-RAY DACILITY IS REQUIRED.					
DX AREA		**BASIC/ MINIMUM**	**RECOMMENDED/ MEDIUM**	**DESIRABLE/ IDEAL**	**NOTES**
HAEMATOLOGY	Anaemia: Hb, Hct, red cell indices	Hb	Hb	Hb and Hct	
	Infection: WBC count, differentiation	WBC count, differentiation	WBC count, differentiation	WBC count, differentiation	
	Emmel test	No	Yes	Yes	
	Coagulation: Thrombocytes	No	Thrombocytes	Thrombocytes	
BLOOD TRANSFUSION	Blood grouping	Yes	Yes	Yes	ANC
	Direct transfusion	Yes	Yes	Yes	
	Blood bank	No	Yes	Yes	Must be related to context (for example high malaria cases in need for transfusion and/or surgery…).
PARASITOLOGY	Malaria: RDT, smear	RDT and smear	RDT and smear	RDT and smear	Lab must have capacity for microscopy
	Microfilariae: Skin snip oncho, blood examination	No	Blood exam and skin snip	Blood exam and skin snip	Where endemic
	Genito-urinary tract: Trichomonas vag., schisto	No	Schisto and Trich. vag	Schisto and Trich. vag	According to context
	Intestinal tract: microscopy, Kato-Katz	Stool microscopy	Stool microscopy, Kato-Katz	Stool microscopy, Kato-Katz	According to context
BACTERIOLOGY	General: gram	Gram	Gram	Gram	
	Meningitis: Pastorex, Pandy, CSF white cell count, CSF chemistry, TI for transport	Full package	Full package	Full package	Use of Pastorex and TI only for outbreak investigation. Glucose requires a spectrophotometer so only applicable in this condition.
	UTI: dipstick, sediment	Dipstick	Dipstick	Dipstick	Sediment is not superior over dipstick for diagnosis of bacterial UTIs. Only sediment of stock rupture of dipsticks.
	STI: Neis. gram, Syph RDT, Syph RPR	Syph RDT and RPR, Gram	Syph RDT and RPR, Gram	Syph RDT and RPR, Gram	Gram for Neisseria only in men because sensitivity in women is too low.
	Cholera: RDT, Cary-Blair	Cary-Blair (RDT when approved test available)	Cary-Blair (RDT when approved test available)	Cary-Blair (RDT when approved test available)	Carry Blair (and RDT when available) as EPREP.
	TB: ZN, bleach, Auramine, Xpert, culture	ZN	ZN/auramine, Xpert, referral to culture	ZN/Auramine, Xpert, referral to culture	Culture only in specialized pro-grams
	EPTB: Rivalta, ADA	Rivalta	Rivalta, Xpert	Rivalta, Xpert, ADA	ADA (feasible just in presence of spectrophotometer) and RIVALTA only when Xpert is not available.
VIROLOGY	HIV: RDTs, EID, CD4, VL	RDT, EID (sample collection)	RDT, CD4, EID (sample collection or testing), VL (sample col-lection or meas-urement)	RDT, CD4, EID (sample collection or testing), VL (sample col-lection or meas-urement)	Note: to be revised upon the availability of Xpert cartridges.

HOSPITAL WITH GENERAL IN-PATIENT AND OUT-PATIENT DEPARTMENT NOTES: HOSPITAL DEFINITION: IPD INCLUDES MEDICAL DOCTORS. SENIOR LABORATORY TECHNICIAN IS PRESENT (NATIONAL OR EXPAT). RADIOGRAPHER(S) (NATIONAL) ARE PRESENT IF AN X-RAY DACILITY IS REQUIRED.					
DX AREA		**BASIC/ MINIMUM**	**RECOMMENDED/ MEDIUM**	**DESIRABLE/ IDEAL**	**NOTES**
	Hepatitis; HBV RDT, HCV RDT, HEV RDT	HbsAg	HbsAg, HCV RDT	HbsAg, HCV RDT	
	Dengue: RDT	No	No	No	Current dengue RDT use is for investigation of suspected out-break only and expat health.
MYCOLOGY	General : KOH, gram	Gram	Gram	Gram, KOH	
	HIV related: Cryp RDT	No	Yes, CrAg/Indian Ink also in WB and CSF	Yes, CrAg/Indian Ink also in WB and CSF	
CLINICAL CHEMISTRY	Poc and/or lab based: Humalyzer test, Reflotron, Piccolo & PoC analzyers	Glucose, creatinine, ALT	Glucose, creatinine, ALT, AST, lactate, K^+, Na^+, CRP, bilirubin. Extra for NCDs: cholesterol, K^+, Na^+	ALT, AST, Creatinine, glucose, K^+, Na^+, Cl^-, Ca^{++}, lactate, CRP, bilirubin, AP, PAmylase, albumin, cholesterol, triglycerides and blood gases and Troponin	Select analysers according to workload and level of training lab techs. A must having Crea and ALT in HIV integrated programs. E'lytes and blood gases only if there is the capacity to give proper treatment. Troponin only if treatment or options for referral for AMI available.
	Coagulation: PT/ INR, PTT, D-Dimer	No	PT/INR (for NCDs)	PT/INR, PTT, D-Dimer	
	Urine: dipstick	Yes	Yes	Yes	
	Pregnancy: dipstick	Yes	Yes	Yes	
	ELISA: TSH	No	No	Yes	In population with frequent hypothyroidism (e.g. middle-eastern countries), 2nd line TB.
	HbA1c	No	Yes	Yes	If diabetes patients seen regularly.
SPECILAIZED DX NTD	Kala azar: RDT, microscopy, DAT	RDT	RDT	RDT	In endemic areas. In vertical programs other tests to be added.
	HAT: CATT, CATT dilution, micros-copy, Woo, mAECT, CSF exam	CATT and CATT dilution	CATT and CATT dilution	CATT and CATT dilution	Maybe replaced with RDTs later. In endemic areas. In vertical programs other tests to be added.
	Chagas: RDT, IHA, ELISA	RDT	RDT	RDT	In endemic areas. In vertical programs other tests to be added.
IMAGING	X-ray	No	Yes	Yes	
	Ultrasound	Yes	Yes*	Yes	US for range of conditions and assist appropriate referral.
	C-arm	No	No	No	Not required
OTHER DX EQUIPMENT	BP cuff	Yes	Yes	Yes	
	Stethoscope	Yes	Yes	Yes	
	Thermometer	Yes	Yes	Yes	
	Otoscope	Yes	Yes	Yes	
	Ophthalmoscope	Yes	Yes	Yes	
	Pulse oximeter	Yes	Yes	Yes	
	ECG	Yes	Yes	Yes	

HOSPITAL WITH GENERAL IN-PATIENT AND OUT-PATIENT DEPARTMENT NOTES: HOSPITAL DEFINITION: IPD INCLUDES MEDICAL DOCTORS. SENIOR LABORATORY TECHNICIAN IS PRESENT (NATIONAL OR EXPAT). RADIOGRAPHER(S) (NATIONAL) ARE PRESENT IF AN X-RAY DACILITY IS REQUIRED.					
DX AREA		**BASIC/ MINIMUM**	**RECOMMENDED/ MEDIUM**	**DESIRABLE/ IDEAL**	**NOTES**
	Fetal heart doppler	Yes	Yes	Yes	As rest of ANC
	Audiometer	No	No	No	
	Monofilament	No	No	Yes	If diabetes patients seen regularly.
	Peak flow meter	Yes	Yes	Yes	If asthma patients seen regularly.
	Spirometry	No	No	Yes	If asthma/COPD patients seen regularly.

3. Add on packages

3.1 Additional specialty: Malnutrition

ADDITIONAL SPECIALTY: MALNUTRITION (ITFC) NOTES: ADD ONS TO HOSPITAL PACKAGE. TO BE ADJUSTED ON THE BASIS OF PAEDIATRIC GUIDELINES.					
DX AREA		**BASIC/ MINIMUM**	**RECOMMENDED/ MEDIUM**	**DESIRABLE/ IDEAL**	**NOTES**
CLINICAL CHEMISTRY	Poc and/or lab based	No	Ca^{++}	Mg^{++}, Ca^{++}, P	

3.2 Additional specialty: Maternal and/or child health care (obs/ANC/neonat.)

ADDITIONAL SPECIALTY: : MATERNAL AND/OR CHILD HEALTH CARE (OBSTETRICS/ANC/NEONATAL CARE) NOTES: ADD ON TO HOSPITAL PACKAGE. EXCLUDING CAESAREAN SECTION.					
DX AREA		**BASIC/ MINIMUM**	**RECOMMENDED/ MEDIUM**	**DESIRABLE/ IDEAL**	**NOTES**
CLINICAL CHEMISTRY	Poc and/or lab based	No	Bilirubin	Bilirubin	Potentially bilirubin to add as basic; depending upon ap-proval of the protocol (for neonatal activities).

3.3 Additional specialty: Neglected tropical diseases

ADDITIONAL SPECIALTY: ADDITIONAL NTDS: CHAGAS, KA, HAT AND SNAKE BITES NOTES: HEALTH CARE STRUCTURE DOES NOT APPLY FOR NTD PROGRAMS (E.G. KA OFTEN IN SHELTER).					
DX AREA		**BASIC/ MINIMUM**	**RECOMMENDED/ MEDIUM**	**DESIRABLE/ IDEAL**	**NOTES**
CHAGAS	RDT	Yes	Yes	Yes	
	ELISA	Yes	Yes	Yes	As referral option or at clinic/hospital.
	IHA	Yes	Yes	Yes	As referral option or at clinic/hospital.
	PCR	No	No	No	Not established test of cure yet.
	ECG	No	Yes	Yes	
SLEEPING SICKNESS	CATT and CATT dilution	Yes	Yes	Yes	
	Microscopy	Yes	Yes	Yes	

ADDITIONAL SPECIALTY: ADDITIONAL NTDS: CHAGAS, KA, HAT AND SNAKE BITES NOTES: HEALTH CARE STRUCTURE DOES NOT APPLY FOR NTD PROGRAMS (E.G. KA OFTEN IN SHELTER).					
DX AREA		**BASIC/ MINIMUM**	**RECOMMENDED/ MEDIUM**	**DESIRABLE/ IDEAL**	**NOTES**
	Woo	Yes	Yes	Yes	
	mAECT	Yes	Yes	Yes	
	CSF examination	Yes	Yes	Yes	
KALA AZAR	RDT	Yes	Yes	Yes	
	DAT	Yes	Yes	Yes	
	Aspirate (lymph node, bone marrow, spleen)	Yes	Yes	Yes	
	Blood transfusion	No	No	Yes	Blood transfusion when a spleen aspirate is done, must be available.
	Ultrasound	No	No	Yes	
SNAKE BITES	Glass clotting test	Yes	Yes	Yes	

3.4 Additional specialty: Multi-drug resistant tuberculosis

ADDITIONAL SPECIALTY: MULT-DRUG RESISTANT TUBERCULOSIS NOTES: ADD ONS TO HOSPITAL PACKAGE.					
DX AREA		**BASIC/ MINIMUM**	**RECOMMENDED/ MEDIUM**	**DESIRABLE/ IDEAL**	**NOTES**
HAEMATOLOGY	Anaemia: Hb, Hk, red cell indices	Yes	Yes	Yes	For linezolid.
	Infection: WBC count, differentiation	Yes	Yes	Yes	For linezolid.
BACTERIOLOGY	Xpert	Yes	Yes	Yes	
	Hain	Yes	Yes	Yes	By referral if not in house.
	Culture	Yes	Yes	Yes	By referral if not in house.
CLINICAL CHEMISTRY	Poc and/or lab based: Humalyzer test, Reflotron, Piccolo & PoC analzyers	Creatinine, K+, ALAT, ASAT	Creatinine, K+, ALAT, ASAT	Creatinine, K+, ALAT, ASAT, Mg++	For 9 month regimen (kanamycin, fluoroquinolones (levofloxacin, moxifloxacin), ethionamide, clofazimine, INH, PZN, ethambutol) and linelozide requires (ALT & AST).
	Poc and/or lab based: Humalyzer test, Reflotron, Piccolo & PoC analzyers	ALT, AST, bilirubin, K^+, Mg^{++}, lipase, albumin	ALT, AST, bilirubin, K^+, Mg^{++}, lipase, albumin	ALT, AST, bilirubin, K^+, Mg^{++}, lipase, albumin	For bedaquiline/delaminide
	Pregnancy: dipstick	Yes	Yes	Yes	
	ELISA: TSH	Yes	Yes	Yes	For PAS, ethionamide
IMAGING	X-ray	Yes	Yes	Yes	Depending on country protocol, smear negative and paediatric pts, high HIV prev., f/u TB and associated pulmonary conditions, EPTB. Bedaquiline regimens.
	Ultrasound	No	No	Yes	For EPTB Dx.
OTHER DX	Audiometry		Yes	Yes	By referral if not in house for 9 month regimen.
	Psychological evaluation	Yes	Yes	Yes	For cycloserine.
	Vision	Yes	Yes	Yes	For linezolid.
	ECG	Yes	Yes	Yes	For bedaquiline.

3.5 Additional specialty: Surgery

ADDITIONAL SPECIALTY: SURGERY INCL. VISCERAL, ORTHOPEDICS, OBS/GYN AND TRAUMA NOTES: ADD ONS TO HOSPITAL PACKAGE. INTERNAL OSTEOSYNTHESIS AND RECONSTRUCTIVE SURGERY ONLY POSSIBLE WHEN DESIRABLE/IDEAL CONDITIONS ARE MET.					
DX AREA		**BASIC/ MINIMUM**	**RECOMMENDED/ MEDIUM**	**DESIRABLE/ IDEAL**	**NOTES**
HAEMATOLOGY	Anaemia: Hb, Hk, red cell indices	Hb	Hb	Hb and Hct	
	Infection: WBC count, differentiation	WBC count, differentiation	WBC count, differentiation	WBC count, differentiation	Analogue IPD
	Coagulation: Throm-bocytes	No	Yes	Yes	For patients on thrombo-prophylaxis
BLOOD TRANSFUSION	Direct transfusion	Yes	Yes	Yes	
	Blood bank	No	Yes	Yes	
BACTERIOLOGY	General: gram	Yes	Yes	Yes	
	Culture + Sensitivity	No	No	Yes (if not by MSF referral to validated lab)	Required if reconstructive surgery or chronic osteomyelitis treatment
	UTI: dipstick, sediment	Dipstick	Dipstick	Dipstick	Sediment is not superior over dipstick for diagnosis of bacterial UTIs
CLINICAL CHEMISTRY	Lab based: Humalyzer test, Reflotron, Piccolo	Glucose	ALT, AST, Creatinine, glucose, lactate, K^+, Na^+, CRP, bilirubin	ALT, AST, Creatinine, glucose, K^+, Na^+, lactate, CRP, Bilirubin, AP, PAmylase, Albumin, Triglycerides	Analogue(ish) to IPD.
	PoC: iSTAT, Piccolo, crea, glucose, lactate	Glucose	ALT, AST, Creatinine, glucose, lactate, K^+, Na^+, CRP, Bilirubin	ALT, AST, Creatinine, glucose, K^+, Na^+, lactate, blood gases other electrolytes, CRP, AP, PAmylase, Albumin, Bilirubin	Analogue(ish) to IPD.
	Coagulation: PT/ INR, PTT, D-Dimer	No	Yes	Yes	
	Urine: dipstick	Yes	Yes	Yes	
	Pregnancy: dipstick	Yes	Yes	Yes	
	ELISA: TSH	No	No	Yes	
IMAGING	X-ray	No	Yes	Yes	X-ray can be considered for general Sx as medium depending on the type / numbers of Sx's.
	Ultrasound	Yeso	Yes	Yes	Ultrasound should be a minimum requirement for all levels of Sx - range of indications from FAST to US guided interventions.
	C-arm	No	No	Yes	Required for internal osteosynthesis, desirable/ ideal for external fixator application and some vascular surgery procedures.

3.6 Additional specialty: Non-communicable diseases

ADDITIONAL SPECIALTY: NON-COMMUNICABLE DISEASES NOTES: HYPERTENSION/CARDIOVASCULAR DISEASE, DIABETES TYPE 1 AND 2, ASTHMA/COPD, EPILEPSY, THYROID DISEASE; DX REQUIRMENTS FOR NCDS ARE INTEGRATED/LISTED IN ROUTINE PROGRAMS – SEE TABLES ABOVE.											
		Basic health care centre / mobile clinic			Primary health care clinic – small lab			Hospital with OPD and IPD			
DX AREA		BASIC/ MINIMUM	RECOMMENDED/ MEDIUM	DESIRABLE/ IDEAL	BASIC/ MINIMUM	RECOMMENDED/ MEDIUM	DESIRABLE/ IDEAL	BASIC/ MINIMUM	RECOMMENDED/ MEDIUM	DESIRABLE/ IDEAL	NOTES
CLINICAL CHEMISTRY	Urine dipsticks	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
	Glucose	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
	Creatinine	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	
	ALT	No	No	No	No	No	Yes	No	Yes	Yes	
	Cholesterol	No	No	No	No	No	Yes	No	Yes	Yes	
	K	No	No	No	No	No	Yes	No	Yes	Yes	
	Na	No	No	No	No	No	No	No	Yes	Yes	
	Calcium	No	No	No	No	No	No	No	No	Yes	
	CRP	No	No	No	No	No	No	No	Yes	Yes	
	Blood gases	No	No	No	No	No	No	No	No	Yes	
	HbA1c	No	No	Yes	No	Yes	Yes	No	Yes	Yes	If diabetes burden is high
	Troponin	No	No	No	No	No	No	No	No	Yes	
	TSH	No	No	No	No	No	No	No	No	Yes	
	INR (PT)	No	No	No	No	No	Yes	No	Yes	Yes	
IMAGING	X-ray	No	No	No	No	No	No	No	Yes	Yes	
OTHER DX	Peak flow meter	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	
	Spirometry	No	No	No	No	No	Yes	No	No	Yes	
	Monofilament - diabetic foot Dx	No	No	Yes	No	No	Yes	No	No	Yes	
	ECG	No	No	No	No	No	Yes*	No	Yes	Yes	Monitoring AMI and *drugs side effect

Annex 2. MSF medical quality complaint form

MSF Medical Quality Complaint Form

1. Please fill one claim form per product; the same form can be used for several batches.

2. For international supply, please inform the concerned European Supply Centers (ESC):

MSF Logistique: qualityMSFLog@bordeaux.msf.org,
(**for OCP copy**: parispharma@paris.msf.org)
MSF Supply : claim-MSFSUPPLY@brussels.msf.org
APU : DL-AMS-qualityAPU@oca.msf.org

3. For locally purchased items,

3a. for OCA dl-ams-quality_oca_lp@amsterdam.msf.org
And please add the intersectional pharmacist in copy when available.
3b. For other sections local supply please inform directly your OC focal point (section pharmacists)

4. **To allow a complete analysis please always attach pictures when sending this claim and provide as many information as possible.**

General information	
Section	
Name	
Position	
Project and Country	
E-mail	
Phone	
Date of submission of the claim form	
Have you informed your medco (Y/N)	

Product details	
Product ITC code and description	
Brand name (if applicable)	
For medical device: manufacturer's reference	
Manufacturer	
Manufacturing site name and address	
Description of primary packaging	
Description of secondary packaging	
Batch/lot number(s)	
Expiry date(s)/Best before date(s)	
Manufacturing date(s)	

MSF Medical Quality Complaint Form

Procurement channel	
International Supply (precise from which ESC)	
Date of order and order number	
Packing reference number(s)	
If the item is part of a kit please indicate: - Kit code: - Manufacturing n° of the kit :	
Local Supply	
Name of the local supplier	
Donation or loan (precise from which entity)	

Quality defect	
Date of 1st observation of the issue	
Who detected the defect? (Patient, hospital staff, pharmacy staff, etc.)	
Circumstances in which the defect was detected	
Detailed description of the defect (tablet friability, abnormal appearance, colour, smell, precipitate, leakage, labelling, seal, insects, etc.)	

Consequences following the use of the defect product (if any)	
Has the concerned product/batch already been used or administrated to patient(s)? If yes how many patients have received the product?	
Has any adverse event or lack of efficacy been observed on the patients following the administration/use of this product/batch (please describe)?	
Has the health staff been affected by the use of this product (please describe)?	

Supply details (write: N/A when not applicable)			
Total quantity received			
Transport	From ESC/supplier to **capital**	From capital to **project**	From project to **end-user**
Date of departure			
Date of arrival			

MSF Medical Quality Complaint Form

Mean of transport			
Temperatures during transport*			
Storage conditions (temp./humidity)*			
Remaining stock per batch			

* Please provide record (log-tag or manual recording) or if not available describe general conditions

Immediate action already taken	
Quarantine (Y/N). If yes please precise location	
Sample returned to country coordination (Y/N)**	
Any other batch that could be used instead?	

** Please keep the affected sample intact for possible analysis and in appropriate storage conditions as recommended by the manufacturer

Annex 3. Stock card

ITEM	DOSAGE/TYPE
CODE	STANDARD UNIT OF DISTRIBUTION
REMARKS	

DATE	ORIGIN / DESTINATION Waybill no. or other reference	IN	OUT	STOCK	REMARKS (incl. expiry.date. & batch nr.)
	Transport from previous stock cards				

Annex 4. Laboratory service manual

LABORATORY SERVICE MANUAL					
NAME OF LABORATORY:					
SUPERVISOR:					
Test	**Container**	**Sample conditions**	**Normal values**	**Panic value**	**Turn around time**

Annex 5. Laboratory request form template

Patient details

First and last name: _____ ID number: _____

Date of birth: ____ / ____ / ____

Gender: ☐ Male ☐ Female

Test(s) requested

Details of referring doctor/clinician

First and last name: _____ Signature:

Department: _____

Note: there is no tick list of available tests on this request form. By experience tick list: increases the workload of the laboratory and the number of unnecessary analysis.

Annex 6. TB register

Date of sample received	Patient identification number, if available	Patient's name, gender, age	Laboratory reference number	Type of sample received	Observation on quality of sputum	Status [i.e. initial examination or follow-up]	Smear and/or culture result	Results for confirmatory test for M. tuberculosis [if applicable]	Date results reported	Name of person responsible for test

Annex 7. Laboratory incident book

Date of accident	Name of person concerned	Description of accident	Sample involved	Extend of injury	Containment and follow-up measures taken

Annex 8. Equipment Log

Local Ref.	Article Code	Description	Brand	Model	Serial Nr.	Other ID nr.	Project Location	Date of first use	Last service	Next service	Comments

Annex 9. RDT QC reporting template

MSF CODE:

MSF DESCRIPTION:

Date	Batch number of test kit	Control Batch number	Negative control	Positive control	Conclusion control samples	Remedial action	Run by

Annex 10. LQAS excel tool

Available only in USB/CD version.

Annex 11. Slide QC reporting template

Name of the Laboratory	
Type of slides/Disease	
Month	

Slide no	**Reader 1 – routine results**	**Reader 2 – Cross checker**			**Investigation done**	**Corrective action taken**
		Results	**Quality of smear**	**Quality of staining**		

	Reader 2	
Reader 1	**Positive**	**Negative**
Positive		
Negative		

Annex 12. Description of the EQA Scheme for semi-automated systems that MSF uses

MSF currently subscribes to a EQA program that based on a collaboration between BIOLABO, which manufactures the reagents, and ASQUALABORATORY (Assurance Qualité des Laboratoires de Biologie Medicale) who performs the statistical analysis of results. This is done by calculating the mean of all the laboratories per analyte and comparing it with the ASQUALABORATORY target value. Each participating laboratory is then compared against the mean of all the laboratories. This EQA program has about 700 participating medical laboratories, mainly in France. The tests included in this EQA program are:

Uric acid
Albumin
Amylase
Bicarbonates
Bilirubin
Calcium
Cholesterol
HDL cholesterol
Creatine Kinase
Creatinine
Iron
Gamma-GT
Glucose
Lactate
LDH
Magnesium
Alkaline phosphatase
Phosphates
Potassium
Proteins
Sodium
TGO / TGP
Triglycerides
Urea

How does the program work?

1. Enroll your laboratory to the EQA program by filling in the form below and sending it to your laboratory advisor/referent.

Suscription to the monthly program of EQA-Biochemistry BIOLABO / ASQUALAB		
Please fill in the white cells carefully		**Explanation on what to fill in**
Name of the laboratory		MSF ...
Hospital		MSF ...
Person in charge of the external quality assurance		First name and last name of the QC in charge or Lab supervisor or Lab country coordinator
Person in charge of the laboratory		MSF Lab supervisor or MSF Laboratory manager
Address		Address of the coordination office were you will receive the DHL parcel
Town (Country)		Town and country of coordination office
Phone		Tel number of MSF Lab supervisor
E-mail(s) (separated by a ";" without spaces before or after)		1. Lab supervisor of field e-mail or Lab country manager 2. Medical coordinator e-mail 3. Lab advisor/referent e-mail
Country DHL account number		

2. Once your laboratory advisor enrolls you into the program, you will receive an email from ASQUALABORATORY containing your user name and password. Please do not delete this email. You will need it to log in to the website where you can post and review your results.

3. You will receive your controls at the address where you have indicated via DHL/hand carried or as part of your international cargo. Please note that controls may be shipped without cold chain and you should put them in the fridge at 2-8 °C as soon as they are received. You will need to brief the coordination logistics department about this.

4. Once you receive the item in the laboratory confirm that:
   a. The box contains 24 vials.
   b. Each vial label has:
      – a reference of the corresponding month (e.g. 2016-03 on the vial in march 2016);
      – a reference code e.g. “Bio 01” or “Bio 02” for the two vials of the first month of the External Quality Assessment.
   c. A kit insert describing which vial you should analyse for which month.

Using the controls

1. Select the correct vials for the month from the box.

2. Add the volume of distilled water indicated on the label to each control sera referenced for the current month and completely dissolve before use. This will take around 30 minutes.

3. Perform the analysis as you would for a patient sample within the next 8 hours for ALL the chemistry tests done in the lab. If you have two machines in the same lab, use the same 2 vials for the month but run them on two machines. Please note you have to enter the results separately per machine.

4. Enter the results online before the last day of the month (It is advisable to run your QC on the same date every month)It is better to enter the results online in advance of the deadline, in case you may have a problem with internet connection on the last day of the month. The procedure to enter these results is described below. If you have a problem with internet connection or the website, contact your laboratory advisor who will enter the results for you.

5. You will receive an email from ASQUALABORATORY confirming that they have received your results.

6. A report of your performance will be sent to you within the first 2 weeks of the next month.

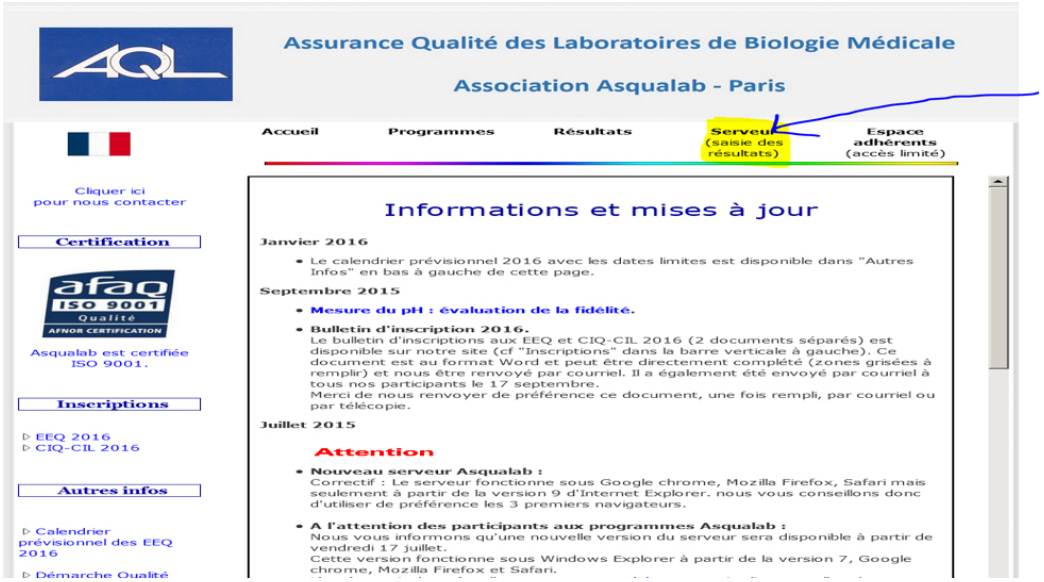
Procedure for entering the EQAS results on the website

You are advised to submit the results before the last day of every month.

If you have problems entering the results, please send them to [*email address of your laboratory advisor/referent***] and they can enter them for you.**

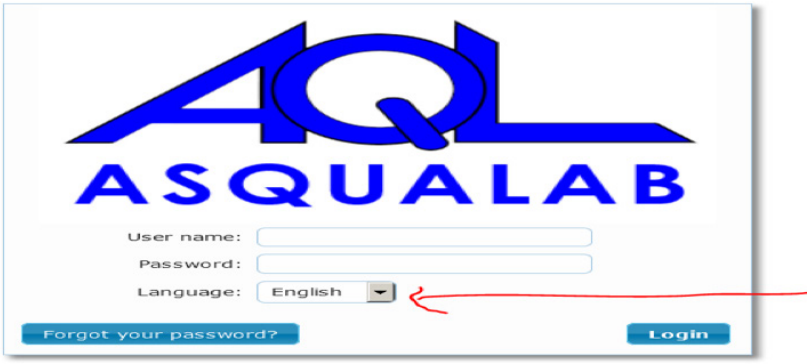
Step 1:
Connect to the following website: www.asqualab.com

Step 2:
Click on 'serveur (saise des resultants)' as shown below.

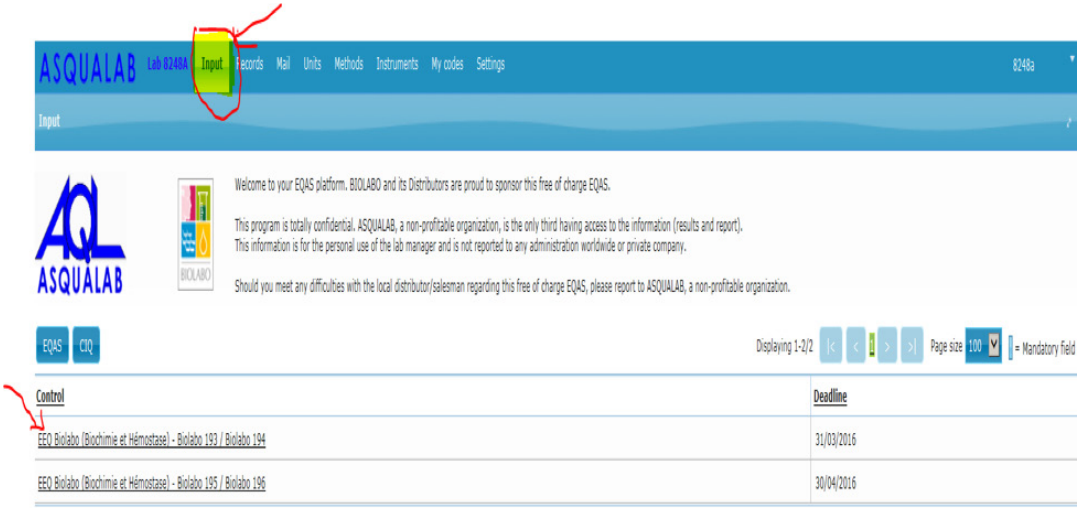


Step 3:
This will bring you into the log in page. Enter your log in name and password which you have received from ASQUALABORATORY by email then click 'login'. If you do not have these details, please refer to the first email you received from ASQUALABORATORY or contact your laboratory advisor.

On this page you can also change the language to English.



Step 4:
Click on 'input'. Then click on the link for the month you want to enter the results for.

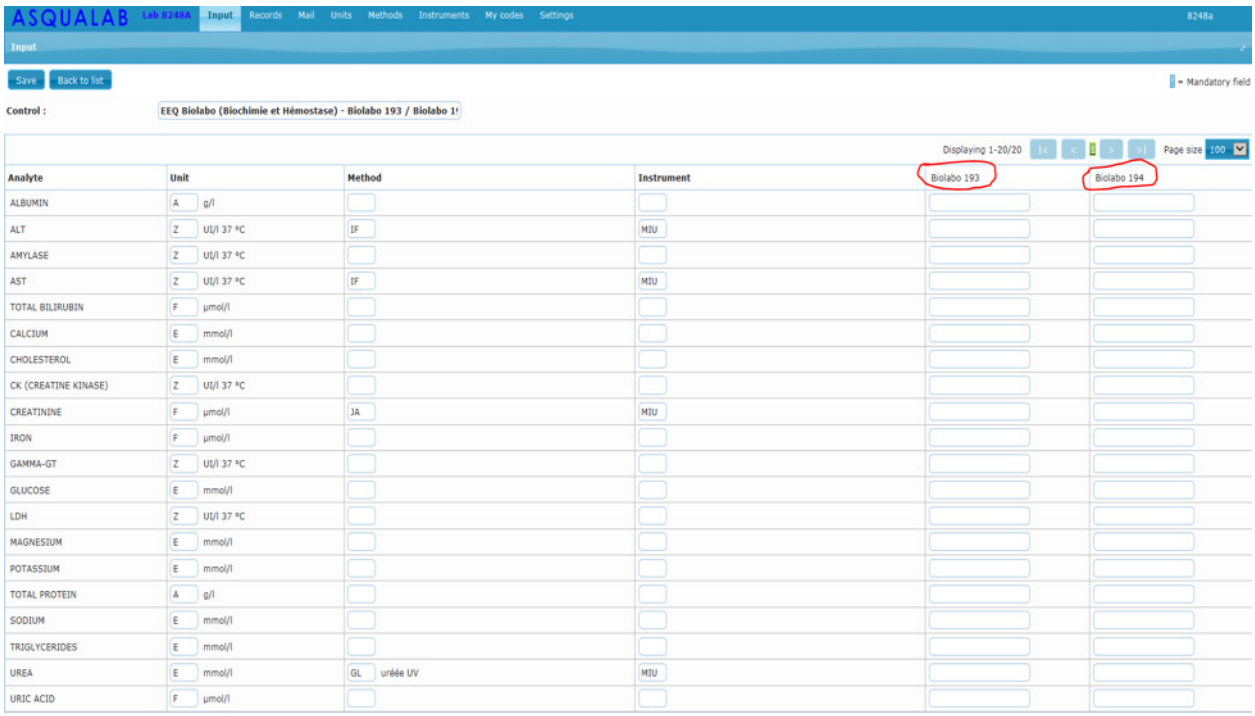


Step 5:
Confirm that there is a code next to the tests that you do. Below is an example of codes.

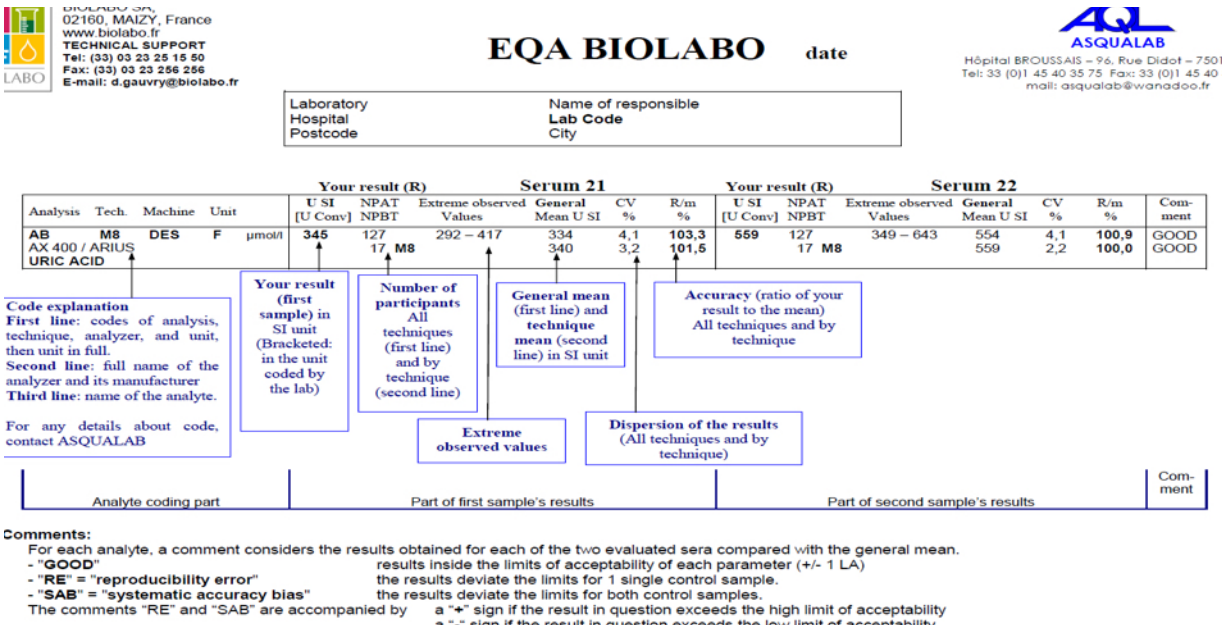
Analyte	MSF method	Unit Code (all equipment)	Method code		Instrument code		
			Humalyser	Reflotron	Humalyse	Reflotron	Spotchem
ALT	IFCC without pyridoxalphosphate	Z- (if reading at 37^{0}C) U- if measuring at 25/30^{0}C	SX	3X	HUM	FLE	FMC
Creatinine	Jaffe reactionat 37	V - If reporting in mg/dl F - if reporting in umol/l	RX	3X	HUM	FLE	FMC
Glucose	GOD-Pap	V - If reporting in mg/dl F - if reporting in umol/l		3X	HUM	FLE	FMC
Urea	Berthelot	V - If reporting in mg/dl F - if reporting in umol/l	EX	3X	HUM	FLE	FMC
Bilirubin-total and direct	modified jendrassik - using diazotised	V - If reporting in mg/dl F - if reporting in umol/l	YX	3X	HUM	FLE	FMC
Cholesterol	COD-PAP peroxide and phenol	V - If reporting in mg/dl F - if reporting in umol/l	EX	XX	HUM	FLE	FMC

Step 6:

Enter your results for each vial in the boxes shown below each vial number. Confirm your results. Check again that you have entered your results correctly then click 'save'.



Step 7:
You will receive an email from Asqualaboratory confirming the receipt of your results shortly after. You are allowed to modify these results until the last day of the month.



02160, MAIZY, France
www.biolabo.fr
TECHNICAL SUPPORT
Tel: (33) 03 23 25 15 50
Fax: (33) 03 23 256 256
E-mail: d.gauvry@biolabo.fr

EQA BIOLABO date

ASQUALAB
Hôpital BROUSSAIS – 96, Rue Didot – 7501
Tel: 33 (0)1 45 40 35 75 Fax: 33 (0)1 45 40
mail: asqualab@wanadoo.fr

Laboratory	Name of responsible
Hospital	**Lab Code**
Postcode	City

Analysis	Tech.	Machine	Unit	Your result (R) Serum 21 U SI [U Conv]	NPAT NPBT	Extreme observed Values	General Mean U SI	CV %	R/m %	Your result (R) Serum 22 U SI [U Conv]	NPAT NPBT	Extreme observed Values	General Mean U SI	CV %	R/m %	Com-ment
AB	**M8**	**DES**	**F** µmol/l	**345**	127	292 – 417	334	4,1	**103,3**	**559**	127	349 – 643	554	4,1	**100,9**	GOOD
AX 400 / ARIUS					17 **M8**		340	3,2	**101,5**		17 **M8**		559	2,2	**100,0**	GOOD
URIC ACID																

Code explanation
First line: codes of analysis, technique, analyzer, and unit, then unit in full.
Second line: full name of the analyzer and its manufacturer
Third line: name of the analyte.

For any details about code, contact ASQUALAB

Your result (first sample) in SI unit (Bracketed: in the unit coded by the lab)

Number of participants All techniques (first line) and by technique (second line)

Extreme observed values

General mean (first line) and **technique mean** (second line) in SI unit

Dispersion of the results (All techniques and by technique)

Accuracy (ratio of your result to the mean) All techniques and by technique

Analyte coding part | Part of first sample's results | Part of second sample's results | Com-ment

Comments:
For each analyte, a comment considers the results obtained for each of the two evaluated sera compared with the general mean.
- "**GOOD**" results inside the limits of acceptability of each parameter (+/- 1 LA)
- "**RE**" = "**reproducibility error**" the results deviate the limits for 1 single control sample.
- "**SAB**" = "**systematic accuracy bias**" the results deviate the limits for both control samples.

The comments "RE" and "SAB" are accompanied by a "**+**" sign if the result in question exceeds the high limit of acceptability

Step 8:
After about 2 weeks the results will be sent to all participating laboratories by email. Analyze the results of your own laboratory carefully with particular attention to theresults that have missed the qualification 'good'.

Belgium
Médecins Sans Frontières/Artsen Zonder Grenzen
46 Rue de l'Arbre Bénit, 1050 Brussels
Tel.: +32 (0)2 474 74 74
Fax: +32 (0)2 474 75 75
E-mail: info@brussels.msf.org

France
Médecins Sans Frontières
14-34 avenue Jean Jaurès, 75019 Paris
Tel.: +33 (0)1 40 21 29 29
Fax: +33 (0)1 48 06 68 68
E-mail: office@paris.msf.org

Netherlands
Artsen Zonder Grenzen
Naritaweg 10, 1043 BX Amsterdam
Tel.: +31 (0)20 52 08 700
Fax: +31 (0)20 62 05 170
E-mail: office@amsterdam.msf.org

Spain
Medicos Sin Fronteras
Calle Zamora 54, 08005 Barcelona
Tel.: +34 933 046 100
Fax: +34 933 046 102
E-mail: oficina@barcelona.msf.org

Switzerland
Médecins Sans Frontières
78 rue de Lausanne - Case postale 116 - 1211 Geneva 27
Tel.: +41 (0)22 849 84 84
Fax: +41 (0)22 849 84 88
E-mail: office-gva@geneva.msf.org

Achevé d'imprimer en France par ISI Print, 93210 La Plaine Saint-Denis
Décembre 2019