European Diagnostic Manufacturers Association

EDMA position paper

LABORATORY ACCREDITATION

12th October 2007

Background

Laboratory Accreditation (for instance under ISO 15189 and ISO 17025) is a welcome development in the clinical laboratory world, which will ultimately lead, if properly implemented, to better results and improved services for healthcare providers and patients. As such, the expansion of accreditation schemes is welcomed in principle by EDMA.

Accreditation does however pose some important challenges to laboratories. Some of those challenges are specific for each individual laboratory, and will need to be addressed solely by the laboratories seeking accreditation. Other challenges will require the collaboration between laboratories and manufacturers of in vitro diagnostic medical devices.

This document is addressed to clinical laboratories, manufacturers of in vitro diagnostic medical devices and accreditation bodies, in order to raise awareness of some of the challenges associated with clinical laboratories, accreditation and to clarify some of the ways in which the IVD industry can assist laboratories in achieving such accreditation.

Issues

The EDMA Accreditation task force has identified a number of issues since the increase in accreditation, particularly according to ISO 15189, throughout the clinical laboratory community. The following issues have been considered as relevant:

- Validation of laboratory procedures
- Establishment of Standard Operating Procedures (SOP) within a laboratory
- Maintenance schedule of laboratory equipment
- Definition of reference values
- Metrological Traceability of measurement results
- Uncertainty of Measurement results

Validation[1] of laboratory procedures

As part of their accreditation under ISO 15189, Clinical Laboratories need to validate their laboratory procedures. The validation of laboratory measurement procedures under ISO 15189 is essentially a verification that their measurement procedures and IVD measurement systems are adequate for the work performed in the laboratory. This should not be confused with the validation of the devices performed by manufacturers prior to the placing on the market of these devices.

In all instances, it is also the responsibility of the laboratory to establish that the procedures being used, including the measurement procedures, produce results which are of clinical value.

There are basically two kinds of situations which the laboratory may find –

1) **The laboratory is using a CE marked device** – In this case the device and the method have already been validated by the manufacturer(s) of the device. The sole responsibility of the laboratory is to validate whether the device performs as expected within

[1] It should be noted that in this document the term validation is used in the same context as in ISO 15189.

the laboratory (validation of the measurement procedure including pre-analytical steps, and any other factors relevant for the use in the laboratory, not validation of the device)

2) **The laboratory is using a device which has not been CE marked, or is using a CE marked device for a use which was not intended by its manufacturer** – In this case, the specific use of the device has not been previously validated, thus it is the responsibility of the laboratory to provide a validation not only of the procedures but also, insofar as possible, of the device itself, according to the relevant requirements of the IVD directive.

Depending on the nature of the device, the nature of the measurement procedure and the relationship between the manufacturer and the laboratory, it may occur in some cases that a manufacturer decides to assist the laboratory in the validation of a new use for his device. However the manufacturer is in no way obliged to do so.

Establishment of Standard Operating Procedures

Standard Operating Procedures (SOP's) must be established by the laboratory as part of its quality system. The SOP's related to measurement procedures should take into consideration many important factors, including but not limited to:

- The manufacturers' instructions for use of the devices which may be used as part of the procedure.
- Other relevant SOP's within the laboratory (e.g.. sample handling procedures)
- Established operational practice within the laboratory
- Results intended to be attained by the procedure

It is thus possible that two different laboratories, which are using the same device to measure the same parameter may establish different SOP's. Because of the presence of many factors intrinsic to the individual laboratory (which need to be taken into account when establishing a SOP's), manufacturers of devices cannot provide generic SOP's suitable for use within multiple laboratories.

Laboratories should in any case ensure that the final established SOP's are in agreement with the manufacturer's recommendations, for instance as regards to the use of reagents, operator training or respecting environmental conditions for operation (temperature, vibrations etc.)

This does not preclude manufacturers helping laboratories to establish their SOP's, either as part of their usual after sales service or as additional contractual arrangements with the laboratories. Such an arrangement would be a collaborative effort between the manufacturer and the laboratory as it would be impossible for a manufacturer to establish SOP's for a laboratory on its own. However, regardless of any assistance provided by the manufacturer, the responsibility for the establishment of laboratory SOP's lies with the laboratory.

Maintenance schedule of laboratory equipment

As part of accreditation it is important for the laboratories to demonstrate that their laboratory equipment is properly maintained in working order. Laboratories should follow the indications laid down by the manufacturer which pertain to the maintenance of the instrument. These indications however are often minimal requirements and laboratories may decide to undertake additional maintenance procedures after consultation with the manufacturer.

When the manufacturer of an instrument or its authorized subcontractor is performing maintenance on an instrument he should provide a report detailing:

- Which maintenance operations have been performed
- Any data pertaining to the final performance of the instrument after maintenance should be made available to the user.

- Any responsibilities of the user (e.g. decontamination of instruments prior to servicing)

It should be noted that the report, while clear, need not be exhaustive. However, all information which may affect the performance of the device should be made available to the user.

Following these maintenance operations the manufacturer or his authorized subcontractor should perform a functional validation of the instrument in order to ensure it will meet stated performance criteria as specified on the report is prior to use by the laboratory. Adequate documentation will be presented to the laboratory to demonstrate that this is the case.

It should be noted that information on the internal calibrations of the device (e.g. dispensing of volumes by automatic pipettes, temperature control, flow rates of pumps) need not always be provided, so long as the overall performance of the device is unaffected.

It should also be noted that the manufacturers' responsibility in terms of maintenance is to ensure and demonstrate that instruments meet the stated performance criteria as specified in the maintenance report after maintenance. It is the responsibility of the laboratory to demonstrate to accreditation bodies that they are meeting the maintenance requirements necessary for accreditation.

Following maintenance the laboratory may decide to re-validate the procedures performed with that instrument, if he deems it necessary.

Definition of Reference Values

Where appropriate manufacturers or their authorized subcontractor are obliged to provide reference values for each parameter measured by their device, as well as information on the nature of the reference population used to establish those values.

However it is the responsibility of the laboratory to determine whether the reference population is comparable to the population from which the samples measured in the laboratory originate. Should the two populations be significantly different, the laboratory may decide to establish new reference values. This can be done either experimentally or if available via appropriate bibliographical references.

Metrological Traceability of Measurement Results[2]

Where appropriate, the manufacturer will provide the laboratory with information, on the traceability of the values assigned to trueness controls and calibrators provided to the user. This information includes the reference material of higher order to which values are traceable.

The final steps in the metrological traceability chain are performed in the laboratory. This usually includes the calibration of the measurement system and measurement procedure on a patient sample. This represents the laboratories important contribution to the establishment of a full chain of metrological traceability.

For details on the establishment of a chain of metrological traceability, see EN ISO 17511: "In vitro diagnostic medical devices – Measurement of quantities in biological samples – Metrological traceability of values assigned to calibrators and (trueness) control materials."

[2] See the EDMA Position Paper on Laboratory Medicine and Traceability: views and needs of industry for compliance with essential requirements of the IVDD.

Uncertainty of Measurement Results

Upon request, manufacturers should provide the laboratories with the uncertainty data associated with the calibrators and trueness control materials provided to the user.

It is the responsibility of the laboratory to do the following:

- Calculate the final measurement uncertainty of the result
- Decide whether and how to present that measurement uncertainty to the clinician.

It should be noted, that because of the nature of the biological samples, and in particular because often the analytes are poorly defined, the uncertainty of results may be large when compared with the reproducibility of results. Similarly the uncertainty associated with biological samples is much greater than that associated with direct measurements of physical properties, such as weight, temperature or distance.

For further guidance on this issue, please see the EDMA Position Paper on Estimation of Uncertainty of Measurement in Medical Laboratories.

References:

EDMA Position Paper on Estimation of Uncertainty of Measurement in Medical Laboratories

EDMA Position Paper on Laboratory Medicine and Traceability: views and needs of industry for compliance with essential requirements of the IVDD

The EDMA Accreditation Task Force