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LAB 31

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Use of Culture Media Procured Ready-To-Use or Partially Completed and Diagnostic Test Kits, in Microbiological Testing

Contents

Changes since last edition

Changes have been made at Edition 4 to include revised title to add equal weight to diagnostic test kits, addition of guidance on expectations for verifying the performance of like-for-like culture media and diagnostic kit changes, updated references to relevant international standards, updated definitions to reference diagnostic kits, reference to other bodies providing recognition bodies and general corrections.

1. Introduction

1.1 Laboratories that have been assessed by UKAS as meeting the requirements of ISO/IEC 17025 *General Requirements for the Competence of Testing and Calibration Laboratories* and/or ISO 15189 *Medical laboratories - Particular requirements for quality and competence* may be granted UKAS accreditation. Whilst ISO/IEC 17025 and ISO 15189 are the authoritative documents, several guidance publications on the application of these requirements are listed under *Publications* on the *Laboratory Accreditation* page of the www.ukas.com website.

1.2 This publication provides guidance on the application of specific requirements for Conformity Assessment Body (CAB) laboratories carrying out microbiological testing. By following the guidance given, such laboratories will be able to demonstrate that they meet the requirements regarding the suitability of media (including diluents) procured ready-to-use or partially completed for microbiological testing purposes. Alternative approaches may be used provided that they are shown to give an equivalent outcome

1.3 The guidance given in this publication applies to the use of any medium procured ready-to-use or partially completed, including identification or diagnostic kits. It is equally applicable to quality assurance of critical reagents used for microbiological, serological or biochemical diagnostic purposes. It does not cover validation/verification of methods, such as described in the relevant BS EN ISO 16140 publication series.

1.4 Demonstration of suitability as outlined in this publication does not replace the need for using positive and negative controls alongside testing when relevant.

2. Definitions

Definitions of the following and other related terms may be found in BS EN 1659 BS EN 12322 and ISO 11133.

Diagnostic test kit
A commercially available product to be used as specified for the purposes of confirmation and or identification of micro-organisms.

Culture media
Formulations of substances, in liquid, semi-solid or in solid form, which contain natural and/or synthetic constituents, intended to support the multiplication, or to preserve the viability of micro-organisms.
Note: This is taken to include diluents and other suspending fluids.

Ready-to-use media
Culture media supplied in containers in ready-to-use form (e.g. Petri dishes, tubes or other carriers and including identification or diagnostic kits that are dependent on microbial growth).

Partially completed media
Culture media which still require one or more additional working steps before their intended use (e.g. melting, pouring, portioning and supplementing).

Reagent
A substance or compound added to a system to cause a chemical reaction or added to test if a reaction occurs.

3. Evaluation of suitability

3.1 The nature of the evaluation of suitability of ready-to-use and partially completed media or test kits for testing purposes is dependent on the source and supplier of those media. The following three categories of such media are recognised:

a) *Media that have been performance tested by a laboratory with accreditation to ISO/IEC 17025 for the performance testing of media*

It is the responsibility of the user laboratory to carry out appropriate commissioning to assess the effects of transport and shelf-life using the relevant organisms before use in accordance with 3.2 to 3.8 below using organisms of relevance to the field of testing.

It is the responsibility of the user laboratory to define acceptable performance specifications against which the medium is to be tested and/or to establish that the criteria applied by the performance testing laboratory meet its own requirements, e.g. by checking that organisms relevant to the user's field of work have been used and that measurements such as growth productivity, selectivity and specificity are appropriate to its own needs.

Media batches procured together with media performance test certificates incorporating decision rules to demonstrate conformity to a specification should not be accepted by the user laboratory without assessment against a defined and accepted specification that is held by the CAB for that medium. Records of chosen specifications and checks against suppliers' data should be held by the laboratory however recorded.

Where user-defined performance testing specifications are demonstrated to be met media may then be used without routine in-house verification, however periodic quality control checks at a

frequency proportionate to usage shall be used to demonstrate on going suitability. The extent and frequency of such reverification exercises shall be sufficiently robust to demonstrate continued suitability. Routine in-house verification may be still required for some sectors in order to meet the expectations of relevant regulator. In these cases CABs are expected to comply with those requirements as per ISO/IEC 17025:2017 Section 5.4, even if they may be interpreted as over and above ISO/IEC 17025:2017 Section 6.4 expectations, for example, regulated pharmaceutical GMP-related testing.

Any relevant factors not covered by the accredited work of the performance testing laboratory need to be tested for acceptability by the user in accordance with (b or c) below.

The manufacturer's release specifications (as opposed to any decision rule applied by the media performance testing laboratory) would not be covered by accreditation to ISO/IEC 17025 and may need to be covered by an agreement. An agreement may also be needed to ensure there is prior notification of changes in testing practices, including scope of accredited testing that could impact on the user's performance testing requirements.

b) *Media supplied by a manufacturer with a quality management system certificated as conforming to ISO 9001 or equivalent in the relevant areas*

It is the responsibility of the user laboratory to commission before use all supplies in accordance with 3.2 to 3.10 below using organisms of relevance to the field of testing.

Having established product specifications and demonstrated their suitability, the user shall apply a sampling and testing rate to subsequent batches in keeping with the expectation of a consistent supply.

An agreement between the user and the manufacturer should be established to ensure prior notification of changes in raw material supply, manufacturing or quality control practices. Any such change would necessitate detailed consideration of the implications, possibly leading to recommissioning. Certificates of conformance with the manufacturer's performance specifications should be reviewed against the laboratory defined/validated specification criteria and held by the user laboratory for every batch of medium supplied.

As with (a), any relevant factors not covered by the manufacturer's quality control practices need to be tested for acceptability by the user in accordance with (c) below.

c) *Media from other manufacturers (including any under a) or b) that cannot be demonstrated to meet the requirements)*

The user laboratory shall define the product specifications required and verify that the media comply with them. Verification should be done before use (or at the time of use where prior testing is not possible), for each batch of medium received for compliance with those specifications. Guidance on the expected methodology for testing is given in ISO 11133 and summarised below but other approaches may be taken if they provide equivalent levels of assurance.

3.2 To enable proper evaluation of suitability, acceptable media performance should be defined quantitatively, with objective parameters being set for associated criteria and taking account of shelf-life. Partially completed media (i.e. those requiring further processing such as re-melting, addition of supplements or rehydrating without subsequent sterilisation) should be tested or otherwise evaluated for suitability as received, with full performance testing carried out after completion.

3.3 A documented plan is necessary for sampling of units for testing which enables suitable comment on the whole batch. A batch of medium shall be considered as a quantity of media prepared on a single occasion with common ingredients and processing including heat treatment, received as a single shipment, ready to use in the laboratory.

3.4 Where control media are used for comparative evaluation of quantitative performance, they should be prepared independently of the media under test and should be demonstrated to be suitable for control use, in that they are shown to provide appropriate consistency of performance.

3.5 Conformance with ISO/IEC 17025 and/or ISO 15189 necessitates use of control strains (i.e. reference materials) traceable to certified materials, where possible. Using cultures obtained from a recognised national culture collection or from a reference materials producer accredited to ISO 17034 would provide a suitable level of assurance. In-house maintenance of control cultures must guard against contamination and deterioration. Guidance on the preservation and handling of control strains may be found in ISO 11133. If microbiological certified reference materials (CRMs) are used, they should comply with the definition for CRMs given in ISO Guide 30 and need to contain an appropriate assigned number of organisms.

3.6 Assessment of the performance of solid media used for isolation and for enumeration of colonies and of media used in conjunction with membranes in colony count procedures needs to include recovery of target organisms and, in the case of selective media, suitable demonstration of inhibition of non-target organisms.

3.7 Liquid media used in procedures for the detection of micro-organisms, including those used for Most Probable Number determinations, should be assessed for suitability in terms of limit of detection of target organisms and growth inhibition of non-target organisms.

3.8 Any differential or diagnostic attributes associated with media should be assessed objectively.

3.9 Relevant physical attributes of media need to meet specified and suitable criteria. Such attributes may include sterility, pH (of the finished medium), volume or quantity, depth, colour, clarity and/or any optical artefacts and gel strength.

3.10 Media designed for the preservation or maintenance, of micro-organisms, including diluents and other suspending fluids, should be shown under conditions of use not to significantly alter the viability or recoverability of micro-organisms, or any other relevant property.

4. Verifying like-for-like replacements

4.1 From time to time a laboratory may need to seek an alternative supplier of a previously validated product, be this culture medium or diagnostic test kit. This eventuality may arise due to manufacturers delisting products or encountering raw material supply issues. In line with ISO/IEC 17025 and/or ISO 15189 CABs are expected to have appropriate mechanisms in place in order to enable a planned response to such events should they occur, whether changes are expected to be temporarily or permanent.

4.2 The expectation is that changes to accredited tests are notified to UKAS in order to determine if assessment of change is considered necessary. Due to the urgency of such changes and where it is determined assessment is required, the UKAS extension to scope process may not always be as responsive as circumstances require before a laboratory can move testing to the alternative replacement. This, however, does not negate the need for a user laboratory to undertake an appropriate level of verification to confirm that any like-for-like replacements from alternative manufacturers have been appropriately evaluated as being comparable and fit for purpose.

4.3 In cases of like-for-like replacements of culture media and diagnostic test kits, laboratories should apply the guidance given in this document in addition to confirming the product truly is like-for-

like, e.g. culture medium formulation is equivalent. Any discrepancies in formulation shall need to be considered including conformity with any particular referenced test standard.

4.4 In addition to the establishment of specification conformity, performance verification will need to be sufficiently rigorous to ensure any difference in performance between old and new product is identified and understood. Such evaluation may include:

a) direct comparison of existing product with new product on internal quality control samples, proficiency test samples and customer work, where supplies of existing product allow;

b) performance against internal quality control samples and proficiency test samples where known target/non target organisms are present, and retained previously confirmed customer sample cultures, where original product is no longer available;

c) sufficient reproducibility studies to provide confidence in the data generated and allow for updated measurement uncertainty estimate where relevant to the test.

4.5 Updated documented procedures and evidence of relevant analyst training as may be needed shall be in place alongside approval for new suppliers if required.

4.6 CABs should notify UKAS of verified changes in order to determine if assessment to confirm continued conformity to ISO/IEC 17025 / ISO 15189 is required. Any such assessment would be handled through the extra assessment process which can likely be undertaken remotely upon receipt of a verification pack addressing clauses 4.3 and 4.4 of this document. The assessment should take place as soon as practical following the change, if not before, and will be chargeable (administrative and assessing time to be determined on a case-by-case basis). A short report shall confirm the changes made by the CAB are appropriate with the usual requirements for any mandatory action findings raised to be closed to the satisfaction of the assessor in order to maintain accreditation for the test in question. Where such an assessment happens retrospectively it should be understood that any significant technical issues identified with verification work or the performance of the new culture medium or diagnostic test kit could result in a mandatory finding requiring work reported as accredited to be withdrawn. Accreditation schedule changes will not normally be necessary except in cases where there is a change to named confirmation test kits if listed on schedules.

4.7 CABs are encouraged to pro-actively validate alternative culture media and diagnostic test kits for business continuity purposes. Where this mechanism has been subject to previous satisfactory assessment by UKAS, CABs should still notify UKAS of intended changes to test methods but the need for extra assessment is likely to be considered unnecessary.

4.8 Should a like-for-like replacement be unavailable, and an alternative medium or kit based on different detection / differentiation principles is needed, then UKAS expectation remains that such a change is subject to the usual extension to scope process and an application is made by the CAB. Again, it is acknowledged that in such circumstances grant may need to be retrospective, however it is usually the case that user laboratories will have forewarning when a product is to be discontinued and no like-for-like replacement is available from elsewhere. The CAB shall communicate intended changes to UKAS at the earliest opportunity.

4.9 Any voluntary change to test culture media and diagnostic test kits that is based on different detection / differentiation principles (e.g. conventional to chromogenic medium or the adoption of non-animal derived medium formulations to meet customer demands) shall remain requiring an extension to scope application to UKAS and must be granted in the usual manner before the laboratory introduces the changes to customer work reported under accreditation.

5. Bibliography

BS EN 1659:1997 *In vitro diagnostic systems - Culture media for microbiology - Terms and definitions*

BS EN 12322:1999 *In vitro diagnostic medical devices - Culture media for microbiology - Performance criteria for culture media*

ISO 11133:2014+A2:2020 *Microbiology of food, animal feed and water. Preparation, production, storage and performance testing of culture media*

ISO Guide 31:2015 *Reference materials - Contents of certificates, labels and accompanying documentation*

ISO 9001:2015 *Quality Management Systems - Requirements*

ISO Guide 30:2015 *Reference materials - Selected terms and definitions*

ISO 17034:2016 *General requirements for the competence of reference material producers*

ISO 16140-1:2016 *Microbiology of the food chain - Method validation - Part 1: Vocabulary*

ISO 16140-2:2016 *Microbiology of the Food Chain - Method Validation - Part 2: Protocol for the validation of alternative (Proprietary) methods against a reference method*

ISO 16140-3:2021 *Microbiology of the food chain – Method validation - Part 3: Protocol for the verification of reference and validated alternative methods implemented in a single laboratory*

ISO/IEC 17025:2017 *General requirements for the competence of testing and calibration laboratories*

ISO 15189:2012 *Medical Laboratories - Requirements for quality and competence*

NOTE: ISO 15189:2022 is due for publication in December 2022, there will be a 3 year transition period with the new version mandatory by December 2025