

NCBI Bookshelf. A service of the National Library of Medicine, National Institutes of Health.

Smith PG, Morrow RH, Ross DA, editors. *Field Trials of Health Interventions: A Toolbox*. 3rd edition. Oxford (UK): OUP Oxford; 2015 Jun 1.

Chapter 17 Field laboratory methods

1. Introduction to field laboratory methods

Laboratory tests may provide the definitive basis for the measurement of outcome variables in field trials, either directly by demonstration of the presence of the pathogenic agent under study or indirectly by demonstration of a host reaction or of biochemical changes due to the pathogen. They may also provide evidence of the mechanism of action of the intervention, for example, directly by measuring the drug or metabolic by-products or indirectly by measuring an immune response to a vaccine. In addition, they may be used to detect or confirm the presence of adverse reactions and prior exposure to an agent or to antimicrobials.

Rigorous laboratory process is crucial to the generation of good-quality data and may be important to ensure the safety of trial participants. Laboratories participating in trials are expected to adopt the Good Clinical and Laboratory Practice (GCLP) guidelines, which govern the conduct of clinical trials globally (Stevens, 2003; World Health Organization, 2009). GCLP provides a framework covering the spectrum of laboratory studies, from planning to analysis and storage of specimens and archiving of data. The WHO publication documents a set of minimum requirements for laboratory involvement in clinical trials, including the use of standard operating procedures (SOPs), monitoring, quality control (QC), and external quality assurance (QA) arrangements (World Health Organization, 2009).

The organization and operation of a field laboratory for the support of a field trial are different from those of a routine medical laboratory and have become more demanding in recent years. Laboratory accreditation (see Section 6) may be necessary when laboratory data are required for the process of product licensure. In field trials, the emphasis is often on the collection and processing of large numbers of samples, on which only a few specific tests will be performed. Aliquots of samples are usually required, so that different aliquots can be used for different tests, for storage as backup specimens, and for shipment for further analysis. Storage of specimens with computerized records, including electronic monitoring and bar coding, has been introduced, even in field laboratories in rural settings.

General aspects of the setting up and running of a field laboratory are discussed in this chapter. Other literature should be consulted for information on specific laboratory tests and specific laboratory methods. Useful general texts containing relevant information for the operation of a field laboratory and for collecting specimens include Cheesbrough (1987), World Health Organization (2003), and World Health Organization (2009). See also Chapter 16.

2. Sample collection

Accurate laboratory results depend on proper collection, processing, and handling of samples. The method of collection, timing, and handling of samples will be determined by the purpose of the trial and specified in the trial protocol. Careful attention must be given to the quantity and quality of samples, aseptic precautions, and prompt transport of samples and their processing and storage in the laboratory. Advances in technology and analytical chemistry have led to the development and use of direct testing in the field, using point of care (POC) diagnostics, and rapid diagnostic tests (RDTs) have been introduced in some areas.

2.1. Types of specimen

The kinds of specimen that are commonly collected in field trials include:

- ◆ specimens from humans, including blood, stool, urine, sputum, skin snips, and other tissue biopsies, and swabs or smears collected from skin or mucosal surfaces
- ◆ entomological specimens for studies of vectors, and animal or malacological specimens for studies of intermediate hosts
- ◆ food, water, and environmental samples.

In this chapter, we discuss only specimens collected from humans, though many of the issues (such as the use of sterile techniques) apply to the other types of specimen.

2.2. Handling specimens

The collection of samples for laboratory studies will usually involve the steps outlined in Box 17.1.

The procedures for collecting and processing samples must be unambiguously specified, including to where they are to be transported and how they will be labelled. Whenever required, the type of shipment must be specified, for example, in dry ice or liquid nitrogen. If samples are to be transported by air, safe shipment of samples is mandatory, and procedures must follow the International Air Transport Association (IATA) guidance for infectious substances and diagnostic specimens, which detail packaging and shipment methods. Each package must contain a primary and a secondary container, and both of these must be leak-proof to avoid accidental spillage during transport. The whole process must be performed only by trained staff, whose competence has been certified. The regulations governing the transport of potentially hazardous samples are designed to ensure that samples reach their destination in good condition and to eliminate exposure of those handling the shipment to any potential hazard. Prior communication with the recipient and tracking information are vital, in order that shipments can be dealt with promptly on arrival. On occasion, this may require staff to receive the specimens outside normal working hours to avoid the specimens sitting around and deteriorating.

All aspects of the collection, transport, and processing of samples must be pilot-tested. Often, much attention is paid to the proper design and testing of questionnaires, but much less care is taken to finding the most appropriate and culturally acceptable methods for the collection of blood, stool, urine, or tissue samples. Yet, this may be crucial to sustained community involvement and participation (see Chapter 9, Section 5).

2.3. Blood

The usual methods by which blood is collected in field surveys are by venepuncture or by finger- or heel-pricks, depending on the nature of the investigations required. If small quantities of blood are required, finger-pricks are usually taken from adults, with heel-pricks more commonly used in infants and young children, whose fingers are very small and whose heels do not yet have calluses. A finger-prick provides an adequate volume of blood for many laboratory tests. Micro-techniques are to be preferred whenever they have acceptable validity, as they either avoid the need for venepuncture altogether or reduce the volume of blood that is needed. Micro-techniques have been, or are being, developed for many assays, and investigations should be conducted before a study starts to find out the latest availability of such techniques (for example, by literature search or contact with those in a central or reference laboratory). It is important to verify that the methods have been adequately validated. Some tests require larger quantities of blood, however, and it will often be necessary to collect blood by venepuncture from at least a sample of the population.

After collection, blood may be separated into several components, including serum, plasma, red cells, and white cells. The separation must be done shortly after the blood has been collected, and it is common for this procedure to be carried out close to where the samples have been collected or in a nearby field laboratory.

A sample of blood taken from a finger-prick may be collected in one of several ways, including:

1. collection into capillary tubes, for example, narrow glass tubes, by capillary action, or microtubes by gentle squeezing of the finger
2. dropping onto a glass slide for direct examination of a blood smear
3. dropping onto strips or discs of absorbent paper (filter paper).

Fingertips are swabbed with alcohol before pricking, and the first drop is wiped off. Sufficient blood can be obtained for two thick, and two thin, malaria smears to do one or two haemoglobin level measurements (for example, with the Haemocue[®] system or the older haematocrit tubes), to collect 50–100 microlitres of blood in a microtube or Microtainer[®] for serum, and to place a drop on filter paper (World Health Organization, 2003). Filter paper samples need to be air-dried, before storing with silica gel. Tubes with plasma or serum can be stored on dry ice, in a freezer, or in liquid nitrogen. The amount of plasma or serum recovered from a finger-prick sample will be sufficient to perform serological tests, such as enzyme-linked immunosorbent assay (ELISA) or Multiplex[®] assays, and is

sufficient for the determination of some micronutrients such as vitamin A or zinc (minimum serum requirements of 25–40 microlitres). Establishing volume requirements for the tests to be conducted is a prerequisite.

If repeated blood sampling is to be undertaken from participants during the course of a study, it is likely to be more appropriate ethically, and easier to maintain the co-operation of most study populations, if finger-prick, rather than venous blood, sampling is used. While filter paper samples are satisfactory in many cases, the larger sample volumes from venous sampling are currently needed for some tests (for example, tests for cell-mediated immunity, human leucocyte antigen (HLA) typing, bacterial cultures). A variety of systems using an evacuated tube, such as Vacutainer[®] or Vacuette[®] collection tubes, and blood culture bottles are suitable for this purpose. For repeated sampling, it is also essential to provide feedback to the individuals involved, and to the community if appropriate, about the earlier results (see also Chapter 9).

If multiple types of collection tubes are to be used, the order of draw should be written into the SOP to minimize cross-contamination of tube additives.

Special care in handling and processing samples is needed if any DNA-based work is to be conducted, as the potential for cross-contamination between samples is high. Blood for bacterial cultures is collected by venepuncture and delivered directly into blood culture bottles containing bacterial growth media, before incubation in the laboratory in either a conventional incubator or an automated incubator system such as the BACTEC[®] series. Blood for immunological and genetic analysis can be collected as whole blood and stored in specialized tubes such as PAXgene[™] or Tempus[™] or, when only small volumes are available, as spots collected on filter paper for later analysis in a specialist laboratory.

Special precautions should be taken when collecting blood. Disposable gloves should be worn, a sharps box provided, and water and detergent should be available for use by those taking blood. All blood samples should be considered to be potentially infectious, and appropriate handling procedures must be employed to safeguard all those who will come into contact with the specimens during their collection, processing, analysis, or storage (World Health Organization, 2004). Guidelines and drugs should be available for use in the event of a needle-stick injury or blood spillage.

2.4. Cerebrospinal fluid

Collection of cerebrospinal fluid (CSF) requires lumbar puncture, which must be performed by a clinically trained member of staff with prior supervised experience. Using aseptic techniques, CSF should be collected into a sterile container for prompt transfer to the laboratory for biochemical and microbiological analysis. An obviously 'bloody' sample may compromise the laboratory results, especially from biochemical analyses.

2.5. Stool and urine

A summary of different methods that may be used for collecting urine and stool samples, with details of different container types, is given in World Health Organization, 2003. The methods considered for use in a particular survey should be discussed with those knowledgeable of local customs and taboos. In some cultures, sensitivity regarding the collection or public display of stool specimens may be greater than that for blood. A container that is technically appropriate may not be acceptable in a particular study community (for example, due to colour, transparency, or resemblance to a cultural design or pattern). In advance of a survey, the proposed stool and urine containers should be shown to the village leaders, and the proposed methods of sample collection discussed. As with all field procedures, it is important to undertake pilot testing to ensure that the procedures planned will be acceptable (both to the investigator and to the study population).

As stool samples can rarely be collected 'on the spot', it is usually necessary to leave the container with an individual overnight and to arrange to pick up the specimen on the following day. A potential hazard in doing this is that containers may be exchanged between individuals or, for example, one person may provide a sample for the whole family. It is difficult to rule out this possibility, but it is important for fieldworkers to stress the importance of participants adhering to the correct procedures and to be alert to possible problems.

2.6. Sputum

The WHO manual (World Health Organization, 2003) gives a concise description of recommended methods of collecting sputum samples, using different kinds of jars, boxes, and containers, including transport media. Two general points merit special attention:

1. all sputum samples should be considered potentially infectious
2. careful attention should be given to the cold-chain requirements if sputum samples have to be sent to another laboratory for culture.

3. Labelling and storage

3.1. Labelling

Proper labelling of samples is essential. The labelling scheme should be as simple as possible, consistent with the study objectives, and must take due account of the size of containers and how the specimens will be handled, transferred, and stored. In most cases, computer-generated, self-adhesive, pre-printed labels, with the individual identification or code numbers duplicated on data sheets, can speed processing. Also, labels in a variety of materials suitable for differing storage conditions, and with each number duplicated several times, are available commercially. Bar codes for specimen containers that can be read automatically by bar code readers are also available commercially.

The information recorded on a label will vary, according to particular requirements. It may include a unique identification number assigned to a study participant, which is utilized during laboratory processing and which may be linked back to an individual by reference to records kept at the time the sample was taken. In some circumstances, it will be appropriate to include on the label a record of the date of collection, the type of specimen, if not evident, and possibly the location (for example, name of the village). Individual names may also be recorded on the label, but this can create problems with blinding and confidentiality, and often names are not a unique identifier, as several individuals may have the same name.

Containers should usually be labelled using waterproof marker pens (but see item 1 in Box 17.2), writing directly onto the container-labelling area or onto adhesive labels attached to the container. If the container has a cap, the marking should be on the body of the container (and possibly on the cap as well, but never on the cap only). For smaller micro- or capillary tubes, an adhesive label with the identification information on it can be wrapped around a container with the two ends joined, such that they protrude (sometimes known as a 'flag'). Flags can be written on with a waterproof marker pen, and tubes may be stored in labelled envelopes, as they are collected in the field.

If smaller tubes are stored in boxes that are too large for them, staff need to be careful to record and maintain the correct numbering and not to invert or tip the box, so that they can fall out and move around in the box. Packing with cotton wool will help to keep the tubes in place in a box, and tape can be used to secure the lid.

Filter paper can be written on either directly or on the protective cardboard surround.

It is not possible to recommend a single standardized form of labelling for different sample containers that will be appropriate in all circumstances. It will be necessary in a particular study to establish, through field testing, a method that guarantees the reliability of the labelling from the time the sample is first collected, through transportation, processing, analysis, and storage. Using sets of labels with series of identical numbers on them, for coding samples and associated record forms, reduces the chances of labelling errors.

Some warnings regarding labelling and storage are given in Box 17.2.

3.2. Storage

The storage area of a field laboratory should be designed to be adequate for the studies to be conducted. This will require estimation of the rate at which samples will be collected and processed and for how long they must be stored before being transported on to another location (for example, for processing or long-term storage in the base laboratory). Serum and plasma samples should be frozen as soon as possible after separation, and storage in a field laboratory at $-20\text{ }^{\circ}\text{C}$ is adequate for most purposes, at least for several weeks, although some tests require immediate storage at $-70\text{ }^{\circ}\text{C}$. The location and positioning of any fridges, freezers, and liquid nitrogen containers need to take account of access, power supply, and consistency of ambient temperature. Specifically designed freezer rooms with conduits to vent air from the freezer exhaust externally are often a good option.

Stool, urine, and tissue samples may be stored under various conditions, using appropriate fixatives and stabilizers; different possibilities are summarized in World Health Organization (2003).

3.3. Aliquoting

Biological samples are easily damaged by repeated freezing and thawing. This can be avoided if samples are divided into small portions (aliquots) before freezing; moreover, this provides a backup sample if problems are encountered during shipping. Ideally, the size of aliquots should be chosen so that there is just sufficient material in each aliquot to perform the tests that will be required at one particular time. This is not always possible, and, in practice, compromise procedures may have to be adopted (for example, on grounds of cost). It is important that the laboratory recording procedures are such that the histories of each aliquot are properly documented (especially recording how many times each one has been thawed and re-frozen), so that any recipient of the samples can be given detailed information about their preparation (for example, whether volumes are precisely measured or are approximate) and subsequent storage.

3.4. Storage system

When large numbers of samples are collected and stored, a storage and record system must be devised that allows the rapid retrieval of particular samples. If this is not done, sorting through large numbers of samples can be a very time-consuming activity. The particular storage system used should be tailored to the design of the specific study. Often, it is appropriate to store samples in batches, according to the date they were collected or frozen, with a record being kept of the contents of each batch. For longer-term storage and/or transport, storage boxes of standardized tube capacities (for example, nine by nine or ten by ten) with coded slots can be used. These boxes can be part of a racking system, for which a detailed inventory can be maintained as part of a computerized laboratory data management system. Generic software systems (some of which are free) are available. These computerized systems are used to record the receipt and storage of samples and can be used to track everything that happens to a sample, from when it was collected until it is disposed of or used up. Two of the most widely used examples are the Laboratory Data Management System (LDMS) and the Laboratory Information Management System (LIMS), though neither of these is free.

4. Documentation of laboratory procedures

There should be clear and explicit documentation of all laboratory procedures as SOPs in the laboratory manual, which should be subject to periodic review. The degree to which the documentation is computer-based will depend on local capacity and, to some degree, on the demands of the sponsors. SOPs will help to ensure reproducibility and will facilitate comparisons with results from other laboratories. Logbooks and records should be made for equipment maintenance, the batches of supplies and reagents used at different times, and for the detailed test procedures and the duties and responsibilities of staff members. Certification of staff competencies can also be included. Specific provision should be made for recording unusual events that may affect the results of a test (for example, power failures and fluctuations—though, in some places, these may not be unusual!).

Depending on the size of the laboratory and the variety of tests and procedures undertaken, the documentation should be arranged in a single or several logbooks that are arranged chronologically (World Health Organization, 2009).

4.1. Supplies

One of the sets of laboratory logbooks should provide information on: the reagents, test kits, laboratory equipment (including brand names), the expiry dates of reagents and test kits, storage conditions, batch or lot numbers, specification sheets, and the relevant re-ordering arrangements (for example, when, how much, and by and through whom). A checklist of itemized activities is important to avoid irregular supplies or shortage of reagents and test kits. Regular, at least monthly, inventories and appropriate documentation of all supplies can help to keep track of expiry dates and check on pilferage. Supplies and reagents that have passed their expiry date should never be used. To avoid this happening, a ‘first in first out’ system should be used for issuing reagents and supplies, i.e. the reagents or test kits that are closest to their expiry date should always be issued before the ones that are further from their expiry date. Where Internet access is available, the website addresses and e-mail addresses of suppliers should be recorded.

4.2. Equipment maintenance

Regular checks should be made on each piece of equipment to ensure that it is in good working order. Such checks should be recorded and, for key items, publicly displayed. Some of the items that should be checked regularly are listed in Box 17.3.

In laboratories in the tropics where air conditioning is not available, humidity may lead to problems with both equipment and storage of certain sample types (for example, blood stored on filter paper). In these circumstances,

storage with silica gel (as a desiccant) in airtight boxes is appropriate, and the silica gel will require regular (monthly) replacement.

Maintenance procedures are usually described in the instruction booklets for the relevant equipment, but these will need to be augmented with details relating to troubleshooting and contacts of qualified staff or engineers. The complete maintenance instructions for each piece of equipment should be incorporated into a dedicated manual, and a logbook with checklists kept for each piece of equipment. Regular maintenance of certain pieces of equipment may be a prerequisite in some studies. It is important therefore that laboratory staff review these logbooks regularly. It is usually a good idea and cost-effective to have a maintenance contract for all major, complex, and expensive laboratory equipment.

4.3. Procedures and staff duties

Laboratory SOPs, detailing step-by-step instructions for individual procedures, should be collected together in a laboratory manual. The author of each SOP and those staff members who have read it and, where appropriate, been trained in it (and who can therefore perform the procedure) should sign the SOP cover sheet. SOPs will specifically detail to whom staff should report and how they should record results, additional observations, mistakes, and other unusual events. These include, for example, any change of kit or batch number of sera, media, or preservatives. Any changes in assay conditions (for example, changes in incubation time or temperature) will require amendments and updating of protocols, which should be validated by the laboratory supervisor. Staff members involved in distinct sequences of the procedures should be indicated on relevant flow charts, and these should be written into the logbook. A separate staff file, containing details of relevant training and certification, may be warranted in some circumstances.

4.4. Unusual or adverse events

The logbook should be used to keep a record of errors in test procedures (operator- or machine-reported) and in the preparation of reagents, power failures, temperature, and humidity changes that might influence the results of the tests or the quality of stored samples. The remedial action taken and results of the rerun of the test should also be documented.

5. Quality control and quality assurance

QC is an inherent component of any good study and a good laboratory. It is a process of routine checks designed to detect any deficiencies that could compromise the results of laboratory analysis and suggest how these might be corrected. An example would be checks that the laboratory always gets the same result for a split specimen. QC checks should be specified in the laboratory work plan and in SOPs. A useful resource that discusses general laboratory QC issues is [Ratliff \(2003\)](#).

QA is a set of activities aimed at evaluating the accuracy of laboratory analysis and to guide improvements if inaccuracies are detected. QA provided by a resource external to the field laboratory is complementary to QC and should be established to monitor and improve the quality of laboratory procedures and validate the effectiveness of a QC programme. For example, a reference laboratory may supply specimens that are analysed 'blind' with the results compared to those of the reference laboratory and all the other laboratories participating in the same QA scheme.

5.1. Reproducibility of test results

The reliability of laboratory results should be tested by regular checks on their reproducibility. The level of acceptable variation will depend both on the test and study. This information is normally predefined in SOPs, test manuals, and the study protocol. Many test systems have inbuilt controls for this purpose, using standardized reagents of known concentration or quantity. The use of such standard controls is important, but not necessarily sufficient, to monitor the quality of test procedures. Depending on the procedure, samples should be tested in duplicate or re-read by a second technician. The frequency with which such repeats are performed depends upon how well the laboratory is running and how long it has been doing the test. Typically, when a test is first introduced or a new staff member is conducting the test, a high frequency of such checking is appropriate, with a decreased frequency as the procedures become more familiar, assuming the re-tests are showing negligible differences to the original results. In many circumstances, it will be appropriate to ensure that duplicate analyses are done on between 5% and 10% of samples on a routine basis. It is sometimes possible and advisable to seed known positive or known negative samples into test runs, which are labelled in such a way that the laboratory staff running the test cannot spot them. This is particularly important if it is expected

that the great majority of samples will either test negative or test positive (for example, seeding a positive result if a long run of negatives is expected). Needless to say, a system will need to be in place to remove these QC test results from the data on the study samples. Where POC diagnostic tests are administered by field staff, it may be essential for a supervisor to review or repeat tests in the field, as results may become less reliable over time.

Reproducibility should be checked within batches, between batches, and from day to day or week to week by the use of appropriate controls. Intra-observer variation can be determined by having duplicate samples processed by the same observer at different times, and inter-observer variation measured by having the same samples processed independently by two different staff members. Inter-product variation is tested by comparing new vs old batches of staining solutions, media, reagents, and so on, on a group of the same samples.

It is essential that immediate remedial action is taken if QC checks reveal a problem.

5.2. Internal quality control

Two types of QC can be distinguished—‘internal’ and ‘external’. Internal QC comprises procedures that are introduced within the field laboratory. External QC involves external monitoring such as the duplicate testing of samples in another reference laboratory to serve as a ‘gold standard’ or ‘blind’ measurement in the field laboratory of a set of samples provided by an external reference laboratory.

The essence of internal QC lies in a tight circle of checks, reporting, evaluation, and action. It is essential to have detailed manuals of every procedure, with a checklist to be consulted each time the procedure is run. Well-kept records, with regular review of these by the supervisors, are key elements in QC. Laboratory QC procedures must be an integral part of the work plan for the study.

5.3. External quality assurance

A major reason for external QA programmes is to check the accuracy of test results. Reproducibility can be assessed adequately by internal QC procedures, but checks on accuracy are best done, for many tests, in collaboration with other laboratories. The results from a laboratory may be highly reproducible within that laboratory but might be consistently incorrect. There are a range of external QA programmes which offer both testing of site-generated samples and/or the provision of a panel of samples with known characteristics that are specific for each assay (for example, biochemistry and haematology analysers). If specimens are selected for QA checks after they have been analysed locally and in such a way that the laboratory staff will not know which specimen will be selected, the use of site-generated QA systems are to be preferred to QA that depends on specimens provided by the external laboratory, since the laboratory staff will know which these QA panel specimens are and may take particular care with them.

SOPs need to be developed for the shipping and reception of samples for QA. An investigation request form should accompany samples that are sent, and every effort should be made to ensure that transport conditions are appropriate and the same for all samples (for example, route, packing conditions, and type of container). Attainment of levels of proficiency by the laboratory and its staff may be a prerequisite prior to involvement in some studies; but, after that, external QA activities would be most frequent during training phases and at the beginning of a field study but should continue throughout. If a problem is detected, it is essential that the reason for this is investigated immediately and that this leads to effective remedial action.

The WHO has produced a list of pre-qualified QC laboratories (http://apps.who.int/prequal/lists/pq_qclablist.pdf), and a link to the United Kingdom National External Quality Assessment Service is <http://www.ukneqas.org.uk/content/Pageserver.asp>.

6. Accreditation and links between laboratories

In some cases, a field laboratory may be set up specifically for the conduct of a particular study and may have no regular links with other laboratories. Increasingly, however, there will be links with other laboratories, either as collaborative partners in projects or to provide specialized expertise and analysis. There should be a clear specification in the study protocol of which procedures and checks will be performed at each laboratory, how arrangements will be made for the transport of specimens and supplies between them, and how and which records will be exchanged. Links with an external reference laboratory may be desirable for independent checks, as part of QA procedures (see Section 5.3).

If samples are to be sent to other laboratories for further storage, processing, or analysis (for example, blood, sera, slides), it will be important to give attention to the following points.

1. It is risky to send entire samples to another laboratory or to send all of the samples from one survey or study at the same time. Duplicates should be kept, even when storage facilities are limited, to guard against loss during shipment.
2. Samples should not be sent to another laboratory without a clear agreement as to what analyses will be done and how these will be reported back. It is essential that an SOP defines *who does what, with what, and when*. These arrangements are defined in Material Transfer Agreements (MTAs). An MTA is a contract that governs the transfer of research materials, such as blood or serum samples, between two organizations. The number of samples to be analysed and type of tests should be agreed beforehand, ideally as part of a predefined analysis plan. It is common practice to send samples to another laboratory in such a way that they are analysed 'blind' (for example, no details are sent of which trial arm the samples are from or of the age and sex of the individual subjects). Agreement with respect to publication procedures should also be made, before specimens are sent.
3. The MTA agreed between the field and other laboratories should be part of the study protocol, in which the division of responsibilities should be specified. All parties must also adhere to the provisions of the MTA, in order to participate in the study (for example, local research clearance and ethical clearance).

7. Coding and linkage of results

In order to remove the possibility of bias, staff working in the laboratory should not know which trial arm any sample is from, and it should not be possible for this to be deduced from the labelling system employed. Specimens must be labelled in such a way, however, that each is identified uniquely, and any test results can be linked back to other records of the individual from whom the specimen was taken. While this seems to be stating the obvious, the problems that arise with these aspects of large studies are often substantial. Special care is necessary in longitudinal studies where individuals may be followed for many years, in studies involving many different research groups or laboratories, and in studies where results need to be linked with census information that may be updated over time (for example, individuals may move house, and this may cause problems if the coding system for individuals is too closely linked to a house code). Pre-printed labels are highly advantageous.

Laboratory results will usually be recorded in laboratory books or on specially prepared forms for data entry. Where the machine used for a particular test prints out the results, these should be carefully transcribed on to data forms, preferably using double entry (see Chapter 20, Section 5.1), and the printed output stored. Some machines generate printouts on heat-sensitive paper. In this case, a heat-stable photocopy must be made and stored. Increasingly, electronic record keeping will render these particular storage methods obsolete. Result codes that identify particular problems or features, such as lost and broken samples, technical problems with batches of samples (for example, staining, storage, transport), and the identification of the technicians involved with each test (to check variations between observers) should be used. Errors in readings on some automated machines (for example, values outside the normal range) will be reported or 'flagged' immediately, so that the assay can be repeated, if necessary.

If the study uses laboratory numbers, in addition to individual identification numbers, as is often the case, both numbers should be entered on a computer form for data entry, so that cross-checks and data linkage can be done in the computer.

If multiple laboratory tests are being performed on samples from the trial population, it may be best to wait until all the results have been assembled and collated before entering them into the computer, so that the checking and linkage back to other data on each individual can be done in relatively few steps. This will depend on how the data entry system is organized, but repeated processing of many small sets of data is liable to lead to confusion and may be unnecessarily time-consuming. However, a compromise may be necessary if results are needed in a timely manner for selection for QC or QA checks so that they can be used for the clinical care of the participant.

8. Laboratory health and safety

Detailed attention to health and safety are key aspects of any laboratory. This may be of special importance in some field laboratories, as they may be relatively accessible by the public or have other specific safety risks. It is important therefore to ensure that each laboratory has its own health and safety manual, addressing both general and specific risks, and that this is read by each new staff member or authorized laboratory visitor. A process of evaluation should

be instituted to make sure that all the staff understand the health and safety rules, before performing laboratory tasks. If field staff are to collect and perform primary processing of samples, they will need to be made aware of potential risks. Procedures that will need to be covered will include disposal of needles, blood, stool, urine, and sputum samples, and of used reagents, chemicals, and detergents. Usually, all sharps should be disposed of in special sharps containers, which should be returned to the base laboratory for final disposal. Special attention should be paid to precautions concerning the transmission of blood-borne infections such as hepatitis B and HIV, and specific instructions given for what staff are to do if they are inadvertently exposed to potential infection. It should be standard procedure that field laboratories have at least a starter supply of antiretroviral drugs for HIV post-exposure prophylaxis if blood is being collected or processed. This is obviously even more important in high HIV prevalence areas. Adequate personal protective equipment should be made available for the type of samples to be collected.

Safety procedures should be regularly reviewed by laboratory supervisors and all staff concerned. Laboratory safety guidelines are given in [World Health Organization \(2004\)](#).

References

- Cheesbrough, M. 1987. *Medical laboratory manual for tropical countries*. London: Tropical Health Technology.
- Ratliff, T. A. 2003. *The laboratory quality assurance system: a manual of quality procedures and forms*. Hoboken, NJ: Wiley-Interscience.10.1002/0471721670 [CrossRef]
- Stevens, W. 2003. Good clinical laboratory practice (GCLP): the need for a hybrid of good laboratory practice and good clinical practice guidelines/standards for medical testing laboratories conducting clinical trials in developing countries. *Quality Assurance*, **10**, 83–9. [PubMed: 14660298]
- World Health Organization. 2003. *Manual of basic techniques for a health laboratory* [Online]. Geneva: World Health Organization. Available at: <<http://www.labquality.be/documents/ANALYSIS/9241545305.pdf>>.
- World Health Organization. 2004. *Laboratory biosafety manual* [Online]. Geneva: World Health Organization. Available at: <<http://whqlibdoc.who.int/publications/2004/9241546506.pdf>>.
- World Health Organization. 2009. *Good Clinical Laboratory Practice (GCLP)* [Online]. Geneva: World Health Organization. Available at: <<http://www.who.int/tdr/publications/documents/gclp-web.pdf>>.

Boxes

Box 17.1 Steps involved in the collection of samples for laboratory studies

1. Collection of specimens from the study participants.
2. Placement in a suitable container.
3. Labelling of the container.
4. Temporary storage at an appropriate temperature.
5. Initial processing (for example, serum separation from whole blood), with appropriate re-labelling.
6. Transport to intermediate or final destination for further processing, testing, and storage.

Box 17.2 Some warnings regarding labelling and storing specimens

1. If the transport cold chain includes a stage where samples are frozen in salt–alcohol mixtures, *never* use felt pens (even waterproof ones). Always use ordinarily pencils or pre-printed highly adhesive labels.
2. Written numbers and letters must be in a clear and standardized form. For example, 191 looks the same as 161 upside down!
3. The methods to be used for collection, storage, and transport of specimens should be thoroughly researched and pilot-tested.
4. Special containers and labels are required if samples are to be stored in liquid nitrogen.

Box 17.3 Equipment and maintenance: items that should be regularly checked

1. Twice-daily (morning and evening) recording of temperatures of refrigerators, freezers, and cool-rooms, using maxima and minima thermometers and/or digital data loggers where available, should be performed without fail—even on weekends and public holidays! These data should be updated daily on standardized forms to allow easy monitoring of any changes away from the norm.
2. Checking on the position of the cap and the level of nitrogen in liquid nitrogen containers.
3. Regular and systematic inspection of all items of equipment which require clean lenses (for example, microscopes, spectrophotometers) and checks on focus and adjustment of light sources.
4. Periodic checks on the position of centrifuge rotors (tight centre bolts) and regular cleaning. Rotor speeds can be calibrated with an anemometer.
5. Many automated pieces of equipment (for example, haematological and biochemistry analysers) will have self-test and self-calibration programmes that run at start-up and shutdown. The results of these runs should be recorded and archived. More elaborate procedures may be required before and after longer periods of storage without use.
6. Any regularly used field equipment, such as thermometers, portable haemoglobin machines, and other POC diagnostics, will need to be calibrated periodically and have new batches of reagents checked.
7. Regular calibration of routinely used equipment such as balances, pH meters, and variable volume pipettes.

This is an open access publication. Except where otherwise noted, this work is distributed under the terms of the Creative Commons Attribution NonCommercial 4.0 International licence (CC BY-NC), a copy of which is available at <http://creativecommons.org/licenses/by-nc/4.0/>. Enquiries concerning use outside the scope of the licence terms should be sent to the Rights Department, Oxford University Press, at the address above.

Monographs, or book chapters, which are outputs of Wellcome Trust funding have been made freely available as part of the [Wellcome Trust's open access policy](#)

Bookshelf ID: NBK305520