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The need for a quality standard for assurance in medical research laboratories

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Abstract

The objective of this article is to show the results of a research study conducted to evaluate the need for a quality standard specific for medical research laboratories based on the shortfalls of ISO 15189 when used for this purpose. A qualitative research methodology was used, which comprised of collecting data from 20 well-qualified and experienced medical laboratory personnel by means of interviews based on a framework developed from a literature review. The data were analysed by means of a thematic technique and the results were verified by a team of medical researchers. The seven themes arising from the analyses were inflexibility; ambiguity; unfair requirements; inappropriate focus; inadequacy for research; renewal; and acceptance for accreditation. The results indicated that the ISO 15189 standard in its present content does not totally suit medical research laboratories and shows support for the development of a standard specific for research laboratories.

Key Words: Medical, Laboratory, Research, ISO 15189, Standards, Quality, Assurance

Introduction

Medical research laboratories perform basic research and develop new techniques and methodologies that provide evidence on which to base the formulation of policies and decisions on health and development. Many of these laboratories are accredited to the ISO 15189 standard, which causes some concern among medical researchers because medical research laboratories are different from routine medical laboratories and ISO 15189 is more suited to the latter. Consequently, a study was conducted to explore the suitability of the ISO 15189 standard as a quality standard in medical research laboratories.

Medical laboratories offer diagnostic testing, which assists clinicians in the monitoring and treating of diseases, and patient management. Some laboratories also conduct research testing in order to develop new assays and technologies, vaccines and drugs. According to the World Health Organisation (WHO) Handbook (TDR, 2006), scientific research plays a vital role in efforts to maintain health and combat diseases, that is, global threats to health security. Research helps to create new knowledge and develop proper tools for the use of existing knowledge. Not only does research enable health care providers to diagnose and treat diseases, but it also provides evidence for policies and decisions on health and development. Research laboratories, as part of the research process, assist in development of new technologies for monitoring disease and the surveillance thereof, whilst diagnostic testing laboratories, on the other hand are directly involved in patient management through laboratory testing and not considered as part of the research process.

Accreditation allows people to make an informed decision when selecting a laboratory. It demonstrates competence, impartiality and capability. According to Dhatt and Peters (2002) many South African medical laboratories were initially accredited to the ISO 17025 Standard and have been advised to change to the ISO 15189 standard. Most South African medical laboratories are accredited or aim to be accredited to the standard ISO 15189. Medical researchers in laboratories have

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mixed feelings when using ISO 15189 on the basis that the standard was developed for routine laboratories. Calabrese and Palm (2008) published an article indicating similar concerns regarding biomedical research and suggested the development of an appropriate standard for biomedical research. According to Prosek et al (2000), in a routine laboratory, the quality control part is more important, while in a research laboratory the quality assessment is dominant. In routine work, a laboratory selects standard methods, performs instrument qualification and validation, educates laboratory personnel and, where necessary, revalidates methodologies. All these processes are well planned and documented prior to the commencement of routine measurements. Adherence to the specifications is the key to the quality of this analytical work. However, Prosek et al (2000) maintains that in a research laboratory, new techniques and methods are developed on an ongoing basis. It is usually not possible to set detailed specifications of requirements prior to the experiments because they are unknown. In this scenario, the quality of the work is ensured with systematic assessment of factors influencing the work. In both types of work, the basic operations are the same, but the way in which they are monitored differs. Hence Prosek et al (2000) suggests that one QA system can be utilised effectively but differently in different laboratory work environments.

Medical research is normally funded by external parties such as government and various donors. In order for laboratory research developments to be accepted and funded by such sponsors, it is a requirement that these laboratories be accredited to known international standards demonstrating confidence of reliability and quality to these funders. According to Burnett (2001), the effectiveness of any accreditation system is crucially dependent on the standards adopted and on the objectivity of assessment of compliance. In addition, standards are required that reflect a quest for quality and promote harmonisation of practices from laboratory to laboratory and from country to country.

According to Vermaercke (2000), a satisfactory quality system for research has many advantages that are comparable with routine laboratories. These are the transparency of the organisation and responsibilities, better traceability of data and uniformity in output goals, thus leading to improvements. He also states that such a system has the following advantages specifically relating to research: a better definition of project structure, goals and objectives and an improvement in the technical quality of the research by enforced validation of the methodology and the creation of a knowledge-based system that can be used for training new personnel. Because research consists of a broad multidisciplinary spectrum ranging from fundamental through subsidised, to contract research or even ad hoc analysis, the QA approach and the standard used may need to be adapted to make it “fit for purpose”.

LITERATURE REVIEW

ISO 15189

ISO 15189 was introduced in 2002 as an international standard, thus developing quality management systems specifically for medical laboratories (2007). It is based on ISO/IEC 17025 (general requirements for the competence of testing and calibration laboratories) and the methodology of ISO 9001 (quality management systems requirements), and focuses on the quality and competence of medical laboratories. ISO 15189 is maintained by the Technical Committee ISO/TC 212 (responsible for clinical laboratory testing and in vitro diagnostic test systems), and produced revised editions in 2007 and 2012. It can be used as a tool for self assessment of laboratory competence as well as for confirming or recognising the competence of the laboratory by laboratory customers, regulating authorities and accreditation bodies. The content of the ISO 15189 standard itself comprises five elements, namely scope, normative references, terms and definitions, management requirements and technical requirements. Like many other ISO standards, the implementation requires demonstrated management commitment,

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elaborate and controlled documentation, regular audits and reviews to ensure that the management system is effective and efficient in performing its basic function. It further lends itself to some elements of bureaucracy and inflexibility, supposedly ensures consistency of quality delivery and is appropriate for routine and established processes, and obviously by the nature of its scope not suited to research processes, which can vary according to different types of projects.

The focus of ISO 15189 is clearly on the safety of laboratory personnel, patients and everyone involved in testing services, including service suppliers, continued competency and improvement of personnel with regard to training and the emphasis on the pre-analytical, analytical and post-analytical stages of testing and the reporting of results.

The establishment of critical levels and reference ranges to indicate normal and abnormal results of all examination and turnaround times that reflect the clinical need are specific requirements for medical testing. These critical alert levels may depend on population, sex, age or method and should be clearly defined in a document. The turnaround time must reflect the clinical needs. There is also a requirement to monitor the transportation of samples to ensure that the samples are received within an appropriate timeframe. The essence of this requirement is based on clinical needs and patient care.

Quality in research

The World Health Organisation released a handbook discussing quality standards in basic biomedical research, which states that the notion of quality in such research has two elements: a fundamental scientific area and a practical experimental section (WHO, 2006). Furthermore, when the underlying science is flawed or the working hypothesis is ill conceived, the results obtained by even the best-conducted experiments will not really advance knowledge. Even the best science or the most brilliantly reasoned working hypothesis will not produce results and answers that are acceptable to the scientific community if they are not supported by high-quality experiments and methodologies (i.e. those that are conducted flawlessly). Scientific research plays a crucial role in efforts to maintain health and combat diseases. Research helps to create new knowledge and develop proper tools for the use of existing knowledge. Not only does it enable healthcare providers to diagnose and treat diseases, but it also provides basic evidence on which to base the formulation of policies and the making of decisions relating to health and development (WHO, 2010).

Quality systems must be adapted to the characteristics of research and tailored to be fit for purpose Robins, 2006). Effective research also demands flexibility, without compromising quality. Such research relies on the competence and motivation of staff and allows deviations from planned programmes to pursue unexpected avenues.

A scheme for quality assurance for different stages of research was developed by Mathur-De-Vre (2002) and is illustrated in figure1. In stages 1 and 2, the quality assurance system is directed towards defining a research project clearly and explicitly. In stage 3, the system is aimed at the quality of the operational technical components required to support the main objectives of the research project and in stage 4, at the quality of the reliability of these operations. Stages 5 and 6 ensure the quality of the results generated and the quality of the interpretation of these results respectively. Stage 7 deals with the quality elements for the process of review and evaluation of performance in terms of the set objectives, with adjustments and improvements being made in stage 10. Finally, the dissemination of information, number and quality of publications (e.g. prestige of the scientific journals, citation index), international recognition, conference papers, etc are included in stages 8 and 9.

Review of ISO 15189 clauses

There are shortcomings in ISO 15189 as regards to its application to research laboratories. The main shortcomings involve

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the pre-analytical phase where research studies would be performed on samples retrospectively thus excluding turnaround times which would be a critical factor in medical diagnostic laboratories. The collection, transportation and receipt of samples would be more critical in a routine testing laboratory where timely reporting of results is a key factor.

Another area where shortcomings would occur would be the post-analytical phase as no patient reports for clinical management would be issued in a research setting. Research laboratories have a focus of attaining results, based on new findings or developments, which would be reported to a sponsor or funder or be published in a peer-reviewed journal; however such results would not impact patient management or care directly.

In examining the clauses, the following are noted as shortcomings of ISO 15189 (ISO, 2012) for research purposes:

- Clause 4.4: Review of contracts: this clause is inadequate as only contracts between external suppliers and subcontractors are discussed. The standard does not include guidelines for contracts or grants between laboratories and funders or sponsors.

- Clause 4.5: Examination by referral laboratories (i.e. outsourced laboratories that perform highly specialised routine testing): this clause does not apply to research laboratories where work is done within the laboratory itself in a developmental process, without being referred or outsourced.

- Clause 5.4: Pre-examination or pre-analytical phase refers to patient or client preparation, as well as sample collection, transportation, receipt and accessioning The pre-examination procedures are a shortcoming particularly where laboratory research work is performed retrospectively on stored (i.e. not freshly collected) samples; therefore turnaround times would not be adhered to. Preparation of the patient, correct and adequate sample collection, transportation to and receipt in the laboratory would be critical in testing laboratories where tight turnaround times are the norm and are critical to outcomes and, therefore, patient management. Research laboratories require sampling and preservation methodologies in a research context as well issues relating to ethics.

- Clause 5.6: Assuring quality of examination procedures would be a shortcoming where, in cases of research or specialised testing, no external quality assurance programmes are readily available for use. Therefore, owing to new methodologies or tests being developed in research laboratories, there would be no benchmark against which to check these new methods because there are no proficiency panels available. The laboratory would need to develop its own in-house measures for quality control of new tests or assays. External quality assurance panels or schemes are readily available for use in diagnostic laboratories where established routine methods are already in use.

- Clause 5.7: Reporting of results would be considered an exclusion criterion in cases where no patient report is generated, for example in research laboratories where new assays are being developed. In such laboratories, a new method or technique is designed and therefore no patient result report is generated. However, new methods or developments, once finalised, would be reported to a sponsor/funder or published in a peer-reviewed journal. In diagnostic, clinical laboratories, a report with test results is issued to the doctor or clinician for patient management and care. The report also highlights whether the results are within expected reference ranges or are abnormal, which directly affects patient treatment outcomes.

- In ISO 15189 there is also no reference to research criteria guided by sponsor or funder requirements, as needed for grant applications or sponsorships for research projects, and no specific criteria

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for assessing the competency of scientists in the absence of peer review.

METHODOLOGY

Qualitative research methodology was followed in this study. Qualitative research involves examining and reflecting on perceptions in order to gain a better understanding of social and human activities (Watkins, 2008). Qualitative methods have a common goal of understanding instead of measuring phenomena from the "bottom up" (i.e. from data to findings) (Forman et al, 2008). In order to do this, the researchers have to start with an open-ended research question and gather information using open-ended data collection techniques such as interviews, focus groups, documents and audio data to address the question. For this study, a framework for the semi-structured qualitative interviews was developed after an extensive literature review. The framework consisted of two sections. Section A provided biographical data such gender, age, qualifications, working experience of quality and standards in the laboratory of the respondents. Section B dealt with issues relating to accreditation, including the relevance, strengths and weaknesses of the ISO standards used in their laboratories. The researcher pretested and refined the framework with five peers before using it in the field.

Thematic analysis was used to interpret the data. Thematic analysis entails searching for themes that emerge as being important for the description of the phenomenon or the research problem being assessed (Fereday and Muir-Cochrane, (2006). Themes are identified by "bringing together components or fragments of ideas or experiences, which often are meaningless when viewed alone" (Leininger, 1985). A panel of research specialists was used to review the results with respect to their value and trustworthiness.

RESULTS

The study on which this article is based comprised twenty medical laboratory quality managers in various areas of South Africa, who were consulted before the appointment and advised of the study, after which they confirmed their willingness to participate. A letter of consent was signed before the actual interviews. The types of laboratories cover a variety of functions, including diagnostics, surveillance, reference activities and research. The respondents consisted of 3 males and 17 females. All of them are over 25 years of age and can be assumed to be mature respondents. Medical technologists with qualifications – either a diploma in medical technology only or with an additional bachelor's degree in biomedical technology – made up 70% of the sample. The other 30% consisted of scientists whose highest qualification was either a bachelor's, honours, master's or doctoral degree in science. This shows that all respondents were well qualified technically to understand and manage laboratories. The respondents also had more than two years' service each, which indicates their experience. All the respondents have adequate knowledge of ISO 15189 and ISO 17025 standards. In summary, the respondents were competent, which meant that the data collected during the interviews were credible. All interviews were recorded and transcribed to facilitate the analyses.

There were seven themes derived from the thematic analyses, namely inflexibility; ambiguity; unfair requirements; inappropriate focus; inadequacy for research; renewal; and acceptance for accreditation.

Some comments by the participants on the issue of inflexibility were as follows: '*the weakness of the standard ISO 15189 is in the inflexibility i.e. training and competency areas require more flexibility*' and '*certain aspects of the current ISO 15189 standard e.g. competency and external quality assessment as well as safety could be kept in a new standard which would be made more flexible for research laboratories*'.

Comments about ambiguity included '*the standard is open to understanding depending on the implementer and accrediting assessor*'; ' *auditors see things differently as opposed to people actually*

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working in the laboratory and their interpretation and their checklists varies'; '*one needs to look at these aspects and clearly define these as there are inconsistencies and lab personnel are frustrated*' and '*there are problems in interpreting the standard in relationship to my lab's roles in particular in research-linked work*'.

Views about unfair requirements included comments such as '*adopting laboratory standards and accreditation for their laboratories would entail more administrative work and thus leave less time for research work*'; '*additional documentation is required for accreditation and quality maintenance purposes*'; ' *there have been complaints regarding paperwork by scientists*'; '*they believe that all the paperwork decreases their productivity*' and '*personnel feel that accreditation or standardisation will limit research capacity and creativity*'.

Concerns about inappropriate focus were ' *the weaknesses are in that ISO 15189 meant for research work is unsuitable as results are not given to patients or clients*' and ' *in research results are provided to sponsors or published but would not have direct impact on patient management*'.

The following statements were made about inadequacy for research: *'ISO15189 is relevant for diagnostics; however disagree that it is suitable for research*'; ' *we use peer-review to assess whether our publications are up to standard. The standard would limit our research capacity and creativity*'; '*the standard used for research depends on the end result emphasis and if this result is a diagnostic result then ISO15189 is most appropriate*' and ' *we have made the standards fit our lab activities and I think ISO15189 and ISO17025 are most suitable for medical diagnostic laboratories whereas neither is relevant for research laboratories*'.

Comments regarding renewal were *'I also believe strongly that there should be a standard specific for research work and functions'*; ' *there should be a specific standard for research labs and it must be flexible for their needs*' and ' *I agree that all medical diagnostic labs should implement ISO15189. I think that there should be a standard specific for research work*'.

On the topic of acceptance for accreditation, comments included ' *my argument is that accreditation is required to ensure that research is of good value. Accreditation is the way forward in this country if we are to compete nationally and internationally with other researchers*'; ' *the strengths of using a standard are that managing the lab as a whole is easier as it provides guidelines for the critical phase of specimen management and transcription*'; *there is a defined process and an audit trail in place. One can pick up errors at an early stage. Benefits are that accreditation to a standard brings in more work from stakeholders and collaborators*'; ' *benefits are huge awareness towards customer service and minimizing waste. Control over quality resulting in accuracy of testing. The standard has defined quality of implementation of new instruments or methods. Clearly documented procedures and standardisation have also occurred* ' and ' *the main benefits are that clients are more confident of the results*'.

The panel of medical research specialists previewed the results. These specialists have been working in laboratories for more than ten years, have done extensive research work and have published numerous publications; this makes them knowledgeable about the requirements for producing high-quality research. There was general consensus about the resulting themes, indicating that ISO 15189 in its present format is unsuitable for quality assurance in medical research laboratories.

DISCUSSION

The various themes are elaborated below;

Inflexibility: This shows a need for the standard to be more flexible when it comes to requirements for research laboratories. The weakness of the standard ISO 15189 is in the inflexibility i.e. training and competency areas require more flexibility. Certain aspects of the current ISO 15189 standard e.g. competency and external quality assessment as well as safety could be kept in a new standard which would be

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made more flexible for research laboratories.

Ambiguity: The current ISO 15189 standard is difficult to interpret for a research environment and auditors and laboratory personnel also have different interpretations of the standard.

Unfair requirements: The adopting of a laboratory standard and subsequent accreditation would entail more administrative work and thus leave less time for research work i.e. preventing time for research creativity and output as the requirements though fair for diagnostic work were unfair for the research environment. In a sense the focussing on a non relevant standard is deemed as wasting time and resources.

Inappropriate focus: This refers to ISO 15189 which has a focus on patient management and reporting of results to clinicians which is not the outcome for medical research laboratories. Research results are generally provided to sponsors or published but would not have direct impact on patient management.

Inadequacy for research: This is an obvious theme in that ISO 15189 is relevant for medical diagnostic work, but not entirely suitable for research. The scope of ISO 15189 does not make any claims on its suitability for medical research laboratories or research processes.

Renewal: This shows that a standard specific for research work in laboratories is required. The use of an existing ISO 15189 with suitable amendments could be acceptable but generally a specific standard for research would be more suitable as it could address specific issues relating to research related functions and outcomes.

Accreditation: Accreditation and quality management to a defined standard is the way forward in this country to compete nationally and internationally with other researchers for funding and sponsorships. The strengths of using a standard are that managing the lab as a whole is easier as it creates guidelines for management. The benefits are that better traceability leads to fewer problems/questions arising from assays performed.

CONCLUSION

The intention of the research was not to slander ISO 15189, but to examine its functionality in a research environment. Obviously, ISO 15189 is not truly intended for a research environment but apparently in the absence of a suitable alternative has been used for accrediting research laboratories. Something is better than nothing.

The results of the analyses suggest that ISO 15189 is unsuitable for medical research laboratories. The various gaps within the ISO 15189 standard for research activities were also highlighted. The laboratory managers who provided the input believe that there should be a specific quality assurance standard for research laboratories, as well as accreditation in order to provide confidence in results, and credibility for the attraction of further funding and sponsorships. Further opportunities for developing appropriate quality assurance standards and best practices should be addressed by the various accreditation bodies and should involve a broader community of research laboratories from other disciplines.

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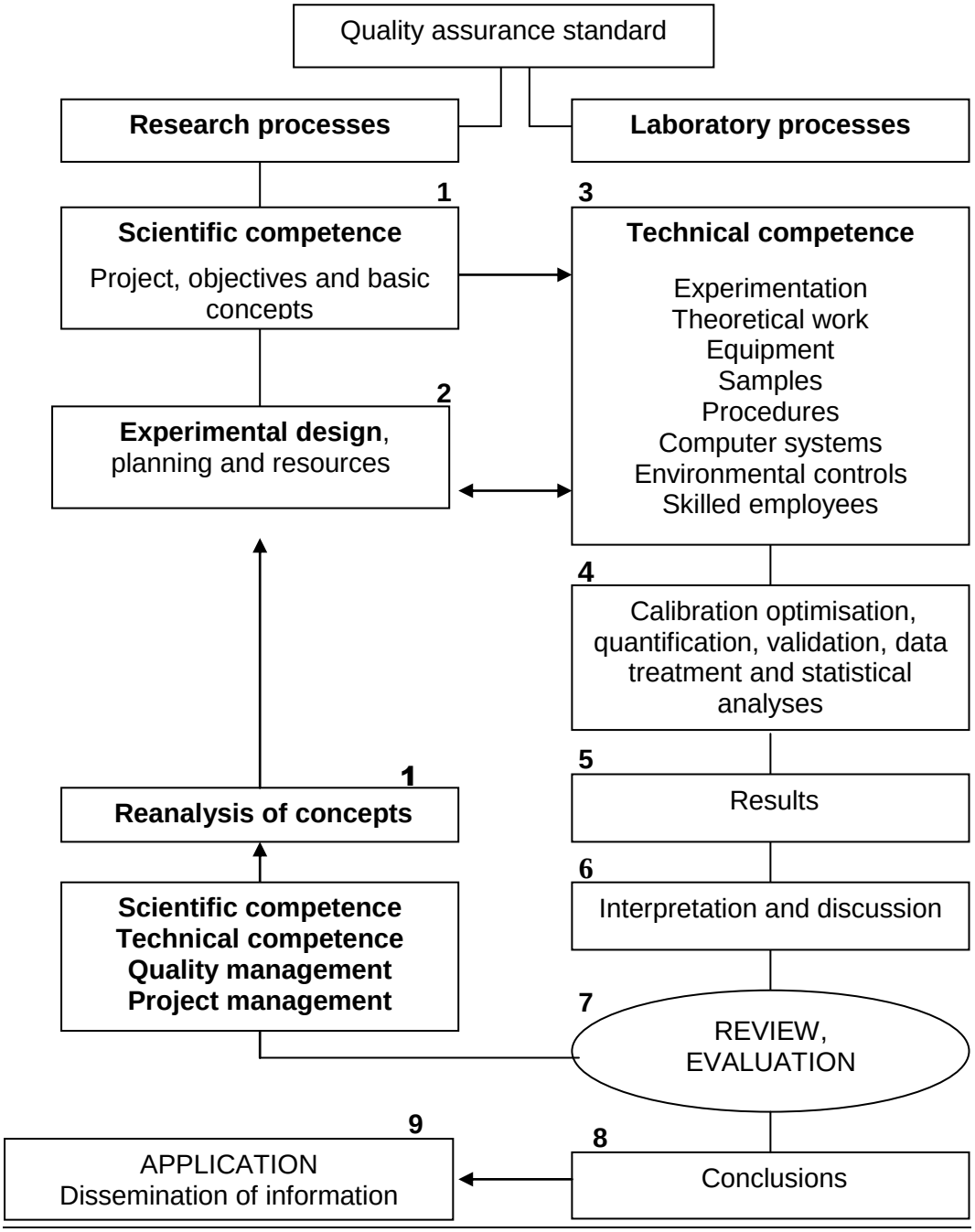

Figure. 1: Scheme for quality assurance in different stages of a research project source: Mathur-De-Vre (2002)