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Accreditation for Microbiological Laboratories

Second Edition 2013

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This document has been produced by Eurachem. It provides microbiological laboratories with appropriate information and guidance on how to be prepared in order to fulfil the requirements of ISO/IEC 17025.

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1 Introduction and scope of the document

1.1 The general requirements for accreditation are laid down in the International Standard *General requirements for the competence of testing and calibration laboratories* (ISO/IEC 17025 2nd Ed., 2005), hereafter referred to as ISO/IEC 17025 [1]. All of these requirements must be met by laboratories seeking accreditation.

1.2 This guide provides laboratories carrying out microbiological testing with appropriate information on how to fulfil the requirements of ISO/IEC 17025, giving detailed guidance on such requirements for those undertaking the examination of materials, products and substances. The guidance is applicable to the performance of all objective measurements, whether routine, non-routine, or as part of research and development. Although this guide is written primarily for food, water and environmental microbiological testing, the general principles may be applied to other areas. Furthermore, it may also be of use in medical laboratories where ISO 15189 [2] applies, as well as in R&D laboratories. ISO/IEC 17025 remains the authoritative document and, in cases of dispute, accreditation bodies will adjudicate on unresolved matters. However, attention should be paid to additional requirements regarding microbiological tests in the medical field, i.e. safety requirements, specimen handling, personnel qualifications. The guidance given in this document may also be of use to those working towards registration under other quality standards such as GLP (Good Laboratory Practice [3]), GMP (Good Manufacturing Practice [4], and GCP (Good Clinical Practice [5]).

1.3 This guide can be considered as a guidance document for microbiological testing as set out in Annex B of ISO/IEC 17025, taking into account EA MLA (EA Multilateral Agreement) requirements. It has been produced by Eurachem in collaboration with EA LC (EA Laboratory Committee) as a means to facilitate microbiological laboratories in complying with accreditation requirements through a better understanding of the provisions of both the accreditation standards and specific sectorial standards as applicable.

1.4 Microbiological testing is taken to include sterility testing, detection, isolation, enumeration and identification of micro-organisms (viruses, bacteria, fungi and protozoa) and their metabolites in different materials and products, or any kind of assay using micro-organisms as part of a detection system as well as the use of micro-organisms for ecological testing. It follows that some of the guidance given, such as on laboratory environment, will need to be interpreted accordingly. This document can also provide guidance to laboratories using techniques in areas related to microbiology, such as biochemistry, molecular biology and cell culture, although there may be additional requirements for such laboratories.

1.5 This guide is concerned with the quality of test results and is not specifically concerned with health and safety matters. However, laboratory practices should conform to national health and safety regulations. It is important to note that in some cases health and safety issues may have an effect on the quality of testing and the laboratory will be required to take this into account. This version of the guide takes into consideration recent trends in microbiology, e.g. real time PCR (polymerase chain reaction) techniques for the detection of micro-organisms. Molecular methods are, nowadays, very important in microbiological analyses, either as confirmation/identification steps, or as alternative detection methods.

1.6 Definitions of the terms used are given in Appendix A.

2 Standards for accreditation of microbiological laboratories

Main Standards used for laboratory accreditation
ISO/IEC 17025, General requirements for the competence of testing and calibration laboratories [1]
ISO 15189, Medical laboratories – Requirements for quality and competence [2]

Terminology
ISO 9000, Quality management systems – Fundamentals and vocabulary [6]
ISO/IEC Guide 99, International vocabulary of metrology – Basic and general concepts and associated terms (VIM 3) (Available as JCGM 200 from www.bipm.org) [7]

Basic standards
ISO 7218, Microbiology of food and animal feeding stuffs – General requirements for microbiological examinations [8]
ISO/TS 19036, Microbiology of food and animal feeding stuffs – Guidelines for the estimation of measurement uncertainty for quantitative determinations (incl. Amd 1: Measurement uncertainty for low counts) [9]
ISO 29201 Water Quality – The variability of test results and the uncertainty of measurement of microbiological enumeration methods [10]
ISO 8199, Water quality – General guidance on the enumeration of micro-organisms by culture [11]

A detailed list of documents to be considered appears in the References.

3 Personnel

ISO/IEC 17025, paragraph 5.2

3.1 Microbiological testing should be either performed or supervised by an experienced person, qualified to degree level in microbiology or equivalent. Alternative qualifications may meet requirements where a member of staff has extensive relevant experience relating to the laboratory's scope of accreditation. Staff should have relevant practical work experience before being allowed to perform work covered by the scope of accreditation without supervision, or before being considered as experienced for supervision of accredited work. Specific national regulations may override the guidance given in this document.

3.2 If the laboratory includes opinions and interpretations of test results in reports, this shall be done by authorised personnel with suitable experience and relevant knowledge of the specific application, as well as legislative and technological requirements and acceptability criteria.

3.3 The laboratory management shall ensure that all personnel have received adequate training for the competent performance of tests and the operation of equipment. This should include training in basic techniques, e.g. plate pouring, counting of colonies, aseptic technique, etc., with acceptability determined using objective criteria. Personnel may only perform tests on samples if they are either recognised as competent to do so, or if they do so under adequate supervision. On-going competence should be monitored objectively with provision for retraining where necessary. Where a method or technique is not in regular use, verification of personnel performance before testing is undertaken may be necessary. The critical interval between performance of tests should be established and documented. The interpretation of test results for identification and verification of micro-organisms is strongly connected to the experience of the performing analyst and should be monitored for each analyst on a regular basis.

3.4 In some cases, it may be more appropriate to relate competence to a particular technique or instrument rather than to methods.

3.5 The competence of personnel to perform tests shall be documented in relation to the results of internal and external quality control. The effectiveness of the training programme, as well as the identification of further training needs, should also be evaluated based on these results.

4 Environment

ISO/IEC 17025, paragraph 5.3
See also ISO 7218 [8], paragraph 3

4.1 Premises

4.1.1 The typical laboratory is comprised of the testing facilities (where specific microbiological testing and associated activities are carried out) and ancillary facilities (entrances, corridors, administration blocks, cloakrooms and toilets, storage rooms, archives, etc.). In general there are specific environmental requirements for the testing facilities. Depending on the type of testing being carried out, access to the microbiological laboratory should be restricted to authorised personnel. Where such restrictions are in force, personnel should be made aware of:

(a) the intended use of a particular area;
(b) the restrictions imposed on working within such areas;
(c) the reasons for imposing such restrictions;
(d) the appropriate containment levels.

4.1.2 The laboratory should be arranged so as to minimise risks of cross-contamination, where these are significant to the type of test being performed. The ways to achieve these objectives are, for example:

(a) to construct the laboratory according to the 'no way back' layout principle;
(b) to carry out procedures in a sequential manner using appropriate precautions to ensure test and sample integrity (e.g. use of sealed containers);
(c) to segregate activities by time or space.

4.1.3 It is generally considered as good practice to have separate locations, or clearly designated areas, for the following:

- sample receipt and storage area;
- sample preparation (e.g. a segregated location should be used for the preparation of powdery products likely to be highly contaminated);
- examination of samples, including incubation;
- maintenance of reference organisms;
- manipulation of presumptive pathogens;
- storage of culture media and reagents;
- media and equipment preparation, including sterilisation;
- sterility assessment;
- decontamination;
- cleaning of glassware and other equipment;
- storage of hazardous chemicals.

The area for washing (after decontamination) may be shared with other parts of the laboratory provided that the necessary precautions are taken to prevent transfer of traces of substances which could adversely affect microbial growth. The need for physical separation should be judged on the basis of the activities specific to the laboratory (e.g. number and type of tests carried out).

Laboratory equipment should not routinely be moved between areas to avoid accidental cross-contamination.

In the molecular biology laboratory, dedicated pipettes, tips, centrifuges, tubes, adequate protective clothing, vials, heating blocks etc. should be located in each work area (i.e. low-medium-high DNA working environments). Where PCR primers and probes are prepared, suitable segregation of these tasks should be ensured to minimise DNA cross-contamination. DNA amplification should be conducted in a dedicated section of the laboratory.

4.1.4 Space should be sufficient to allow work areas to be kept clean and tidy. The space required should be commensurate with the volume of analyses handled and the overall internal organisation of the laboratory. The space should meet the requirements of national regulations when available.

4.1.5 Workrooms should be appropriately ventilated and at a suitable temperature. This may be done by natural or forced ventilation, or by the use of an air conditioner. Where air conditioners are used, filters should be appropriate, inspected, maintained and replaced according to the type of work being carried out. Natural ventilation is not recommended in clean rooms or workrooms handling pathogens.

4.1.6 Reduction of contamination may be achieved by having:

- smooth surfaces on walls, ceilings, floors and benches (the smoothness of a surface is judged on how easily it may be cleaned). Tiles are not recommended as bench covering material;
- concave joints between the floor, walls and ceiling;
- minimal opening of windows and doors while tests are being carried out;
- sun shades placed on the outside;
- easy access for cleaning of internal sun shades if it is impossible to fit them outside;
- fluid conveying pipes not passing above work surfaces unless placed in hermetically sealed casings;
- a dust-filtered air inlet for the ventilation system;
- separate hand-washing arrangements, preferably non-manually controlled;

- cupboards up to the ceiling;
- no rough and bare wood;
- wooden surfaces of fixtures and fittings adequately sealed;
- stored items and equipment arranged to facilitate easy cleaning;
- no furniture, documents or other items other than those strictly necessary for testing activities.

This list is not exhaustive, and not all examples will apply in every situation. Ceilings, ideally, should have a smooth surface with flush lighting. When this is not possible (as with suspended ceilings and hanging lights), the laboratory should have documented evidence that they control any resulting risks to hygiene and have effective means of overcoming them, e.g. a surface-cleaning and inspection programme.

4.1.7 Where laboratories are on manufacturing premises, personnel must be aware of the potential for contamination of production areas, and should demonstrate that they have taken appropriate measures to avoid any such occurrence.

4.1.8 When PCR primers and probes are prepared, suitable segregation of these tasks should be ensured to minimise DNA cross-contamination. DNA amplification should be conducted in a dedicated section of the laboratory in a positive pressurised room

4.1.9 Negative pressurised rooms are required for manipulation of high risk micro-organisms.

4.2 Environmental monitoring

4.2.1 An appropriate environmental monitoring programme shall be devised, including, for example, frequent use of air settlement plates for bacterial and fungal contaminants as well as periodic surface swabbing for a variety of relevant micro-organisms, especially pathogens. Acceptable background counts should be assigned and there should be a documented procedure for dealing with situations in which these limits are exceeded. Analysis of data should enable trends in levels of contamination to be determined.

4.2.2 Where molecular techniques are undertaken, monitoring for DNA contaminants should be undertaken by employing a No Template Control (NTC).

4.3 Hygiene

4.3.1 There shall be a documented cleaning programme for laboratory fixtures, equipment and surfaces. It should take into account the results of environmental monitoring and the possibility of cross-contamination. There should be a procedure for dealing with spillages.

4.3.2 Measures should be taken to avoid accumulation of dust, by the provision of sufficient storage space, by having minimal paperwork in the laboratory and by prohibiting plants and personal possessions in the laboratory work area.

4.3.3 Protective clothing appropriate to the type of testing being performed (including, if necessary, protection for hair, beard, hands, shoes, etc.) should be worn in the microbiological laboratory and removed before leaving the area. This is particularly important in the molecular biology laboratory, where for example, movement from an area of high DNA load to one of low DNA load may unwittingly introduce cross-contamination. A change of the laboratory coat may suffice when moving between areas.

4.3.4 Adequate hand washing facilities should be available and a policy regarding appropriate glove use should be in place to avoid the spreading of micro-organisms in the laboratory.

5 Validation and Verification of test methods

ISO/IEC 17025, paragraph 5.4.5
See also ISO/TS 12869 [12], ISO 7218 [8], ISO 17994 [13], ISO/TR 13843 [14], ISO 16140 [15]

5.1 Selection of test methods

The laboratory shall use appropriate test methods to meet the specific needs in each case. To this end it is preferable to use standard methods, i.e. the ones published in international, regional or national standards, or in scientific textbooks or by widely recognised and reputable organisations. These methods have normally been validated. However, other methods could be used provided that they are validated by the laboratory as described in 5.2.1 and 5.2.2. This is the case with laboratory-designed/developed methods and standard methods used outside their intended scope or modified in a way that an influence on the test results must be assumed. Further to this, the detailed procedure to be followed in each case varies with the nature of the method, i.e. qualitative, semi-quantitative and quantitative. The method/technique used will dictate the aspects of validation to be considered.

The following standards can assist laboratories in obtaining method validation data: ISO/TR 13843, ISO 16140 and ISO 17994.

5.2 Validation

The validation of microbiological test methods should reflect actual test conditions. This may be achieved by using naturally contaminated products or products spiked with a predetermined level of contaminating organisms. The analyst should be aware that the addition of contaminating organisms to a matrix only mimics in a superficial way the presence of the naturally occurring contaminants. However, it is often the best and o nly solution available. The extent of validation necessary will depend on the method and the application. The laboratory shall validate standard methods applied to matrices not specified in the standard procedure.

5.2.1 Qualitative microbiological test methods, such as where the result is expressed in terms of detected/not detected, and confirmation and identification procedures, should be v alidated by determining, if appropriate, the specificity, sensitivity, relative trueness, positive deviation, negative deviation, limit of detection, matrix effect, repeatability and r eproducibility (see Appendix A for definitions).

5.2.2 For quantitative microbiological test methods, the specificity, sensitivity, relative trueness, positive deviation, negative deviation, repeatability, reproducibility and the limit of quantification within a defined variability should be c onsidered and, if necessary, quantitatively determined. The differences due to the matrices must be taken into account when testing different types of samples. The results should be evaluated with appropriate statistical methods.

5.2.3 Laboratories shall retain validation data on commercial test systems (kits) used in the laboratory. This validation data may be obtained through collaborative testing and f rom validation data submitted by the manufacturers and subjected to third party evaluation (e.g. AFNOR, NordVal, Microval, AOAC). If the validation data are not available, or not wholly applicable, the laboratory shall be responsible for completing the validation of the method.

5.2.4 If a m odified version of a method is required to meet the same specification as the original method, then the modified method must be validated for those parameters that are likely to be affected by the revision. Experimental design and analysis of results must be statistically valid.

5.2.5 Even when validation is completed, the user will still need to verify, as appropriate, (e.g. when there is a change in the critical factors) that the documented performance can be met. This can be accomplished by the use of spiked samples or reference materials incorporating relevant matrices.

5.3 Verification

In the preferable case of standard and validated methods being used, the laboratory is still required to prove that it can implement them in a reliable way. This is called verification – see further “Eurachem Terminology in Analytical Measurement”. For verification of quantitative methods the laboratory has, in most cases, to determine repeatability, measurement uncertainty (see section 6) and limit of quantitation, and for qualitative methods the limit of detection.

6 Uncertainty of measurement

ISO/IEC 17025, paragraph 5.4.6
See also ISO/TS 19036 [9], EA-4/16 [16], ISO 29201 [10] and HPA (UK) QSOP4 [17]

6.1 The international definition of uncertainty of measurement is given in the ISO International Vocabulary of Metrology (VIM 3) [7] and the concept in general is treated in the Eurachem guide on uncertainty [28]. Both ISO/IEC 17025 and ISO 15189 specify the need for laboratories to estimate the measurement uncertainty taking into account all components that may affect the result. Measurement uncertainty can only be determined for the results from quantitative methods. The general approaches to evaluating and expressing measurement uncertainty in microbiological testing of food and water are based either on ISO/TS 19036 (for food), or ISO 29201 and HPA (UK) QSOP4 (for water). ISO 29201 is more versatile, covering both colony counts and MPN (Most Probable Number) results, and presents two different approaches to uncertainty estimation (component approach and global approach) that can be used for different matrices.

6.2 Microbiological tests generally come into the category of those that preclude the rigorous, metrologically and statistically valid calculation of measurement uncertainty as described in the ISO Guide to the expression of uncertainty in measurement [18]. It is generally appropriate to base the estimate of measurement uncertainty on repeatability and intermediate precision (within-laboratory reproducibility) data. The individual uncertainty components should be identified and demonstrated to be under control and their contribution to the variability of results evaluated. Some components (e.g. pipetting, weighing, dilution effects and incubator effects) may be readily measured and easily evaluated to demonstrate a negligible contribution to the overall measurement uncertainty. Other components (e.g. sample stability and sample preparation) cannot be measured directly and their contribution cannot be evaluated in a statistical manner but their importance to the variability of results should also be considered.

6.3 It is expected that accredited microbiological testing laboratories will have a good understanding of the distributions of organisms within the matrices they test, and will take this into account when sub-sampling by following good laboratory practices and/or regulatory requirements where applicable. However, it is not always practical that this component of measurement uncertainty is included in estimates unless the customer's needs dictate otherwise. The principal reasons for this are:

- the uncertainty due to the distribution of organisms within the product matrix is not a function of the laboratory's performance and may be unique to individual samples tested;
- test **methods should specify the sample size to be used taking into** account poor homogeneity.

6.4 The concept of measurement uncertainty cannot be applied directly to qualitative test results such as those from detection tests or the determination of attributes for identification. Nevertheless, individual sources of variability, e.g. consistency of reagent performance and analyst interpretation, should be identified and demonstrated to be under control. Additionally, for tests where the limit of detection is an important indication of suitability, the measurement uncertainty associated with the inocula used to determine the limit should be estimated and its significance evaluated. Laboratories should also be aware of the incidence of false positive and false negative results associated with the qualitative tests they use.

6.5 In the case of microbiological laboratories performing molecular testing for the detection and quantification of genetically modified organisms (GMOs), measurement uncertainty is estimated according to JRC/IRMM Guidance EUR 22756 EN [19].

7 Equipment – maintenance, calibration and performance verification

ISO/IEC 17025, paragraph 5.5
See also ISO 7218 [8], paragraph 5 and ILAC P10 [20]

7.1 Maintenance

7.1.1 Maintenance of essential equipment shall be carried out at specified intervals as determined by factors such as the frequency of use. Detailed records shall be kept. Examples of maintenance of equipment and intervals are given in Appendix E.

7.1.2 Attention should be paid to the avoidance of cross-contamination arising from equipment, for example:

- disposable equipment should be clean and sterile when appropriate;
- re-used glassware should be properly cleaned and sterilised when appropriate;
- ideally, laboratories should have a separate autoclave for decontamination. However, one autoclave is acceptable provided that adequate precautions are taken to separate decontamination and sterilisation loads, and a documented cleaning programme is in place to address both the internal and external environment of the autoclave.

7.1.3 Typically, the following items of equipment will be maintained by cleaning and servicing, inspecting for damage, by general verification of suitability and, where relevant, sterilising:

- general service equipment – filtration apparatus, glass or plastic containers (bottles, test tubes), glass or plastic Petri dishes, sampling instruments, wires or loops (platinum, nickel/chromium or disposable plastic);
- water baths, incubators, microbiological cabinets (laminar flow and safety cabinets), autoclaves, homogenisers, fridges, freezers;
- volumetric equipment – pipettes, automatic dispensers, spiral platers;
- measuring instruments – thermometers, timers, balances, pH meters, colony counters.

7.2 Calibration and performance verification

7.2.1 The laboratory must establish a programme for the calibration and performance verification of equipment which has a direct influence on the test results. The frequency of such calibration and performance verification will be determined by documented experience, being based on need, type and previous performance of the equipment. Intervals between calibration and verification shall be shorter than the time the equipment has been found to take to drift outside acceptable limits. Examples of calibration intervals and typical performance checks for various laboratory instruments are given in Appendix C and Appendix D.

7.2.2 Temperature measurement devices

(a) Where temperature has a direct effect on the result of an analysis or is critical for the correct performance of equipment, temperature measuring devices (for example thermocouples and platinum resistance thermometers (PRTs) used in incubators and autoclaves) shall be of an appropriate quality to achieve the accuracy required. It is preferable that, for health and safety reasons, mercury and toluene liquid-in-glass thermometers are not used in the laboratory.

(b) Calibration of these devices shall be traceable to national or international standards for temperature. However, if accuracy requirements permit, measurement devices that can be demonstrated to conform to an appropriate and nationally or internationally accepted manufacturing specification may also be used. Such devices may, for example, be used for monitoring storage fridges and freezers and also incubators and water baths where acceptable tolerance around the target temperature permits. Verification of the performance of such devices is necessary.

7.2.3 Incubators, water baths, ovens

The stability of temperature, uniformity of temperature distribution and time required to achieve equilibrium conditions in incubators, water baths, ovens and temperature-controlled rooms shall be established initially, and then periodically, at a documented frequency, in particular with respect to typical usage (for example position, space between, and height of, stacks of Petri dishes). The constancy of the characteristics recorded during initial validation of the equipment shall be checked and recorded after each significant repair or modification. Laboratories shall monitor daily, or according to usage, the operating temperature of this type of equipment and retain records.

7.2.4 Autoclaves, including media preparators

The following paragraphs outline the generally accepted approach to calibration, and the establishment and monitoring of performance. However, it is recognised that quantitative testing of materials and items processed by autoclaving may also provide equivalent assurance of quality.

(a) Autoclaves should be capable of meeting specified time and temperature tolerances. Pressure cookers fitted only with a pressure gauge are not acceptable. Sensors used for controlling or monitoring operating cycles require calibration and the performance of timers should be verified.

(b) Initial validation should include performance studies (spatial temperature distribution surveys) for each operating cycle and each load configuration used in practice. This process must be repeated after significant repair or modification (e.g. replacement of thermo-regulator probe or programmer, modification of loading arrangements or operating cycle) or where indicated by the results of quality control checks on media. Sufficient temperature sensors should be positioned within the load (e.g. in containers filled with liquid/medium) to enable location differences to be demonstrated. In the case of media preparators, where uniform heating cannot be demonstrated by other means, the use of two sensors, one adjacent to the control probe and one remote, would generally be considered appropriate. Validation and re-validation should consider the suitability of come-up and come-down times as well as time at sterilisation temperature.

(c) Clear operating instructions should be provided based on the heating profiles determined for typical uses during validation/re-validation. Acceptance/rejection criteria should be established and records of autoclave operations, including temperature and time, maintained for every cycle.

(d) Monitoring may be achieved by one of the following:

(i) using a thermocouple and recorder to produce a chart or printout;

(ii) direct observation and recording of maximum temperature achieved and time at that temperature.

In addition to directly monitoring the temperature of an autoclave, the effectiveness of its operation during each cycle may be checked by the use of chemical or biological indicators for sterilisation/decontamination purposes.
Autoclave tape or indicator strips should be used only to show that a load has been processed, not to demonstrate completion of an acceptable cycle.

7.2.5 Weights and balances

Weights and balances shall be calibrated traceably at regular intervals (according to their intended use).

7.2.6 Volumetric equipment

(a) Volumetric equipment such as automatic dispensers, dispenser/diluters, mechanical hand pipettes and disposable pipettes may all be used in the microbiology laboratory. Laboratories should carry out initial verification of volumetric equipment and then make regular checks to ensure that the equipment is performing within the required specification. Verification should not be necessary for glassware which has been certified to a specific tolerance. Equipment should be checked for the accuracy of the delivered volume against the set volume (for several different settings in the case of variable volume instruments) and the precision of the repeat deliveries should be measured.

(b) For 'single-use' disposable volumetric equipment, laboratories should obtain supplies from companies with a recognised and relevant quality system. After initial validation of the suitability of the equipment, it is recommended that random checks on accuracy are carried out. If the supplier has no recognised quality system, laboratories should check each batch of equipment for suitability.

7.2.7 Thermal cyclers

Laboratories should carry out verification of temperature, ramp rate, overshoots/undershoots, hold time.

7.2.8 Other equipment

Conductivity meters, oxygen meters, pH meters and other similar instruments should be verified regularly or before each use. The buffers used for verification purposes should be stored in appropriate conditions and should be marked with an expiry date. Where humidity is important to the outcome of the test, hygrometers should be calibrated, the calibration being traceable to national or international standards. Timers, including the autoclave timer, should be verified using a calibrated timer or national time signal. Where centrifuges are used in test procedures, an assessment should be made of the criticality of the centrifugal force. Where it is critical, the centrifuge will require calibration.

8 Reagents and culture media

ISO/IEC 17025, paragraph 4.6 and 5.5
See also ISO/TS 11133-1 [21] and ISO/TS 11133-2 [22]

8.1 Reagents

Laboratories should ensure that the quality of reagents used is appropriate for the test concerned. They should verify the suitability of each batch of reagents critical for the test, initially and during its shelf-life, using positive and negative control organisms which are traceable to recognised national or international culture collections.

8.2 In-house prepared media

8.2.1 The suitable performance of culture media, diluents and other suspension fluids prepared in-house should be checked, where relevant, with regard to:

- recovery or survival maintenance of target organisms;
- inhibition or suppression of non-target organisms;
- biochemical (differential and diagnostic) properties;
- physical properties (e.g. pH, volume and sterility).

Quantitative procedures for evaluation of recovery or survival should be performed according to ISO 11133.

8.2.2 Raw materials (both commercial dehydrated formulations and individual constituents) should be stored under appropriate conditions, e.g. cool, dry and dark. All containers, especially those for dehydrated media, should be sealed tightly. Dehydrated media that are caked or cracked, or show a colour change, should not be used. Distilled deionised, or reverse osmosis produced water, free from bactericidal, inhibitory or interfering substances, should be used for preparation unless the test method specifies otherwise.

8.2.3 Shelf-life of prepared media under defined storage conditions shall be determined and verified.

8.3 Ready-to-use-media

8.3.1 All media, including diluents and other suspension fluids procured ready-to-use or partially complete, also require performance evaluation as in 8.2.1 before use. Evaluation of performance in recovery or survival of target organisms, and the inhibition or suppression of non-target organisms should be fully quantitative. Attributes (e.g. physical and biochemical properties) should be evaluated using objective criteria.

8.3.2 Where the manufacturer of media procured ready-to-use or partially complete is covered by a recognised quality system (i.e. ISO 9000 series) and the media are quality controlled according to ISO 11133, relevant information (certificates) needs to be reviewed for acceptability but quality control does not need to be repeated. Checks by the user laboratory may only involve initial checks for every new manufacturer, and indirect checks through internal quality control procedures. In other circumstances, quality control according to ISO 11133 must be fully performed on every batch received.

8.3.3 As part of this performance evaluation, the user laboratory needs to have adequate knowledge of the manufacturer's quality system and the product specifications, which include at least the following:

- name of the media and list of components, including any supplements;
- shelf-life and the acceptability criteria applied;
- storage conditions;
- sterility check;
- check of growth of target and non-target control organisms used (with their culture collection references) and acceptability criteria;
- physical checks and the acceptability criteria applied;
- date of issue of specification.

All the above, including the validation exercise, should be taken into consideration by the laboratory to set acceptability criteria for incoming batches of media appropriate for its testing needs.

8.3.4 Batches of media should be identifiable. Each one received should be accompanied by evidence that it meets the quality specification. The user laboratory should ensure that it will be notified by the manufacturer of any changes to the quality specification.

Note:
Batch: A homogeneous and fully traceable unit of a culture medium or reagent referring to a defined amount of bulk, semi-finished product or end-product, which is consistent in type and quality and which has passed the requirement of production (in-process control) and performance testing and which has been produced within one defined production period, having been assigned the same number.

8.4 Labelling

Laboratories shall ensure that all reagents (including stock solutions), media, diluents, and other suspending fluids are adequately labelled to indicate, as appropriate, identity, concentration, storage conditions, date of opening, preparation date, validated expiry date and/or recommended storage periods. The person responsible for preparation should be identifiable from records.

9 Reference materials and reference cultures

ISO/IEC 17025, paragraph 5.6.3
See also ISO/TS 11333 [21, 22]

9.1 Reference materials

Reference materials and certified reference materials (see definition in Appendix A) provide essential traceability in measurements and are used, for example:

- to demonstrate the accuracy of results;
- to calibrate equipment;
- to monitor laboratory performance;
- to validate methods;
- to enable comparison of methods;
- to demonstrate quality of culture media;
- to demonstrate consistent performance of kits.

If possible, reference materials should be used in appropriate matrices.

9.2 Reference cultures

9.2.1 Traceable reference cultures are required for establishing acceptable performance of media (including test kits), for validating methods and for assessing/evaluating on-going performance. To demonstrate traceability, laboratories shall use reference strains of micro-organisms obtained directly from a recognised national or international collection, where these exist. Where traceable reference cultures are not readily available, commercial derivatives traceable to them could alternatively be used, provided that the relevant properties for its intended use have been shown by the laboratory to be equivalent at the point of use.

9.2.2 Reference strains may be sub-cultured once to provide reference stocks. Purity and biochemical checks should be made in parallel as appropriate. It is recommended to store reference stocks in aliquots either deep-frozen or lyophilised. Working cultures for routine use should be primary subcultures from the reference stock (see Appendix B on preparation of working stocks). If reference stocks have been thawed, they must not be re-frozen and re-used.

9.2.3 Working cultures should not be sub-cultured unless it is required and defined by a standard method or laboratories can provide documentary evidence that there has been no change in any relevant property. Working stocks shall not be sub-cultured to replace reference stocks. Commercial derivatives of reference strains may only be used as working cultures.

10 Sampling

ISO/IEC 17025, paragraph 5.7
See also ISO 7218 [8], paragraph 8 and ISO 19458 [23]

10.1 In many cases, testing laboratories are not responsible for primary sampling to obtain test items. Where they are responsible, it is strongly recommended that this sampling be covered by quality assurance and ideally by accreditation.

10.2 Transport and storage should be under conditions that maintain the integrity of the sample (e.g. chilled or frozen where appropriate). The conditions should be monitored and records kept. Where appropriate, responsibility for transport and storage, between sampling and arrival at the testing laboratory, shall be clearly documented. Testing of the samples should be performed as soon as possible after sampling and s hould conform to relevant standards and/or national/international regulations.

10.3 Sampling should only be performed by trained personnel. Whenever the laboratory is responsible for sampling, the personnel to be i nvolved shall also be authorised for sampling. It should be carried out aseptically using sterile equipment. Environmental conditions, for instance air contamination and temperature, should be monitored and recorded at the sampling site. Time of sampling should be recorded.

11 Sample handling and identification

ISO/IEC 17025, paragraphs 5.7 and 5.8
See also ISO 7218 [8], paragraph 8, ISO 6887 [24] and ISO 19458 [23]

11.1 Microbial flora may be sensitive to factors such as temperature or duration of storage and transport, so it is important to check and record the condition of the sample on receipt by the laboratory.

11.2 The laboratory shall have procedures that cover the delivery of samples and sample identification. If there is insufficient sample or the sample is in poor condition due to physical deterioration, incorrect temperature, damaged packaging or deficient labelling, the laboratory should consult with the customer before deciding whether to test or refuse the sample. In any case, records should be maintained and the condition of the sample should be indicated on the test report.

11.3 The laboratory shall record all relevant information, in particular the following:
(a) date and, where relevant, the time of receipt;
(b) condition of the sample on receipt and, when necessary, temperature;
(c) characteristics of the sampling operation (sampling date, sampling conditions, etc.).

11.4 Samples awaiting test shall be stored under suitable conditions to minimise changes to any microbial population present. Storage conditions should be defined and recorded.

11.5 The packaging and labels from samples may be highly contaminated and should be handled and stored with care so as to avoid any spread of contamination.

11.6 Sub-sampling by the laboratory immediately prior to testing is considered to be part of the test method. It shall be performed according to national or international standards, where they exist, or by validated in-house methods. Sub-sampling procedures should be designed to take account of uneven distribution of micro-organisms (general guidance given in ISO 6887 and ISO 7218).

11.7 A procedure for the retention and disposal of samples shall be written. Samples should be stored until the test results are obtained or longer, if required and if applicable, based on legislative requirements or customer's request. Laboratory sample portions that are known to be highly contaminated should be decontaminated prior to being discarded (see 12).

12 Disposal of contaminated waste

ISO/IEC 17025, paragraph 5.8
See also ISO 7218 [8]

The correct disposal of contaminated materials may not directly affect the quality of sample analysis, although procedures should be designed to minimise the possibility of contaminating the test environment or materials. However, it is a matter of good laboratory management and should conform to national/international environmental or health and safety regulations.

13 Quality assurance of results/quality control of performance

ISO/IEC 17025, paragraph 5.9
See also EA-4/18 [25], Eurachem Proficiency Testing Guide [26]

13.1 Internal quality control

13.1.1 Internal quality control consists of all the procedures undertaken by a laboratory for the continuous evaluation of its work. The main objective is to ensure the consistency of results day-to-day and t heir conformity with defined criteria.

13.1.2 A programme of periodic checks is necessary to demonstrate that variability (i.e. between analysts and between equipment or materials etc.) is under control. All tests included in the laboratory's scope of accreditation need to be covered. The programme may involve:

- the use of spiked samples with variable contamination levels, including target and background flora;
- the use of spikes/naturally contaminated samples from a range of matrices;
- the use of reference materials (including proficiency testing scheme test materials);
- replicate testing;
- replicate evaluation of test results, i.e. counting of colonies in petri dishes by two analysts.

The internal quality control programme must be adapted to the actual frequency of tests performed by the laboratory. It is recommended that, where possible, tests should incorporate controls to monitor performance. It is also advised that data from reference materials and s piked samples be plotted to assist in the evaluation of trends in a visual manner.

13.1.3 In special instances, a l aboratory may be accredited for a test that it is rarely called on to do. It is recognised that in such cases an on-going internal quality control programme may be inappropriate and that a scheme for demonstrating satisfactory performance which is carried out in parallel with the testing, may be more suitable. However, this does not eliminate the need to participate in proficiency testing schemes at acceptable frequency. In any case, the laboratory should be aware of the inherent risk associated with such an approach and take all appropriate measures.

13.2 External quality assessment (proficiency testing)

13.2.1 Laboratories should regularly participate in proficiency testing (PT), relevant to their scope of accreditation. Preference should be given to proficiency testing schemes which use appropriate matrices.

13.2.2 Participation in proficiency testing schemes is mandatory, provided that appropriate schemes are available. If this is not the case, the laboratory should participate in interlaboratory comparisons organised by a s ufficient number of other laboratories on the basis of a well-documented protocol.

13.2.3 Laboratories should use external quality assessment not only to assess laboratory bias but also to check the validity of the whole quality system.

13.2.4 Although Accreditation Bodies may specify minimum participation in proficiency testing schemes, it is the responsibility of the laboratory to demonstrate that the frequency and extent of their participation is appropriate for their scope. The document EA-4/18 may give useful support with the use of sub-disciplines, i.e. an area of technical competence defined by a m inimum of one measurement technique, property and product, which are related. This facilitates the optimisation of the extent of participation in proficiency testing. Further to this, the Eurachem guide on selection, use and interpretation of PT schemes [26] may help in the interpretation of the results from proficiency testing participation.

13.2.5 Laboratories are encouraged to subscribe to ISO/IEC 17043 [27] accredited PT schemes; other providers should only be used where the laboratory has assessed their competency.

14 Test reports

ISO/IEC 17025, paragraph 5.10
See also ISO 19036 [9], ISO 8199 [11], ISO 7218 [8]

14.1 In quantitative methods, results are expressed as number of colony forming units (cfu) per volume or grams of sample analysed. Below 10 cfus per plate, precision decreases significantly and laboratories are advised to reflect this on their test reports. If the result of the enumeration is negative, it should be reported as “not detected for a defined unit” or “less than the detection limit for a defined unit”. If preferred, and in order to comply with national technical and health regulations, the result may also be reported as “zero for a defined unit”.

14.2 Qualitative test results should be reported as “detected/not detected in a defined quantity or volume”. They may also be expressed as “less than a specified number of organisms for a defined unit” where the specified number of organisms exceeds the detection limit of the method and this has been agreed with the customer.

14.3 Where an estimate of the measurement uncertainty of the test result is expressed on the test report, any limitations (particularly if the estimate does not include the component contributed by the distribution of micro-organisms within the sample) have to be made clear to the customer.

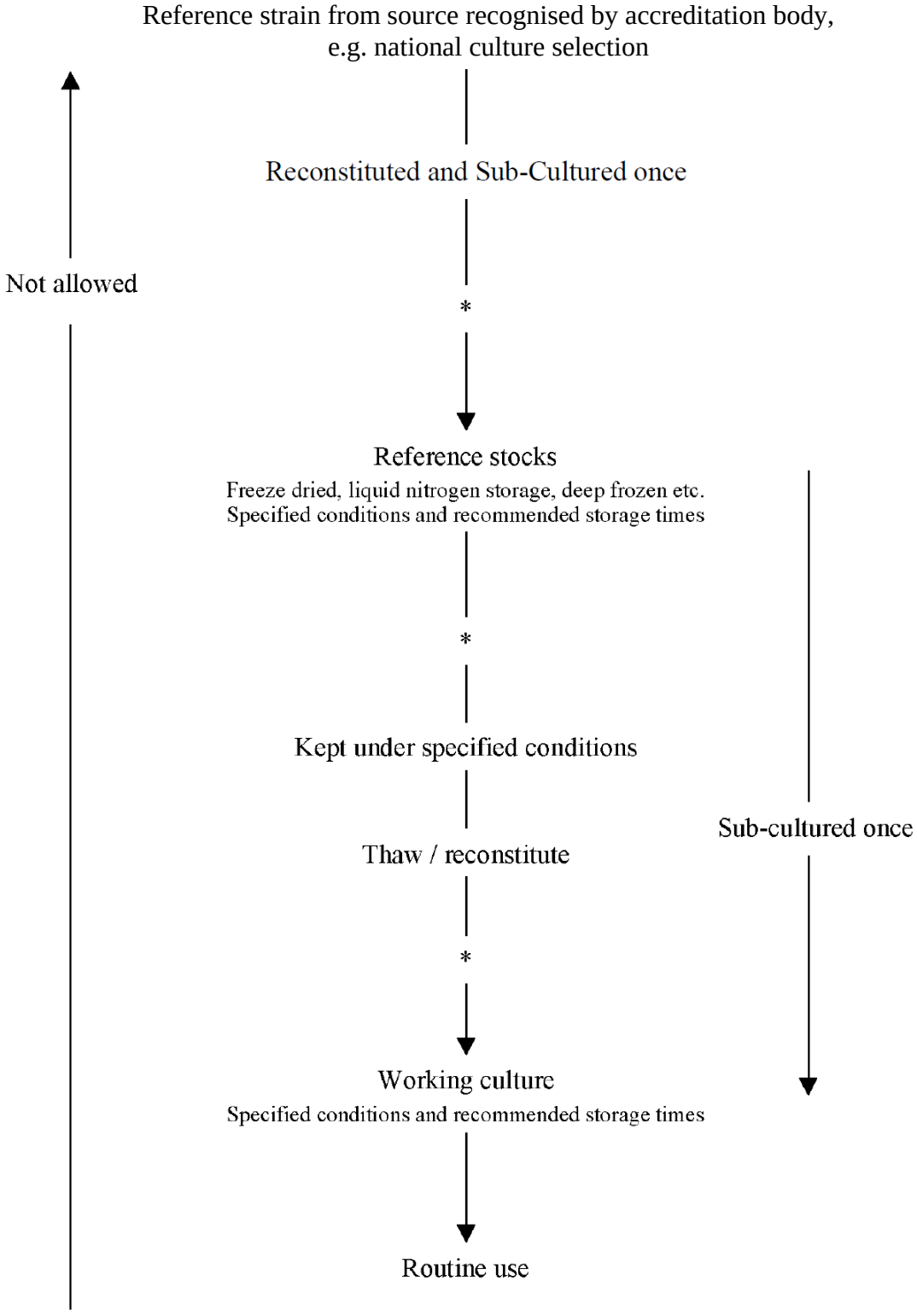
14.4 Laboratories may have to check if the standards used have their own specific requirements regarding the expression of results. Examples include: ISO 11731-2:2004 *Water quality -- Detection and enumeration of Legionella -- Part 2: Direct membrane filtration method for waters with low bacterial counts* and ISO 6222:1999 *Water quality -- Enumeration of culturable micro-organisms -- Colony count by inoculation in a nutrient agar culture medium.* .

Appendix A Glossary of terms

Calibration	Operation that, under specified conditions, in a first step, establishes a relation between the quantity values with measurement uncertainties provided by measurement standards and corresponding indications with associated measurement uncertainties and, in a second step, uses this information to establish a relation for obtaining a measurement result from an indication. *NOTE 1* A calibration may be expressed by a statement, calibration function, calibration diagram, calibration curve, or calibration table. In some cases, it may consist of an additive or multiplicative correction of the indication with associated measurement uncertainty. *NOTE 2* Calibration should not be confused with adjustment of a measuring system, often mistakenly called "self-calibration", nor with verification of calibration. *NOTE 3* Often, the first step alone in the above definition is perceived as being calibration. [VIM 3]
Certified reference material	Reference material, accompanied by documentation issued by an authoritative body and providing one or more specified property values with associated uncertainties and traceabilities, using valid procedures. [VIM 3]
Limit of detection	Applied to qualitative microbiological tests: The lowest number of micro-organisms that can be detected, but in numbers that cannot be estimated accurately.
Limit of quantification	Applied to quantitative microbiological tests: The lowest number of micro-organisms within a defined variability that may be determined under the experimental conditions of the method under evaluation.
Measurement precision	Closeness of agreement between indications or measured quantity values obtained by replicate measurements on the same or similar objects under specified conditions. [VIM 3]
Negative deviation	Occurs when the alternative method gives a negative result without confirmation when the reference method gives a positive result. This deviation becomes a false negative result when the true result can be proved as being positive.
Positive deviation	Occurs when the alternative method gives a positive result without confirmation when the reference method gives a negative result. This deviation becomes a false positive result when the true result can be proved as being negative.
Reference cultures	Collective term for reference strain, reference stocks and working cultures.
Reference material	Material, sufficiently homogeneous and stable with reference to specified properties, which has been established to be fit for its intended use in measurement or in examination of nominal properties. [VIM 3]
Reference method	Thoroughly investigated method, clearly and exactly describing the necessary conditions and procedures, for the measurement of one or more property values that has been shown to have trueness and precision commensurate with its intended use and that can therefore be used to assess other methods for the same measurement, particularly in permitting the characterisation of a reference material. Normally a national or international standard method.

Reference stocks	A set of separate identical cultures obtained by a single sub-culture from the reference strain. [ISO 11133]
Reference strains	Micro-organisms defined at least to the genus and species level, catalogued and described according to its characteristics and preferably stating its origin. [ISO 11133] Normally obtained from a recognised national or international collection.
Relative trueness	The degree of correspondence of the results of the method under evaluation to those obtained using a recognised reference method.
Repeatability	Measurement precision under a set of repeatability conditions of measurement. [VIM 3]
Repeatability condition	i) For quantitative methods Condition of measurement, out of a set of conditions that includes the same measurement procedure, same operators, same measuring system, same operating conditions and same location, and replicate measurements on the same or similar objects over a short period of time. [VIM 3] (ii) For qualitative methods *An interpretation analogous to the above could be used, namely:* Conditions of test…. (instead of conditions of measurement…)
Reproducibility	Measurement precision under reproducibility conditions of measurement. [VIM 3]
Reproducibility condition	(i) For quantitative methods Condition of measurement, out of a set of conditions that includes different locations, operators, measuring systems, and replicate measurements on the same or similar objects. [VIM 3] (ii) For qualitative methods *An interpretation analogous to the above could be used, namely*: Conditions of test…. (instead of conditions of measurement…)
Sensitivity	The fraction of the total number of positive cultures or colonies correctly assigned in the presumptive inspection. [ISO/TR 13843]
Specificity	The fraction of the total number of negative cultures or colonies correctly assigned in the presumptive inspection. [ISO/TR 13843]
Validation	The confirmation by examination and the provision of objective evidence that the particular requirements for a specific intended use are fulfilled. [ISO/IEC 17025] Note: Primary validation. An exploratory process with the aim of establishing the operational limits and performance characteristics of a new, modified or otherwise inadequately characterised method. It should result in numerical and descriptive specifications for the performance and include a detailed and unambiguous description on the target of interest (positive colony, tube or plaque). [ISO 13843]
Verification	Provision of objective evidence that a given item fulfils specified requirements. [VIM 3] Note: Verification (secondary validation) takes place when a laboratory proceeds to implement a method developed elsewhere. Verification focuses on gathering evidence that the laboratory is able to meet the specifications established in primary validation. [adopted from ISO 13843]
Working culture	A primary sub-culture from a reference stock. [ISO 11133]

Appendix B General use of reference cultures



*Parallel purity checks and biochemical tests as appropriate

All parts of the process shall be fully documented and detailed records of all steps must be maintained

Appendix C Guidance on calibration and calibration checks

This information is provided for guidance purposes and the frequency will be based on the need, type and previous performance of the equipment.

Type of equipment	Requirement	Suggested frequency
Reference thermometers (liquid-in-glass)	Full traceable re-calibration Single point (e.g. ice-point check)	Every 5 years Annually
Reference thermocouples	Full traceable re-calibration Check against reference thermometer	Every 3 years Annually
Working thermometers & Working thermocouples	Check against reference thermometer at ice-point and/or working temperature range	Annually
Balances	Full traceable calibration	Annually in the first 3 years, followed by less frequently, based on satisfactory performance
Calibration weights	Full traceable calibration	Every 5 years
Check weight(s)	Check against calibrated weight or check on balance immediately following traceable calibration	Every two years
Volumetric glassware	Gravimetric calibration to required tolerance	Annually
Pipettors/pipettes	Full traceable calibration	Annually
Microscopes	Traceable calibration of stage micrometre (where appropriate)	Initially
Hygrometers	Traceable calibration	Annually
Centrifuges	Traceable calibration or check against an independent tachometer, as appropriate	Annually

Appendix D Guidance on equipment validation and verification of performance

This information is provided for guidance purposes and the frequency will be based on the need, type and previous performance of the equipment.

Type of equipment	Requirement	Suggested frequency
Temperature controlled equipment (incubators, baths, fridges, freezers)	(a) Establish stability and uniformity of temperature (b) Monitor temperature	(a) Initially, periodically, at documented frequency, and after repair/ modification (b) Daily .each use
Sterilising ovens	(a) Establish stability and uniformity of temperature (b) Monitor temperature	(a) Initially, periodically, at documented frequency, and after repair/ modification (b) Daily/each use
Autoclaves	(a) Establish characteristics for loads/cycles (b) Monitor temperature/time	(a) Initially, periodically, at documented frequency, and after repair/ modification (b) Daily/each use
Safety cabinets	(a) Establish performance (b) Microbiological monitoring (c) Air flow monitoring	(a) Initially, every year and after repair/ modification (b) Weekly (c) Daily/each use
Laminar air flow cabinets	(a) Establish performance (b) Check with sterility plates	(a) Initially, and after repair/modification (b) Weekly
Timers	Check against national time signal	Annually
Microscopes	Check alignment	Daily/each use
pH meters	Adjust using at least two buffers of suitable quality	Daily/each use
Balances	Check zero, and reading against check weight	Daily/each use
De-ionisers and reverse osmosis units	(a) Check conductivity (b) Check for microbial contamination	(a) Weekly (b) Monthly
Gravimetric diluters	(a) Check weight of volume dispensed (b) Check dilution ratio	(a) Daily/each use (b) Daily/each use
Media dispensers	Check volume dispensed	Each adjustment or replacement
Pipettors/pipettes	Check accuracy and precision of volume dispensed by gravimetric method	Regularly (to be defined by taking account of the frequency and nature of use)
Spiral platers	(a) Establish performance against conventional method (b) Check stylus condition and the start and end points (c) Check volume dispensed	(a) Initially and annually (b) Daily/each use (c) Monthly

Type of equipment	Requirement	Suggested frequency
Colony counters	Check against number counted manually	Annually
Centrifuges	Check speed against a calibrated and independent tachometer	Annually
Anaerobic jars/incubators	Check with anaerobic indicator	Daily/each use
Laboratory environment	Monitor for airborne and surface microbial contamination using, e.g. air samplers, settle plates, contact plates or swabs	Weekly for total count and moulds: Biannually for pathogens or as otherwise decided by the laboratory based on activities and historical trends and results

Appendix E Guidance on maintenance of equipment

This information is provided for guidance purposes and the frequency will be based on the need, type and previous performance of the equipment.

Type of equipment	Requirement	Suggested frequency
(a) Incubators (b) Fridges (c) Freezers, ovens	Clean and disinfect internal surfaces	(a) Monthly (b) When required (e.g. every 3 months) (c) When required (e.g. annually)
Water baths	Empty, clean, disinfect and refill	Monthly, or every 6 months if biocide used
Centrifuges	(a) Service (b) Clean and disinfect	(a) Annually (b) Each use
Autoclaves	(a) Make visual checks of gasket, clean/drain chamber (b) Full service (c) Safety check of pressure vessel	(a) Regularly, as recommended by manufacturer (b) Annually or as recommended by manufacturer (c) Annually
Safety cabinets Laminar flow cabinets	Full service and mechanical check	Annually or as recommended by manufacturer
Microscopes	Full maintenance service	Annually
pH meters	Clean electrode	Each use
Balances, gravimetric diluters	(a) Clean (b) Service	(a) Each use (b) Annually
Stills	Clean and de-scale	As required (e.g. every 3 months)
De-ionisers, reverse osmosis units	Replace cartridge/membrane	As recommended by manufacturer
Anaerobic jars	Clean/disinfect	After each use
Media dispensers, volumetric equipment, pipettes, and general service equipment	Decontaminate, clean and sterilise as appropriate	Each use
Spiral platers	(a) Service (b) Decontaminate, clean and sterilise	(a) Annually (b) Each use
Laboratory	(a) Clean and disinfect working surfaces (b) Clean floors, disinfect sinks and basins (c) Clean and disinfect other surfaces	(a) Daily, and during use (b) Weekly or more frequently if required (c) Every 3 – 12 months depending on type of laboratory work

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