Publishable Summary for 16SIP01 Bio-stand
New underpinning standards for improved bio-analytical measurement in Biotechnology & In vitro Diagnostics

Overview

This project will use outputs from two previously completed EMRP projects (SIB54 (Bio-SITrace) and HLT08 (INFECT-MET)), which used state of the art techniques to develop methodology and guidelines for achieving traceability and comparability in biological measurements. Knowledge gained during these projects will be used to input into the development of new standards and revision of an existing standard through two ISO committees (ISO/TC 276 Biotechnology and ISO/TC 212 Clinical laboratory testing and in vitro diagnostic test systems) as well as supporting events to disseminate these standards and guidelines to user communities. The project's primary supporter, DIN, has recognised that the traceable measurement of biomolecules is a key problem in many sectors and is fundamental to the progress of biotechnology and clinical diagnostics.

Need

Accurate measurement of biological analytes (nucleic acids, proteins and cells) underpins the future of many sectors including healthcare, environment, biotechnology and food. However, a lack of higher order reference methods and standards is a major hindrance for deriving traceability and measurement comparability, which impacts upon accreditation and regulatory development and compliance. This in turn compromises patient and consumer safety and efficacy of products.

Objectives

The project addresses the following objectives:

1. To incorporate the outputs from SIB54 (Bio-SITrace) for the quantification of nucleic acids and cells into ISO/TC 276 (Biotechnology), in order to support their wider dissemination and uptake.
2. To incorporate the results and best practice guidance developed in SIB54 (Bio-SITrace) and HLT08 (INFECT-MET) for the quantification of nucleic acids in clinical matrices into ISO/TC 212 (Clinical laboratory testing and in vitro diagnostic test systems) in order to support compliance with Regulation (EU) 2017/746 of the European Parliament and of the Council on in vitro diagnostic medical devices and wider dissemination and uptake by the clinical community.

Results

1. *To incorporate the outputs from SIB54 Bio-SITrace for the quantification of nucleic acids and cells into ISO/TC 276 (Biotechnology) in order to support their wider dissemination and uptake.*
   - LGC led the UK Delegation at the ISO/TC 276 Biotechnology documentary standards meeting held in Beijing, China. It was agreed at the meeting to move ISO/DIS 20395-1 (Requirements for evaluating the performance of quantification methods for nucleic acid target sequences: Part 1 qPCR and dPCR) to the Draft International Standard (DIS) part of the development process, a significant step towards publication of a final standard.
   - Outputs from SIB54 (Bio-SITrace) have been incorporated into ISO 20391-1 (Biotechnology - Cell counting - Part 1: General guidance on cell counting methods) which was published in January 2018 and ISO 20391-2 (Biotechnology - Cell Counting - Part 2: Experimental design and statistical analysis to quantify counting method performance which is now registered as a Draft International Standard (DIS).
2. *To incorporate the results and best practice guidance developed in SIB54 Bio-SITrace and HLT08 INFECT-MET for the quantification of nucleic acids in clinical matrices into ISO/TC 212 (Clinical laboratory testing and in vitro diagnostic test systems) in order to support compliance with* Regulation (EU) 2017/746

The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States

of the European Parliament and of the Council *on in vitro diagnostic medical devices and wider dissemination and uptake by the clinical community.*

- Outputs from SIB54 (Bio-SITrace) with respect to establish SI-traceability of bio-measurements via counting methods have now been incorporated into the main text of the revision of ISO 17511 (In vitro diagnostic medical devices -- requirements for establishing metrological traceability of values assigned to calibrators, trueness control materials and human samples).
- Outputs from HLT08 (INFECT-MET) have been incorporated into the committee draft of ISO 17822-2 (In vitro diagnostic test systems -- Qualitative nucleic acid-based in vitro examination procedures for detection and identification of microbial pathogens -- Part 2: Quality practices for nucleic acid amplification).

Impact

Direct impact for the primary supporter

ISO/TC 276 is concerned with standardisation in the field of biotechnology processes. The consortium will lead on the development of one new standard and input into the development of a second standard within the TC 276 committee. These standards will be fundamental base documents and will provide guidelines for evaluating and ensuring the quality of nucleic acid (NA) quantification and cell counting required specifically to support the analytical requirements of both TC 276/WG 2 (biobanks) and TC 276/WG 4 (bioprocesses). They will also support the broader biotechnology, R&D, industrial biotechnology, synthetic biology, gene editing, and advanced therapeutics industries which have to comply with quality and emerging regulatory requirements.

ISO/TC 212 is concerned with standardisation and guidance in the field of laboratory medicine and in vitro diagnostic test systems. The consortium will input into the development of two standards which are being revised/developed within the TC 212 committee. These standards will describe the particular laboratory practice requirements to ensure the quality of detection, identification and quantification of microbial pathogens using NA amplification-based methods. They will help users and developers of such clinical tests to comply with Regulation (EU) 2017/746 of the European Parliament and of the Council on in vitro diagnostic medical devices.

Direct impact on biotechnology industry

The standards developed in this project will provide confidence in the data produced and be useful for selecting or optimising a measurement process. They will also provide supporting performance parameters that may be utilised during performance qualification of a particular measurement process. Biotechnology and bioscience industry data with higher measurement confidence will enable data interoperability, reduced risks and costs, engender regulatory confidence and compliance and facilitate international trade.

Direct impact on healthcare providers and diagnostics developers

The standards developed in this project will be used by IVD medical device manufacturers, medical laboratories and research and development laboratories that develop NA amplification-based in vitro diagnostic examination procedures for the detection and identification of microbial pathogens in human specimens. In this context, these guidelines support molecular diagnostic laboratories to demonstrate conformity with IVD regulatory requirements worldwide.

Wider industry impacts

Accurate measurement of biological analytes (nucleic acids, proteins and cells) underpins the future of many sectors including healthcare, environment, biotechnology, and food. The guidelines disseminated deal with cross-cutting fundamental measurements of targeted NA quantification and cell counting and will provide generic support to practitioners in the field undertaking such measurements.

Economic and Societal impact

Low reproducibility rates within life science measurements undermine cumulative knowledge production and contribute to both delays and costs of product development. Whilst it is difficult to put a precise figure on the amount of money that can be saved as a result of the guidance documents produced in the project, it can be assumed that even a low level of uptake will have significant cost benefits.

Laboratory developed tests serve an increasingly important role in health care today. They also have become significantly more complex and higher risk, with several notable examples of inaccurate tests placing patients

at otherwise avoidable risk. The standards and guidance documents produced in this project will help to mitigate against the use of inaccurate and unreliable tests.

<table>
<tr><td colspan="2">Project start date and duration:</td><td>01 April 2017, 36 months</td></tr>
<tr><td colspan="3">Coordinator: John Black, LGC Tel: +44 (0) 208 943 7000 E-mail: john.black@lgcgroup.com
Project website address: http://www.lgcgroup.com/our-science/national-measurement-laboratory/european-metrology-programme-for-innovation-and-re/biostand/#.WoQsQa5l_cs</td></tr>
<tr><td colspan="3">Primary Supporter: Lena Krieger, DIN e.V., Tel: +49 30 26011231 E-mail: lena.krieger@din.de</td></tr>
<tr><td>Internal Funded Partners:
1. LGC, United Kingdom
2. PTB, Germany</td><td>External Funded Partners:</td><td>Unfunded Partners:</td></tr>
</table>