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Making the most out of proficiency testing participation for a medical laboratory from the standardization point of view

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Any laboratory defines a policy regarding quality assurance with respect to its results. In case of medical laboratories such a policy is emphasized because of the impact its results have on medical decision. Technical competence can be demonstrated in various ways such as positive results at voluntary audits (e.g. private certification schemes), scientific publications, staff qualifications, repeated proficiency testing participation with positive results etc. Accreditation by its defintion (at least with respect to Regulation (EC) No 765/2008 of the European Parliament and of the Council is a pathway to demonstrating technical competence. There are several clear advantages of working within an accredited system, which can be organized in three groups: i) ensure public confidence in the results delivered by the laboratory, ii) minimise technical failures, iii) facilitate cross-border results acceptance. It is very important to point out that while accreditated results of a laboratory should be considered trustworthy and, therefore, eligibile for acceptance in another country (i.e. economy), it does not necesarily mean that a non-accredited laboratory provides questionable results. Differently put, an accredited result benefits by default from the premises of conformity since the issuing laboratory has been technically assesed against relevant technical standards by an accreditation body. One must make a clear difference between accreditation and certification. While accreditation is the highest-level of conformity assesment, the certification is an audit which determines if a product or an individual conforms to criteria specified in a certification scheme. In case of medical laboratories, the accreditation standard is ISO 15189, current edition rolled-out in 2012.

With regard to medical laboratories, there are several reasons why one would seek accreditation besides having a guarantee of the quality of results and thus maximize acceptance regionally and/or worldwide. France and Hungary declared full ISO 15189 accreditation mandatory for all the laboratory scope. Belgium, Lithuania and Ireland declared partial mandatory accreditation for several scopes (e.g. molecular biology in Belgium, blood transfusion in Ireland). In Romania, laboratories seeking a contractual relation with National Health Insurance House must be accredited for at least 50% of the basic national healthcare package[1]. One can notice that at the European Union level there is a currently heterogenous approach with respect to accreditation of medical laboratories. However, all the countries that use the concept of accreditation of medical laboratory, irrespective of the level of implementation use of ISO 15189. The reason for this accreditation standard (ISO 15189) and not other national standards is because of its comprehensive approach, wide acceptance at the international level, and continous update from a well respected independent institution in the field standardization (International Standard Organization). Another rationale for accreditation is that of clinical research. The relevant part of the research for a laboratory is usually required to be carried out in an accredited scope.

A laboratory seeking accreditation must identify the appropriate accreditation body and, at least in Europe, Regulation (EC) No 765/2008 of the European Parliament and of the Council has very clear statements about this[2]. Accreditation bodies must define an accreditation scope and, if they pass a peer-review assesment can become signatories of regional and/or international agreements which facilitate cross-border results acceptance. For better understanding this concept, we introduce the figure below which shows the pyramidal organization of the most important mutual agreements which are of interest for a medical laboratory. (Figure. 1)

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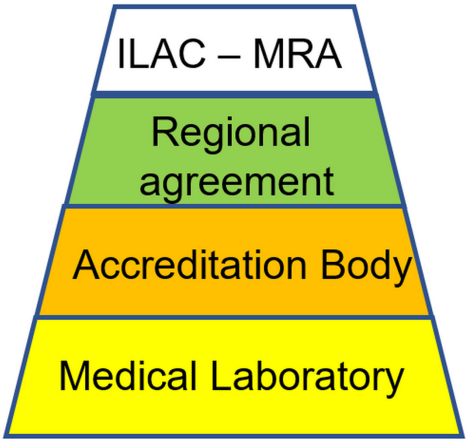

Fig. 1. Pyramidal display of the relationships between Conformity Assessment Bodies (CAB) – medical laboratory and accreditation bodies, Regional Agreements (Inter American Accreditation Cooperation (IAAC), European co-operation for Accreditation (EA), Asia Pacific Accreditation Cooperation Incorporated (APAC), Arab Accreditation Cooperation (ARAC), African Accreditation Cooperation (AFRAC). A medical laboratory can identify if its accreditation is endorsed just by an accreditation body and/or regional/international agreements of which the respective accreditation body is signatory of. The figure shows that a laboratory that is accredited by an accreditation body signatory of an agreement, has its results facilitated towards recognition by other accreditation bodies signatory of those agreements.

Having signed an agreement with a Recognised Regional Cooperation Body, an accreditation body is eligible to become a signatory of the ILAC- MRA agreement (without any further assesment), which facilitates the widest possible international results recognition. Updated list of signatories and the scope is publicly available[3].

Reliable, high-quality results are achieved by having implemented a complex system of items, the most important ones being internal quality control, proficiency testing participation, metrological tracebility, and records control. Proficiency testing participation is clearly outlined: "*The laboratory shall participate in an interlaboratory comparison programme(s) (such as an external quality assessment programme or proficiency testing programme) appropriate to the examination and interpretations of examination results*"[4]. However, the accreditation standard does not provide any details regarding the level of participation, neither the frequency of participation nor any other information of how to select an adequate proficiency testing provider. The main rationale for this approach is that there is such a variety of laboratories and situations that they cannot be encompassed within a single requirement. It is therefore the laboratory's sole responsability to select an appropriate proficiency testing provider. It is important however to highlight that a laboratory should not participate in proficiency testing schemes solely because it needs to fulfill an accreditation requirement. In fact, proficiency testing is a powerful tool to assess different aspects in a daily laboratory activity. For example, ensuring a new equipment performs adequately can be verified by a combination of methods, one of them being succesful participation in a proficiency testing scheme[5]. Proficiency testing can also be used to identify measurement issues, compare procedures and methods. Moreover, participation in proficiency testing can be used as viable educational tool in the framework of the induction program of new staff or continuous education.

The first question needed to be answered when selecting a proficiency testing provider is whether it should be an accredited one or not[6]. It is generally well known that accredited proficiency providers have significantly more expensive services (at least 50%). If the laboratory is an accredited one, the policy of the accreditation body should be carefully examined since each accreditation body has its own policy regarding proficiency testing participation and accreditation status of the providers. All these policies are peer-reviewed by the Regional Cooperation Body (European co-operation for Accreditation- EA with respect to European Union and associated states). A detailed examination of various European accreditation bodies points out a heteregenous approach in this regard. Some accreditation bodies accept results only from accredited proficiency providers while others recommend using services of accredited proficiency testing provides. With respect to frequency of participation, the approach is even more heterogenous. For example, in Hungary a medical laboratory must participate at least four times a year, while in Romania a medical laboratory must participate at least two times a year. However, the EA has published two documents: i) Guidance on the level and frequency of proficiency testing participation[7] which is meant to provide laboratories indicators of how to define an optimum level of participation, and ii) Guidelines for the assessment of the appropriateness of small interlaboratory comparisons within the process of laboratory accreditation [8] which, even though is primarily meant for assesors, it can and should be used by laboratories in order to better understand what the expectations are from the accreditation point of view.

From a technical perspective, without implying that services of non-accredited proficiency testing providers are questionable, selecting an accredited one offers several key advantages besides the classical benefits of accreditation. Firstly - an accredited proficiency testing

provider must have transparent policies regarding: i) communcation with participants, ii) appeals and complaints, iii) the assigned values and the statistic processes, iv) intended use of the scheme. All these data allow a medical laboratory to make an informed decision before contracting a proficiency testing scheme. In case of selecting an accredited provider, the laboratory is further safeguarded by the accreditation body which ensures compliance with all the requirements of the applicable accreditation standard (ISO 17043). In contrast with this, using a non-accredited provider leaves only one option to the laboratory: the commercial contract between the parties which most of the times does not include any technical requirements. Suplementary confidence is added if the accreditation body that accredited the provider is signatory of a regional agreement with respect to proficiency testing[6]. In case of the European accreditation bodies, detailed updated information is available on the webpages of the EA[9].

If the proficiency testing provider is selected also for fulfilling the accreditation requirements, careful consideration should be be given in terms of the policies with respect to proficiency testing of the accreditation body. If the parameter, matrix, analytical principle of the scheme offered by the proficiency provider and confirmed by the annex of the accreditation certificate does not fully match the ones in the annex of the accreditation certificate of the laboratory, then the scheme might be assesed as inadequate as it did not mimic the routine examinations performed by the laboratory – Clause 5.6.3.1 of ISO 15189. In the special case of flexible scope accreditation of the proficiency testing provider, it is the responsability of the laboratory to obtain evidence of the accredited parameters, matrix and analytical principle from the provider itself and not the accreditation body. Otherwise, there is a risk of participating in an inadequate proficiency testing round.

Irrespective of the type of proficiency scheme sought by the laboratory (quantitative or qualititative) it has to be fit for purpose. This does not mean just that the analyzed sample mimics the actual test samples routinely run by the laboratory. Fit for purpose also means that the sample should be compatible with the techiques and equipment implemented in the laboratory. It is the responsability of the proficiency testing provider to ensure commutability of the sample between equipment or, if that is not possible whatever the reasons, not enrol the laboratory into the round. This is documented in Clause 4.4.1.3 of the applicable accreditation standard[6]. Safeguarding the proficiency testing round against tampering requires the provider to keep confidential the assigned value or any other information that might lead to finding out the assigned value. Therefore, limited information can and should be provided to interested potential participations with respect to the sample. However, Clause 4.9.1 of the applicable accreditation standard[6] guarantees the right of the participants to obtain information about the sample for the purpose of deciding whether the scheme is fit for a specific laboratory or not before signing up for the round. Also, this Clause ensures the interested laboratories that participation criteria are available such that an informed decision regarding participation is made. When collecting information about the methods/equipments the interested laboratories plan to use for the prospective round, the proficiency testing provider should inform based on this information if the objective of the scheme can be achieved by the laboratory and if the laboratory meets the participation criteria – Clause 4.4.1.3 of the accreditation standard[6]. Also, the provider may also choose not to communicate technical information to the interested potential participant, but in that case it should emit a binding confirmation that the sample is adequate or not for the particular case of the enquiring participant. Participation in a fit for purpose scheme is a key factor in ensuring the objectives of the external quality control from the laboratory perspective. Accepting only laboratories that can fully integrate the sample in their daily workflow is also a compliace guarantee with several clauses of the accreditation standard applicable to the proficiency provider.

The role of assigned value also plays a key role in a proficiency testing round. However, the proficiency testing accreditation standard does not provide any mandatory requirements other than the fact the statistics used in the scheme design should be adequate and a theoretical demonstration should be available. It is therefore the responsability of the provider to develop the mathematical apparatus for data processing such that the results are adequate and provide a sound feedback to the laboratory. Besides the results themselves that are disseminated to the participants, it is worthwhile mentioning that these results have a quantifiable impact on the laboratory- most of the time, a financial one. However, there is a standard ISO 13528 [10] which details various mathematical models for the assigned value for different types of proficiency testing schemes and it is generally accepted that if a proficiency testing provider strictly implements the mathematical models [10], then there is no further need for theoretical demonstration of the mathematical model. While the detailed mathematical models do not need to be available to participants, by being accredited, it is assumed that accreditation body has previously assesed if these models are both adequante and rigorously implemented. Clause 4.4.4 of the accreditation standard for proficiency testing providers[6] supports this view. The most popular methods for determin-

ing the assigned value are by consensus of participations and by reference. The provider has the full authority and responsibility to apply mathematical processing in order to ensure that the results are meaningful and reflect the performance of the participating laboratories.

Participating in a proficiency testing scheme where the assigned value is given by consensus offers several unique information like how well (measured in standard deviation units from a central tendancy) the laboratory performed compared to other participant laboratories. The resulting information is very useful because, generally, the number of participants in consensus schemes is usually high enough such that the assigned value does not deviate too much from the true value[12]. There are several limitations to this approach: i) number of participants- a limited number of participants (below 30) may negatively influence the assigned value since there might not be enough information to derive an assigned value close enough to the true value; ii) heterogeneity (either of technical experience of participants, participants' performance) may negatively influence the assigned value in the sense that a large number of participants using an inferior technology will have a higher impact on the assigned value than a smaller number of participants using a superior technology.

The limitations of these schemes can be overcome by using a reference value for the assigned value. That is, a laboratory is sent a sample which is actually a certified reference material and the assigned value is the reference value specified in the quality assurance certificate. Having an assigned value straight forward from a certified reference material certificate is different than having an assigned value from formulation[10]. This latter case is used when the provider is actually manufacturing the samples and does it in such a way to obtain a specific value. Using a reference material as sample, which may be more expensive since this has higher costs, offers the advantage that the number of participants cannot influence the scheme results. However, usually certified reference materials have a standard uncertainty generally far less than the uncertainty used by the laboratory in its routine workflow. This means that a laboratory may perform a high-quality work by its standards but a suboptimal one from the proficiency testing participation. In this case, the laboratory should use the criteria and objectives of the schemes publicly available from the provider to decide if the participation in such a particular scheme is fit for purpose or not. Ideally, the laboratory should identify a provider which runs schemes with uncertainities in the same range as the routine measurements of the lab. This view is supported by the laboratory accreditation standard – Clause 5.6.3.1[4].

The paper highlighted several key points which should enable a laboratory to define objective criteria for selecting an adequate proficiency testing provider. These criteria should also take into consideration the policies regarding proficiency testing of the accreditation body – in case the results will be used to confirm fulfilment of the ISO 15189 proficiency testing participation. The advent of globalization, the removal of trade barriers, spread of the IT systems, development of high-speed internet, also made proficiency testing providers readily available even though the laboratory and the providers operate in different economies or sometimes in different geographic regions. In these cases careful attention should be paid to the accreditation status of the provider and/or the signatory status of the accreditation body of regional/international agreements. The most relevant agreements and their hierarchy were documented above.

Selecting the proficiency testing provider, especially nowadays has become quite a challenge because it requires knowledge, not only technical (laboratory medicine), but also in the field of IT, legal and even international trade. Arguably laboratories usually seek a minimum number of proficiency testing providers, mainly for non-technical reasons (familiarity with the IT reporting platform, background experience with cooperation terms, etc). However, this approach increases the risk of participating in testing rounds with more or less the same laboratories, therefore the comparison pool narrows. This means that the laboratory will be compared more or less with the same other laboratories and the relevance of results will be somewhat limited. Therefore, a laboratory might take into consideration participation in proficiency testing rounds organized by several providers.

Accredited vs non-accredited provider certainly has financial implications as non-accredited proficiency testing schemes are signifcantly cheaper and not necessarily inferior from the quality point of view to the accredited ones. An accredited proficiency testing provider has to demonstrate sample homogeneity and stability for the length of the entire round which also is a key component of a successful participation with reliable results. Also, an accredited provider most certainly will succesfully meet the technical criteria for which it was selected and if not, right to appeals and complaints by the laboratory is guaranteed by the applicable accreditation standard. All these requirements are documented by the accreditation standard for the proficiency testing providers and are regularly assessed by an accreditation body thus supplying confidence that the laboratory benefits from a high quality service.

With respect to type of proficiency testing schemes that a laboratory should participate in, both consensus

and reference assigned value schemes have their own particular advantages and provide useful information for the laboratory. Therefore, the laboratory might participate in both consensus and reference assigned value schemes independent of the requiremets of the accreditation body.

The paper detailed several key aspects which should be taken into account when contracting proficiency testing participation in order to meet the necessities of the laboratory which are technical and can be even regulatory. This is because most of the time laboratories do not contract just one participation, but several (usually yearly or even multiannual). Having obtained relevant results from the proficiency testing participations is a step forward in maintaining/improving overall technical competency of the laboratory. The proficiency testing providers market has become global and most of the providers will deliver their services in different geographic regions. Other traditional providers terminate the business and accreditation status may change yearly or even sooner. This means there is also a high volatility in this niche market. In these cases, it is the laboratory which is responsible for determining if, at the selection time, the provider met the eligibility criteria and its schemes were deemed as fit for purpose.

AUTHORS' CONTRIBUTION

Authors declare equal contribution in all regards.

CONFLICT OF INTEREST

None to declare.

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