UPCOMING QUALITY REQUIREMENTS FOR MOLECULAR PATHOLOGY

SPIDIA4P CONSORTIUM: C. STUMPTNER[1], U. OELMUELLER[2], K.F. BECKER[4], F. BETSOU[15], S. BONIN[12], C. CINISELLI[19], G. DAGHER[16], C. FONSECA[8], T. FORSHEW[7], C. FOY[3], A. GAINAUX[15], S. GELMINI[10], D. GROELZ[6], C. HARTMAN[2], O. KOFANOVA[15], L. KRIEGER[5], M. KUBISTA[9], P. KUNGL[1], C. MARCHIO[13], H. PARKES[3], M. PAZZAGLI[10], M. PLEBANI[19], P. PINZANI[10], M. PUGH[7], P.H.J. RIEGMAN[17], K. RODENKIRCHEN[2], A. SAPINO[13], M. SCHMITZ[2], U. SCHRÖDER[5], R. SJOBAC[9], G. STANTA[12], E. STEINFELDER[14],'M TAUSSIG[8], A. TROMBETTA[13], P. TURANO[11], P. VERDERIO[19], A. WUTTE[14], K. ZATLOUKAL[1].

[1]Diagnostic- and Research Center for Molecular Biomedicine, Instit. of Pathology, Medical University of Graz, Austria; [2]QIAGEN GMBH, Hilden, Germany; [3]LGC LIMITED, Teddington, United Kingdom; [4]Technische Universität München, Germany; [5]DIN Deutsches Institut für Normung, Berlin, Germany; [6]PreAnalytiX GMBH, Hombrechtikon, Switzerland, [7]Inivata Ltd, Cambridge, UK; [8]Cambridge Protein Arrays LTD, Cambridge, UK; [9]TATAA Biocenter AB, Goteborg, Sweden, [10]Dipartimento di Scienze Biomediche, Univerita Degli Studie Di Firenze, Italy; [11]Magnetic Resonance Center, Consorzio Interuniversitario Risonanze Magnetiche Di Metallo Proteine, Sesto Fiorentino, Italy; [12]Molecular Histopathology Laboratory, Universita Degli Studi Di Trieste, Italy; [13]Medical Sciences, Universita Degli Studi Di Torino, Italy; [14]BBMRI-ERIC, Graz, Austria; [15]IBBL, Luxembourg Institute of Health, Luxembourg; [16]Inserm US 13, Institut National De La Sante, Paris, France; [17]Dept. of Pathology, Erasmus Universitair Medisch Centrum Rotterdam, Netherlands; [18]Centro Nacional de Analisis Genomico (CNAG-CRG), Fundacio Centre De Regulacio Genomic, Barcelona, Spain; [19]Unit of Medical Statistics, Biometry and Bioinformatics, Fondzione IRCCS Istituto Nazionale Dei Tumori, Milano, Italy

BACKGROUND & AIM

The reliability and reproducibility of molecular analyses critically relies on sample quality which is to a great part influenced by pre-analytical factors.

Findings from literature, the EU project SPIDIA and the NIH provided the basis for a series of international sample pre-analytics standards.

METHOD

The CEN (European Committee for Standardization) Technical Committee 140 has developed a series of sample quality standards under the title “In-Vitro Diagnostic examinations - Specifications for Pre-examination Processes”. These documents were forwarded to ISO (International Organization of Standards) to be prepared as ISO Standards).

In the context of the H2020 project SPIDIA4P further standards are developed and their dissemination and implementation supported.

RESULTS

Pre-analytical sample quality standards by CEN and ISO: “In-Vitro Diagnostic examinations - Specifications for Pre-examination Processes for…”

1 Why Standards?

To harmonize pre-analytical sample handling because pre-anaytical errors

- Make up 50-70% of clinical laboratoryerrors[1]
- Cause unnecessary expenditure in hospitals[2]
- Can lead to diagostic errors which account for 10% patient deaths[3]
- Leads to irreproducible pre-clinical research results (30%)[4]

2 Examples of Standards

Published:[5]

- FFPE tissue - Part 1: RNA (CEN/TS 16827-1:2015)
- FFPE tissue - Part 2: proteins (CEN/TS 16827-2:2015)
- FFPE tissue - Part 3: DNA (CEN/TS 16827-3:2015)
- Snap frozen tissue - Part 1: RNA (CEN/TS 16826-1:2015)
- Snap frozen tissue - Part 2: proteins (CEN/TS 16826-2:2015)

In development:

- FFPE tissue - Part 4: In situ detection (ISO)
- CTCs in blood - Part 1-3: RNA/DNA/staining (CEN)
- Human specimen - microbiome DNA (CEN)

3 Content

- **Standards contain requirements / recommendations what shall / should be done or documented**
- **along the entire pre-analytical clinical workflow:**

e.g. FFPE Tissue – RNA (CEN/TS 16827-1:2015)

Outside the laboratory
Collection of biospecimen
Transport requirements
Inside the laboratory
Primary tissue sample receipt
Fixation of the specimen
Evaluation of the pathology
Processing and paraffin embedding
Storage requirements (paraffin blocks & sections)
Isolation of total RNA
General information (FFPE)
Quantity & quality assessment of RNA
Storage of isolated RNA

4 Relevance for Molecular Pathology

- To establish and improve quality management particularly in accredited / certified institutions

- To harmonize Standard Operation Procedures (SOPs) and processes
- To fullfill requirements of the In-Vitro Diagnostic (IVD) Regulation: Sample pre-analytics are needed for lab and industry developed test

Excerpt from IVDR Annex II

6. PRODUCT VERIFICATION AND VALIDATION

6.1. Information on analytical performance of the device

6.1.1. Specimen type

This Section shall describe the different specimen types that can be analysed, including their stability such as storage, where applicable specimen transport conditions and, with a view to time-critical analysis methods, information on the timeframe between taking the specimen and its analysis and storage conditions such as duration, temperature limits and freeze/thaw cycles

- The standards also specify the role of pathologists in molecular testing

SUMMARY

Compliance with these standards will become important in the light of the new IVDR that has to be applied for laboratory and industry developed tests. They will also be relevant for pathology in the context of quality management audits of ISO accredited/certified laboratories.

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