ORIGINAL ARTICLE

Conformity evaluation checklists of Panbio COVID-19 Ag Rapid Test Device for internal auditing: a quality compliance tool for ISO 15189:2012 accredited medical laboratories

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ABSTRACT

Objectives: The aim of this study was to develop a compliance tool that can be used by internal auditors to audit the conformity status of the use of Panbio COVID-19 Ag Rapid Test Device examination kit when ISO 15189:2012 accreditation is specified. The objectives include the identification of relevant conformance requirements in Clauses 4 (Management requirements) and 5 (Technical requirements) of ISO 15189:2012 and specific requirements for accreditation from accreditation bodies relating to areas of audit and the development of Panbio COVID-19 Ag Rapid Test Device examination kit conformity evaluation checklists for internal auditing.

Methods: The relevant conformance requirements in Clauses 4 and 5 of ISO 15189:2012 and specific requirements for accreditation from 83/101 (82 %) accreditation bodies in 80/249 (32 %) countries were identified as specific audit criteria for Panbio COVID-19 Ag Rapid Test Device examination kit conformity evaluation checklists for reagents, test device and reference equipment.

Results: A total of 22/1515 (1.5 %) conformance requirements relating to the use of Panbio COVID-19 Ag Rapid Test Device examination kit was identified in Clauses 4 and 5 of ISO 15189:2012, and specific accreditation requirements for calibration of reference equipment were identified and selected from 12/83 (14.4 %) accreditation bodies in 12/80 (15 %) countries; together these requirements were used to develop conformity evaluation of Panbio COVID-19 Ag Rapid Test Device examination kit checklists (n = 4) and an interpretation checklist.

Conclusions: The present study has provided a practical contribution to existing knowledge of ISO 15189:2012 accreditation compliance management by providing internal auditors with a reasonably practicable approach to conduct comprehensive determination of conformity status of the use of Panbio COVID-19 Ag Rapid Test Device examination kit in accordance with ISO 15189:2012 and specific requirements for accreditation.

Key words: compliance, conformity, ISO 15189:2012, quality management, SARS-CoV-2.

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INTRODUCTION

The pathology services industry plays a competitive role in providing reliable diagnostic information for treatment of human pathological conditions. Medical laboratories can demonstrate their ability to provide competent results by undergoing an accreditation with a relevant accreditation body that is a signatory to the International Laboratory Accreditation Cooperation (1,p.1830) mutual recognition arrangement (2). Medical laboratory accreditation requires fulfilment of requirements from accreditation-related documents that include supplementary criteria and International Standard ISO 15189:2012 (3) prepared by the International Organization for Standardization (ISO) (1,p.1886). The implementation of ISO 15189:2012 to support the medical laboratory quality management system remains a formidable task for management of any laboratory (4,5), largely due to the ongoing effort required to maintain its currency (6-8).

The medical laboratory can monitor whether the examination processes are within its quality management system specifications effectively and efficiently by conducting internal audits at planned intervals, as specified in Subclause 4.14.5 (Internal audit) of ISO 15189:2012 (3,p.17). More specifically, the medical laboratory is required to ensure fulfilment of the conformance requirements (CReqs) of Clause 4 (Management requirements) of ISO 15189:2012 (3,pp.6-19) and Clause 5 (Technical requirements) of ISO 15189:2012 (3,pp.19-39) as well as requirements established by the medical laboratory, as specified in Subclause 4.14.5 a) of ISO 15189:2012 (3,p.17). The medical laboratory can establish its own requirements by consulting with accreditation-related documents that include general and specific guidance and criteria as well as international, national, and regional regulations. In sum, relevant requirements in relation to the examination processes of the medical laboratory quality management system must be met as per specifications of the medical laboratory.

Recent quantitative studies have established that 1515/1515 (100 %) CReqs are associated with Clauses 4 and 5 of ISO 15189:2012 (9) and 22/1515 (2 %) CReqs are associated with examination kits using the API 20 E identification system (10). Clauses 4 and 5 of ISO 15189:2012 contained 3/22 (14 %) CReqs and 19/22 (86 %) CReqs respectively (10), therefore the same CReqs could be used as audit criteria for the Panbio COVID-19 Ag Rapid Test Device examination kit for which the tool to determine compliance status thus far remains unelucidated. The aim of this paper was to develop a compliance tool that can provide an administrative support to accreditation of medical laboratories by determining the compliance status of the use of Panbio COVID-19 Ag Rapid Test Device examination kit. The internal audit areas of focus include documented information

management in acceptance testings as well as calibration and metrological traceability of Panbio COVID-19 Ag Rapid Test Device examination kit reagents (buffer, negative control, and positive control), test device and reference equipment. The development comprised three steps. First, relevant CReqs (*n* = 22) for the areas of audit in Clauses 4 and 5 of ISO 15189:2012 were identified. The relevant CReqs were established from a published quantitative analysis, as previously described (10). Second, specific requirements for accreditation prepared by accreditation bodies that are signatories of the International Laboratory Accreditation Cooperation mutual recognition arrangement were analysed. Third, compliance checklists were developed based on the CReqs and specific requirements for accreditation, and the overall results were then summarised in a final interpretation checklist. The compliance checklists have been designed to ensure that medical laboratories using Panbio COVID-19 Ag Rapid Test Device examination kit to detect SARS-CoV-2 are fulfilling the relevant CReqs in ISO 15189:2012 and specific requirements for accreditation of the accreditation body.

MATERIALS AND METHODS

Elicitation of conformance requirements for the conformity evaluation of Panbio COVID-19 Ag Rapid Test Device examination kit

Audit criteria that could be performed against for the conformity evaluation of Panbio COVID-19 Ag Rapid Test Device examination kit were established by the identification of relevant CReqs in ISO 15189:2012. The technique of content analysis was selected for the quantitative analysis of ISO 15189:2012 and accreditation guidance documents due to its suitability to provide quantitation of requirements in accreditation-related documents (11) and International Standards (9,12). Relevant CReqs pertaining to the conformity evaluation of reagents, test device and reference equipment were identified, as previously described (10). Relevant operating instructions information, as specified in Subclause 7.1.2 of ISO/IEC Guide 37:2012 (13,p.5) and Subclause 7.1.6 of ISO/IEC Guide 37:2012 (13,p.6), were extracted from the Panbio COVID-19 Ag Rapid Test Device examination kit instructions for use (14).

Elicitation of specific requirements for accreditation for the conformity evaluation of Panbio COVID-19 Ag Rapid Test Device examination kit

Relevant specific requirements for accreditation that could be performed against for the conformity evaluation of Panbio COVID-19 Ag Rapid Test Device examination kit were identified and selected from accreditation guidance documents from accreditation bodies that operate in countries listed in International Standard ISO 3166-1:2020 (15) prepared by the ISO that are operating according to International Standard ISO/IEC 17011:2017 (16) prepared by the ISO and the International Electrotechnical Commission (IEC) (1,p.1729) and are signatories to the International Laboratory Accreditation Cooperation mutual recognition arrangement (17). Relevant specific requirements for accreditation pertaining to the conformity evaluation of reagents, test device and reference equipment were identified.

Selection of graphical symbols for use in the development of Panbio COVID-19 Ag Rapid Test Device examination kit conformity evaluation checklists

Relevant graphical symbols (*n* = 10) were selected from International Standard IEC 60417:2002 DB (18) prepared by the IEC and International Standard ISO 7000:2019 (19) prepared by the ISO, to present information in the development of Panbio COVID-19 Ag Rapid Test Device examination kit conformity evaluation checklists. The following symbols were selected: IEC 60417-5662 (2002-10), IEC 60417-5664 (2002-10), ISO 7000-0632 (2014-06), ISO 7000-2493 (2004-01), ISO 7000-2495 (2004-01), ISO 7000-2496 (2004-01), ISO 7000-2498 (2004-01), ISO 7000-2607 (2004-01) and ISO 7000-5132 (2002-10). The format of the calendar date adjacent to graphical symbols conforms to International Standard ISO 8601-1:2004 (20) prepared by the ISO. Specifically, the calendar date is presented in the extended format, as specified in Subclause 5.2.2.1 b) of ISO 8601-1:2004 (20,p.19).

Development of Panbio COVID-19 Ag Rapid Test Device examination kit conformity evaluation checklists for reagents

The Panbio COVID-19 Ag Rapid Test Device examination kit contains a buffer, a negative control, and a positive control to support the examination processes. The performance of buffer, negative control and positive control are required to be verified before use in examinations, as specified in Subclause 5.3.2.3 (Reagents and consumables — Acceptance testing) of ISO 15189:2012 (3,p.26). More specifically, relevant information can be retrieved from records, if maintained, as specified in Subclause 5.3.2.7 (Reagents and consumables — Records) of ISO 15189:2012 (3,p.26). Relevant acceptance status can be established from records, as previously described (10).

Development of Panbio COVID-19 Ag Rapid Test Device examination kit conformity evaluation checklists for test device

The Panbio COVID-19 Ag Rapid Test Device examination kit contains test devices (*n* = 25) that require verification to ensure quality of examination results, as specified in Subclause 5.6.1 (General) of ISO 15189:2012 (3,p.33). The performance of the test device is required to be verified before use in examinations, as specified in Subclause 5.3.2.3 of ISO 15189:2012. More specifically, relevant information can be retrieved from records, if maintained, as specified in Subclause 5.3.2.7 of ISO 15189:2012. Relevant verification status can be established from records, as previously described (10).

Development of Panbio COVID-19 Ag Rapid Test Device examination kit conformity evaluation checklists for reference equipment

The Panbio COVID-19 Ag Rapid Test Device examination kit requires the use of a thermometer and a timer to support the examination processes. The thermometer used to assess the operating temperature of the testing environment (21) and the timer to assess the examination reaction timeframe (22) need to be calibrated, as specified in Subclause 5.3.1.4 (Equipment calibration and metrological traceability) of ISO 15189:2012 (3,p.24). The calibration is to be performed by a facility that has obtained accreditation in International Standard ISO/IEC 17025:2017 (23) prepared by the ISO and the IEC. The temperature information should be expressed in degrees Celsius, as specified in Item 5-2 of International Standard ISO 80000-5 (24,p.3) prepared by the ISO, in alignment with the manufacturer's instructions for use (14). More specifically, relevant information can be retrieved from records, if maintained, as specified in Subclause 5.3.1.7 (Equipment records) of ISO 15189:2012 (3,p.25). Relevant calibration status can be established from records, as previously described (10).

Limitations of Panbio COVID-19 Ag Rapid Test Device examination kit conformity evaluation

The Panbio COVID-19 Ag Rapid Test Device examination kit evaluation process was subject to three limitations.

The first limitation was that the internal auditor needs to assume the test was performed on a relatively level surface to allow the extracted specimens laterally flowing through the test device. The internal auditor can measure the level of a horizontal plane by using a level measuring instrument (25), if required. The second limitation was that the internal auditor needs to assume the result was read with good task visibility in an appropriate level of maintained illuminance, as specified in Clause 5 (Schedule of lighting requirements) of International Standard ISO 8995:2002 (26,pp.9‑17) prepared by the ISO. The internal auditor can take photometric measurements around the examination area using a luminance meter (27), if required. The third limitation was that the internal auditor needs to take into consideration requirement(s) established by the medical laboratory that are highly unlikely to be included in the compliance tool.

RESULTS

Quantitation of conformance requirements for the conformity evaluation of Panbio COVID‑19 Ag Rapid Test Device examination kit

Content analysis was used to identify the relevant CReqs from Clauses 4 and 5 of ISO 15189:2012, as previously described (10), that pertain to the conformity evaluation of Panbio COVID‑19 Ag Rapid Test Device examination kit. A total of 22/1515 (1.5 %) CReqs was identified and used for the conformity evaluation (Figures S2 to S6).

Quantitation of specific requirements for accreditation from accreditation guidance documents for the conformity evaluation of Panbio COVID‑19 Ag Rapid Test Device examination kit

A total of 83/101 (82 %) accreditation bodies in 80/249 (32 %) countries was identified as International Laboratory Accreditation Cooperation mutual recognition arrangement signatories to ISO 15189:2012 (28); of these, the 12/83 (14.4 %) accreditation bodies in 12/80 (15 %) countries were identified that provide specific requirements for accreditation for thermometer calibration (Figure S1); and, 8/83 (9.6 %) accreditation bodies in 12/80 (15 %) countries were identified that provide specific requirements for accreditation for timer calibration (Figure S1). It was identified that 1/83 (1.2 %) accreditation bodies (National Accreditation Board for Testing and Certification Laboratories) have specific requirements for accreditation relating to lot verification of examination kits (Table S1).

Graphical symbols for Panbio COVID‑19 Ag Rapid Test Device examination kit conformity evaluation checklists

Selected graphical symbols (n = 10), as previously described (10), were used in checklists to support the transmission of information (Figures S2 to S6).

Panbio COVID‑19 Ag Rapid Test Device examination kit conformity evaluation checklists for reagents

The Panbio COVID‑19 Ag Rapid Test Device examination kit conformity evaluation checklists for reagents were developed based primarily on Subclause 5.3.2.3 of ISO 15189:2012, as previously described (10). The first checklist evaluated the Panbio COVID‑19 Ag Rapid Test Device examination kit buffer (Figure S2). The second checklist evaluated the Panbio COVID‑19 Ag Rapid Test Device examination kit negative control and positive control (Figure S3) which require medical laboratory established procedures for the verification.

Panbio COVID‑19 Ag Rapid Test Device examination kit conformity evaluation checklist for test device

The Panbio COVID‑19 Ag Rapid Test Device examination kit conformity evaluation checklists for the test device were developed based primarily on Subclause 5.3.2.3 of ISO 15189:2012, as previously described (10). The first checklist evaluated the Panbio COVID‑19 Ag Rapid Test Device examination kit test device in relation to acceptance testing (Figure S4). The second checklist evaluated the Panbio COVID‑19 Ag Rapid Test Device examination kit reactivity of SARS‑CoV‑2 antigen with specified conditions of incubation and duration (Figure S5).

Panbio COVID‑19 Ag Rapid Test Device examination kit conformity evaluation checklists for reference equipment

The Panbio COVID‑19 Ag Rapid Test Device examination kit conformity evaluation checklists for reference equipment were developed based primarily on Subclause 5.3.1.4 of ISO 15189:2012, as previously described (10). The first checklist evaluated treatments with a specified environmental condition [(15 °C to 30 °C) (Figures S2 to S5)]. The second checklist evaluated treatments with specified durations [(30 min) (Figures S2 to S5) and (15 min) (Figures S2 to S5)].

Summary of results for Panbio COVID‑19 Ag Rapid Test Device examination kit conformity evaluation checklists

The final results were summarised in accordance with the acceptability of Panbio COVID‑19 Ag Rapid Test Device examination kit checklists (Figures S2 to S4). The summary of results can be presented in a final interpretation checklist (Figure S5).

DISCUSSION

The present study was designed to develop a reasonably practical tool for ISO 15189:2012 accredited medical laboratories to determine the conformity status of the use of Panbio COVID‑19 Ag Rapid Test Device examination kit in accordance with the relevant CReqs (n = 22) in Clauses 4 and 5 of ISO 15189:2012 and specific requirements for accreditation. The developed conformity evaulations checklists have the potential to provide an effective support to the internal audit process, as specified in Subclause 4.14.5 of ISO 15189:2012, and the continual improvement process, as specified in Subclause 4.12 (Continual improvement) of ISO 15189:2012 (3,pp.14‑15). The results of this study found that a comprehensive structured approach could offer the medical laboratory enhanced internal audit effectiveness and efficiency.

The use of Panbio COVID‑19 Ag Rapid Test Device examination kit conformity evaluation checklists has three technical considerations that need to be considered by the internal auditor. First, the internal auditor should ensure that the calibration requirements need to be fulfilled in accordance with Subclause 5.3.1.4 of ISO 15189:2012 and specific requirements for accreditation by the accreditation body before the information can be considered valid. Although only 12/83 (14.1 %) accreditation bodies provide specific information relating to check and calibration of reference equipment, it is important to note that ISO 15189:2012 accredited medical laboratories must calibrate equipment that directly or indirectly affects examination results. The reference equipment is to be calibrated by a facility that has achieved accreditation to International Standard ISO/IEC 17025:2017 (23) prepared by the ISO and the IEC or by an in‑house facility capable of providing equivalent results. Second, the internal auditor should ensure that the locality of temperature detection is relevant to the locality of the testing environment before the information

can be considered valid. It is important that the recording is at an appropriate proximity of the performance of the examination processes and could represent the specified environmental condition. Although the level of proximity is open to interpretation, but the term 'appropriate' can be defined as 'specially fitted or suitable, proper' (29,p.109). Nevertheless, the medical laboratory must limit its exposure to non-conformity by ensuring that the recorded environmental condition is representative of the specified testing condition. Third, the internal auditor should ensure the personnel who make judgments with reference to examinations have met the established criteria of medical laboratory. In addition to relevant qualification and experience appropriate to the task, the medical laboratory may require personnel to hold valid local registration. In the case that the medical laboratory requires personnel to hold valid registration to provide professional judgements, then the personnel must hold relevant registration to perform the examination to meet conformity necessities, as specified in Subclause 5.1.2 (Personnel qualifications) of ISO 15189:2012 (3,p.19). It is important to note that any form of special exemption in registration to practice by any entities or parties does not of itself confer immunity from accreditation compliance obligations. The medical laboratory's practices are defensible by reference to accreditation risk management requirements.

CONCLUSIONS

The present study was undertaken to develop practical work documents for the medical laboratory to conduct internal audits to ensure practices relating to the use of Panbio COVID-19 Ag Rapid Test Device examination kit conform to the relevant CReqs of ISO 15189:2012 and specific requirements for accreditation. The main strength of this study is to provide a structured approach to perform relevant internal audits for an examination kit. In sum, this study has developed a reasonably practicable solution for conformity evaluation relating to use of the Panbio COVID-19 Ag Rapid Test Device examination kit in ISO 15189:2012 accredited medical laboratories.

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