Documentary standards update for Coronavirus Standards WG Steering Committee

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24 July 2020
SCOPE
Standardization in the field of biotechnology processes that includes the following topics:

- Terms and definitions;
- biobanks and bioresources;
- analytical methods;
- bioprocessing;
- data processing including annotation, analysis, validation, comparability and integration;
- metrology.

ISO/TC 276 Biotechnology will work closely with related committees in order to identify standardization needs and gaps, and collaborate with other organisations to avoid duplications and overlapping standardization activities.

The committee will not pursue subjects within the scope of other TCs including but not limited to ISO/TC 212 and ISO/TC 34/SC 16.
Scope of ISO TC 276 WG3: Analytical Methods

The Analytical Methods Working Group aims to develop standards for **accurate, reproducible and robust measurement and analysis** in support of biotechnologies.

WG 3 will develop a package of International Standards for **biologically relevant molecules and entities**, including nucleic acids, proteins, and cells.

This WG will develop horizontal standards and, when applicable, vertical / particular standards for industry sectors.

The WG will also coordinate with relevant technical committees and standardization initiatives.
Suite of standards to address all sectors of emerging biotechnology

By molecules & entities
- Nucleic acids*
- Protein
- Cells*
- Virus/viral vectors
- Others

By attribute
- Count*
- Purity*
- Viability
- Potency

By method
- qPCR/ddPCR*
- NGS*
- Genome Editing*
- Photometric*
- Microscopy*
- Flow cytometry
- ELISA

By application
- Cellular therapeutics*
- Biotechnology
- Biodiversity
- Infectious disease

* Ongoing efforts or completed standards
Example: Analytical methods for supporting SARS-CoV-2 diagnostics and therapeutics

By molecules & entities
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- Flow cytometry
- ELISA

By application
- Cellular therapeutics
- Biotechnology
- Biodiversity
- Infectious diseases (+ other ISO TC documents)

NOTE: For illustrative purpose only, may not be comprehensive or correct
WG3 Programme Summary

(Almost) Published
- Published
- FDIS ➔ DIS/DTS/DTR
- Cell Counting Pt 1
- Cell Counting Pt 2
- NA Quantification
- NA Synthesis Pt 1
- NGS Pt 2
- Cell Characterization

Ongoing
- CD ➔ WD/AWI/NP
- NGS Pt 1
- Genome Editing Terminology
- Cell Line Auth
- RMTM
- Photometric Methods
- NA Synthesis Pt 2

Potential
- PWI ➔ Idea
- Cell Morphology
- Contamination of Mammalian Cells
- Cell Viability
- Pre-analytics
- Barcode for biodiversity
- SARS-CoV-2 by molecular method
ISO 20395:2019
Biotechnology — Requirements for evaluating the performance of quantification methods for nucleic acid target sequences — qPCR and dPCR

This standard is available for free in read-only format

ABSTRACT
This document provides generic requirements for evaluating the performance and ensuring the quality of methods used for the quantification of specific nucleic acid sequences (targets).
This document is applicable to the quantification of DNA (deoxyribonucleic acid) and RNA (ribonucleic acid) target sequences using either digital (dPCR) or
ISO 20688-1:2020
Biotechnology — Nucleic acid synthesis — Part 1: Requirements for the production and quality control of synthesized oligonucleotides

ABSTRACT
This document specifies minimum requirements for the production and quality control of synthesized oligonucleotides (nominally up to 250 bases).

This document also describes general quality attributes for synthesized oligonucleotides as well as common methods for evaluating quality attributes.

GENERAL INFORMATION
Status: ® Published
Publication date: 2020-02
Edition: 1
Number of pages: 28

Technical Committee: ISO/TC 276 Biotechnology

Relevant stds to COVID-19
ISO/AWI 20688-2
Biotechnology — Nucleic acid synthesis — Part 2: General definitions and requirements for the production and quality control of synthesized gene fragment, gene, and genome

GENERAL INFORMATION

Status: Under development
Edition: 1
Proposal from BGI and China National Institute of Standardization (CNIS): Considerations for quality evaluation for detecting Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by RT-qPCR

**Scope**

This document describes considerations for evaluation of assays for detecting Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by RT-qPCR, including the terms and definitions, abbreviations, evaluation procedure, evaluation methodology, factors affecting the evaluation results and evaluation examples.

This document is applicable to the process of kit development and laboratories performing RT-qPCR testing for detection of SARS-CoV-2.
Standard proposal introduction

Standard Framework

1 Scope
2 Normative references
3 Terms and definitions
4 Abbreviation
5 Quality evaluation requirements
6 Quality evaluation parameters and methods
7 Reagent and facility requirements
8 Reagent kit requirements
9 Test report
10 Waste and cross contamination management

Presented during June ISO TC 276 Meeting
Standard proposal introduction

Scope:
This guidance documented the terms and definitions as well as the criteria, parameters and methods of quality evaluation for qRT-PCR testing for SARS-CoV-2.

Normative references:

ISO 15198:2004
Clinical laboratory medicine — diagnostic medical devices — Validation of user quality control procedures by the manufacturer

ISO 20395:2019
Biotechnology — Requirements evaluating the performance of quantification methods for nucleic acid target sequences — qPCR and dPCR

ISO 17511:2020
In vitro diagnostic medical devices — Requirements for establishing metrological traceability of values assigned to calibrators, trueness control materials and human samples

Presented during June ISO TC 276 Meeting


<table>
<thead>
<tr>
<th>Evaluation parameters</th>
<th>Requirements</th>
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</thead>
<tbody>
<tr>
<td><strong>Nucleic acid extraction</strong></td>
<td>Laboratories must test and validate the nucleic acid extraction kit for its nucleic acid extraction rate and nucleic acid purification efficacy.</td>
</tr>
<tr>
<td><strong>Lower detection limit</strong></td>
<td>Lower detection limit must be no more than 1×102 copies/mL.</td>
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<tr>
<td><strong>Precision</strong></td>
<td>Coefficient of Variation must be no more than 5 percent.</td>
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<tr>
<td><strong>Specificity</strong></td>
<td>Potential contamination by nucleic acid from other pathogen must be documented, including name, type and concentration of the pathogen.</td>
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<td><strong>Validation</strong></td>
<td>Validation must be performed using reference material fulfilling national or international standard.</td>
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<tr>
<td><strong>Stability</strong></td>
<td>Factors that would impact reagent stability including period of validity, transportation, freezing and thawing.</td>
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</tbody>
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Presented during June ISO TC 276 Meeting
Presented during June ISO TC 276 Meeting

Standard proposal introduction

Reagent requirements
Storage, Sterilization, Nuclease,
......

Reagent kit requirements
Package label, Instructive document,
Traceability document

Test report:
Quality control report, Logic of result interpretation

Waste and cross contamination management
Considerations

- Appropriate ISO technical deliverables
- Coordination with other ISO Technical Committee(s)
- Building consensus towards a global standard
Appropriate ISO technical deliverables

INTERNATIONAL STANDARDS

Provides rules, guidelines or characteristics for activities or for their results, aimed at achieving the optimum degree of order in a given context. Forms: Product standards, test methods, codes of practice, guideline standards and management systems standards.

TECHNICAL SPECIFICATION

Addresses work still under technical development, or where it is believed that there will be a future, but not immediate, possibility of agreement on an International Standard.

TECHNICAL REPORT

Contains information of a different kind from that of the previous two publications. It may include data obtained from a survey, for example, or from an informative report, or information of the perceived “state of the art”.

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**Deliverables**
- First CD (Committee draft)
- or ISO/PAS (Publicly Available Specification)
- DIS or ISO/TS (Technical Specification)
- ISO/TR (Technical Report) for non-normative documents
- Final text for processing as FDIS (Final Draft International Standard)
- Final text of International Standard
- ISO International Standard
- International workshop Agreement
Coordinated efforts

ISO/TC 212
Clinical laboratory testing and in vitro diagnostic test systems

**Scope:** Standardization and guidance in the field of laboratory medicine and in vitro diagnostic test systems. This includes, for example, quality management, pre- and post-analytical procedures, analytical performance, laboratory safety, reference systems and quality assurance.
Coordinated effort (continued)

ISO/TC276 and ISO/TC212 agreed on a path forward:

• A joint working group (JWG) will form (Convened from TC212, with JWG Manager from TC276).
• Experts from both TC will be able to participate.

Next steps:

• Both TCs will put forward a resolution to form a JWG as soon as the scope of ISO/NP TR 20398 can be updated.
• Joint expert meeting to be schedule for the week of July 25, 2020
  • Review outline of document
  • Review and update scope/title statement
  • Derive a project management schedule with action items.
Building consensus

Version July 20, 2020
4. Technical procedure to evaluate the quality attributes

- **Nucleic acid extraction**
  - Assess the nucleic acid extraction rate and purity
- **Limit of Detection**
  - Test a serial dilution of a positive certified reference material
- **Quality Evaluation**
  - **Precision**
    - Operator
    - Analyzer
    - Location
    - Detection Reagents
    - Test round
  - **Verification of reference materials**
    - Negative references
    - Positive references
    - Precision
    - Sensitivity
  - **Specificity**
    - Wet lab testing
    - Dry lab testing
    - Within the period of validity
    - After transportation
    - After unsealing and freezing and thawing
  - **Stability**
    - Evaluate the performance by interfering pathogen/nucleic acid
    - Evaluate the performance under different conditions
5. Evaluation Methodology

• 5.1 Extraction / purification performance of nucleic acid (RNA)
• 5.2 Verification of the inclusiveness of virus samples in different regions
• 5.3 Metrology traceability
• 5.4 Precision
• 5.6 Specificity （Selective detection）
• 5.7 Stability
• 5.8 linearity
• 5.9 Conformity rate of reference materials
• 5.10 Instrument suitability
• 5.11 Sample types
• 5.12 Positive threshold
6. Factors affecting the evaluation results

• 6.1 Reagent and facility
• 6.2 Laboratory personnel
• 6.3 Package
• 6.4 Instructions
• 6.5 Waste and cross contamination
Reporting as an additional section?

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Laboratory design

The new TC will stipulate technical design requirements for a diverse range of laboratories with different functions and responsibilities. It will include, but not limited to:

1. site selection and planning;
2. layouts and selection of model furniture (e.g. workbenches, fume hoods, safety showers, biological safety cabinets, etc);
3. electrical, water and gas supply systems, drainage, fire prevention, HVAC, auto-control and decoration;
4. laboratories featuring bio-safety, constant temperature and humidity, and other special laboratories;
5. laboratory safety, staff health and wellness, environmental protection, and energy saving;
6. Smart laboratory (Use of big data, cloud computing, Internet of things, blockchain, artificial intelligence and other digital technologies to monitor and control the environmental conditions of the laboratory, so as to have better performance operation of facilities, energy conservation, environmental protection and personnel health).
Purpose

• Note: the proposed TC will help laboratory design industry to address a wide range of global issues. Outbreaks of zoonotic disease like Avian Influenza (H5N1), Middle East Respiratory Syndrome (MERS), Ebola virus, Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS) and Coronavirus (COVID-19) has highlighted the worldwide lack of adequate laboratory capacity, especially in low-resource environments. This proposal should address this situation, early during the design stage, by providing a standardised approach on laboratory function, health and safety, energy efficiency, environmental impact and regulatory compliance issues.
## ISO Deliverables

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<td>Normative (i.e. contains reqts)</td>
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<td>Informative (No requirements)</td>
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<tr>
<td><strong>Consensus Level for Pub.</strong></td>
<td>TC (+ input from all ISO MBs)</td>
<td>TC</td>
<td>WG</td>
<td>TC</td>
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<tr>
<td><strong>Voting Requirements for Pub.</strong></td>
<td>ISO MBs + 2/3 of TC P-members approval (&lt;1/4 votes disapprove)</td>
<td>2/3 of P-members approval</td>
<td>Simple majority of P-members</td>
<td>Simple majority of P-members</td>
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<td><strong>Intended Use</strong></td>
<td>Technologies that are sufficiently mature for a longer term standard</td>
<td>Less mature technologies/methods, etc that are likely to change in the short term</td>
<td>TC wishes to publish collected relevant information (e.g., test results) and/or guidance</td>
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<td><strong>Systematic Review (SR) Cycle / Doc Lifetime</strong></td>
<td>No life limit (SRs every 5 yrs or less)</td>
<td>SR after 3 yrs Recommended maximum life=6 yrs</td>
<td>SR after 3 yrs Max life = 6 yrs (convert or withdraw)</td>
<td>No life limit</td>
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</tbody>
</table>

Normative: necessary for application of standard / Informative: assist in particular subject area
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