SPIDIA4P

SPIDIA4P Newsletter 01/2020

SPIDIA4P AT THE EU PARLIAMENT!

New CEN and ISO standards published! See page 5

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EDITORIAL

Dear reader,

there is meanwhile broad international consensus that improved and standardised preanalytical workflows are key for reliable and correct laboratory test results. During last year, SPIDIA4P has therefore continued to develop additional new ISO and CEN standards for preanalytical workflows via the CEN/TC 140 and the ISO/TC 212 and associated External Quality Assurance Schemes (EQAs).

A new ISO Standards series 20186 addressing preanalytical workflows for Blood Cellular RNA, Blood Genomic DNA and Blood Circulating Cell-free DNA was published in 2019. In total, 8 ISO Standards are meanwhile published (see page 5). Furthermore, new CEN/Technical Specifications for Frozen Tissue DNA, Saliva DNA and Circulating Tumor Cells were published. Additional 9 documents are under development (see page 3).

SPIDIA4P has also achieved strong progress in developing new EQA Schemes that accompany the standard documents. In total 13 processing schemes were developed so far (see page 5).

Furthermore, SPIDIA4P is focusing on the implementation of standards and EQA schemes. A highlight was the event "Tackling issues on in vitro diagnostics for personalised medicine" in the EU Parliament (see page 9). The consortium's dissemination activities were broadened including new education videos, intensified co-work with professional societies and other stakeholder organizations as well as with the new EU Horizon 2020 projects EASI-Genomics and EU-STANDS4PM and other running partner consortia projects such as CANCER-ID. Various scientific papers were published including a SPIDIA4P Special Issue of the journal New Biotechnology. In addition more than 20 training courses and lectures were run and more than 30 invited talks and presentations were presented at congresses (see pages 10-13).

More detailed information about our activities and publications can be found on the new SPIDIA website.

Dr. Uwe Oelmueller, Coordinator, QIAGEN GmbH

Publication Highlight: SPIDIA4P Special Issue of New Biotechnology

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NEW ISO Standard: ISO 20186-3:2019, Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for venous whole blood – Part 3: Isolated circulating cell free DNA from plasma

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WP1 GET THE NEW STANDARDS! // ULRIKE SCHRÖDER

ULRIKE SCHROEDER

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A lot of work has been done in 2019 to reach the goal of creating and implementing a comprehensive portfolio of 22 pre-analytical CEN Technical Specifications and ISO International Standards[1] (together with the existing standard documents initiated by SPIDIA) for selected high priority pre-analytical workflows needed for personalized medicine as described in Work package 1 (WP1) in SPIDIA4P.

The working group CEN/TC 140/WG 3 "Quality management in the medical laboratory", responsible for the development of the standard documents on European level, came together several days almost every three months in 2019 to draft, discuss and finalize the documents. Amongst the experts in the working group are a high number of SPIDIA4P partners as well as further pan-european professionals.

Together, they achieved great progress for the 12 new CEN/TS and 2 new ISO standards under the main title "Molecular in vitro diagnostic examinations – Specifications for pre-examination processes…":

Task	Project/document title	Status
1.1	…for circulating tumour cells (CTCs) in venous whole blood – Part 1: Isolated RNA	Published as CEN/TS 17390-1
1.1	…for circulating tumour cells (CTCs) in venous whole blood – Part 2: Isolated DNA	Published as CEN/TS 17390-2
1.2	…for circulating tumour cells (CTCs) in venous whole blood – Part 3: Preparation for analytical CTC staining	Published as CEN/TS 17390-3
1.3	…for saliva – Isolated DNA	Published as CEN/TS 17305 NWI in proposal (ISO)
1.4	…for frozen tissue – Part 3: Isolated DNA	Published as CEN/TS 16826-3 Accepted NP (ISO)
1.5	…for exosomes and other extracellular vesicles in venous whole blood – Isolated RNA, DNA and proteins	Finalization of Working draft Stage 20
1.5	…for venous whole blood – Isolated circulating cell free RNA from plasma	Preparatory Stage Stage 20
1.6	…for urine and other body fluids – Isolated cell free DNA	Preparatory Stage Stage 20
1.7	…for Fine Needle Aspirates – Part 1: Isolated cellular RNA	Finalization of Working draft Stage 20
1.7	…for Fine Needle Aspirates – Part 2: Isolated proteins	Finalization of Working draft Stage 20
1.7	…for Fine Needle Aspirates – Part 3: Isolated genomic DNA	Finalization of Working draft Stage 20
1.8	…for human specimen – Isolated microbiomes	Finalization of Working draft Stage 20
1.9	…for metabolomics in urine, venous blood serum and plasma	Preparatory Stage (ISO)
1.10	…for formalin-fixed and paraffin-embedded (FFPE) tissue – Part 4: In situ detection techniques	Preparatory Stage (ISO)

Key: PWI – Preliminary work item, NWI – New work item

[1] On the European level, the standardization projects are developed within the European standard organizations (CEN) Technical Committee CEN/TC 140 "In vitro diagnostic medical devices" as CEN technical specifications (CEN/TS) to be later introduced into the international organization of standardizations (ISO) technical committee ISO/TC 212 "Clinical laboratory testing and in vitro diagnostic test systems" with EN ISO standards as envisioned documents.

Out of the first wave of SPIDIA4P projects, referred to as Task 1.1 to Task 1.4, the documents on circulating tumor cells (Task 1.1 to 1.2) received 100% positive approval during the European approval ballot and were published by CEN in January 2020, marking another important milestone within the project. After the publication, it is expected to bring these documents into proposal stage as ISO standards.

The saliva document (Task 1.3) was published as CEN/TS 17305 in April 2019 and simultaneously brought into proposal stage as an ISO standard, while the frozen tissue document (Task 1.4), published as CEN/TS 16826-3:2018, is already an accepted new project on ISO level currently being worked on.

In 2019, the majority of work within WP 1 has been done on the second wave of projects (Task 1.5 to Task 1.8). The documents on isolated RNA, DNA and proteins from extracellular vesicles (Task 1.5), different FNA analytes (Task 1.7) and isolated microbiome DNA (Task 1.8) have been drafted by the according project teams, discussed by the CEN working group and are now being prepared to enter the final European approval stage by 2020/Q1.

While the above mentioned projects are finalized, the drafting work on the documents on isolated circulating cell free RNA from plasma (Task 1.5) and isolated cell free DNA from body fluids (Task 1.6) will commence.

For the new projects ISO/NP 23118 on metabolomics and ISO/NP 20166-4 on in situ detection techniques on ISO level under the Vienna Agreement, work in the preparatory stage for Task 1.9 and Task 1.10 is continuously brought forward and actively supported by SPIDIA4P partners within the international working group ISO/TC 212/WG 4 „Microbiology and molecular diagnostics".

After the publication of the EN ISO-series 20166, Molecular in vitro diagnostic examinations – *Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue* and EN ISO-series 20184, *Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for frozen tissue,* the list of high-level standards initiated by SPIDIA and SPIDIA4P was extended even further in 2019 by the publication of the EN ISO-series 20186, Molecular in vitro diagnostic examinations – *Specifications for pre-examination processes for venous whole blood.*

Standardization is a process open to everyone and further input and expertise is always needed and appreciated.

If You, Your company or Your research institute are interested in working on the above mentioned projects, please contact Your national standardization body or the secretariat of CEN/TC 140/WG 3 "Quality management in the medical laboratory" *ulrike.schroeder@din.de* **for further details on how to get involved!**

PUBLICATION OF THE FIRST ROW OF EN ISO STANDARDS

THE SPIDIA AND SPIDIA4P PROJECT HAS LED TO THE PUBLICATION OF THE FOLLOWING CEN/TS AND ISO STANDARDS IN 2018–2019

ISO-series 20166	
ISO 20166-1:2018, Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue – Part 1: Isolated RNA	www.iso.org/standard/67179.html
ISO 20166-2:2018, Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue – Part 2: Isolated proteins	www.iso.org/standard/69802.html
ISO 20166-3:2018, Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue – Part 3: Isolated DNA	www.iso.org/standard/69803.html
ISO-series 20184	
ISO 20184-1:2018, Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for frozen tissue – Part 1: Isolated RNA	www.iso.org/standard/67215.html
ISO 20184-2:2018, Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for frozen tissue – Part 2: Isolated proteins	www.iso.org/standard/69801.html
ISO-series 20186 ISO-series 20186	
ISO 20186-1:2019, Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for venous whole blood – Part 1: Isolated cellular RNA	www.iso.org/standard/67217.html
ISO 20186-2:2019, Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for venous whole blood – Part 2: Isolated genomic DNA	www.iso.org/standard/69799.html
ISO 20186-3:2019, Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for venous whole blood — Part 3: Isolated circulating cell free DNA from plasma	www.iso.org/standard/69800.html NEW

INITIATED BY THE SPIDIA4P PROJECT AND PUBLISHED AS CEN/TS – MORE TO COME!

CEN/TS 16826-3:2018, Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for frozen tissue – Part 3: Isolated DNA	www.din.de/en/wdc-beuth:din21:281615991
CEN/TS 17305:2019, Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for saliva – Isolated human DNA	https://standards.cen.eu/dyn/www/f?p=204:110:0::::FSP_PROJECT:62239&cs=130B991FE0957A5743F90225BBCACEABB
CEN/TS17390-1:2020: Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for circulating tumor cells (CTCs) in venous whole blood – Part 1: Isolated RNA	https://standards.cen.eu/dyn/www/f?p=204:110:0::::FSP_PROJECT:65450&cs=1799CD1DD5E0FBEEBE1246AC9CE6AB2F1 NEW
CEN/TS17390-2:2020: Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for circulating tumor cells (CTCs) in venous whole blood – Part 2: Isolated DNA	https://standards.cen.eu/dyn/www/f?p=204:110:0::::FSP_PROJECT:65452&cs=1B8E3EC3BB49D6FF8A6AA7684A31C122 NEW
CEN/TS17390-1:2020: Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for circulating tumor cells (CTCs) in venous whole blood – Part 3: Preparations for analytical CTC staining	https://standards.cen.eu/dyn/www/f?p=204:110:0::::FSP_PROJECT:65451&cs=1406EA2E6FBA608D914F22B25BFD6A1BC NEW

Raising awareness and acceptance of the importance of standards is one of the biggest goals of the SPIDIA4P project. Thus, we very much appreciate that in February 2019, CEN CENELEC announced the publication of a new series of standards via different channels: press release, website, social media:

New ISO standard: Better diagnoses, thanks to EN ISO 20166:2018 series on pre-examination processes for FFPE Tissues.

European Standards have a fundamental role in providing safe access to healthcare for patients by setting safety, quality and performance requirements for medical devices. In this context, an important part of ensuring high levels of healthcare and prevention derives from making sure that diagnoses are correct and timely.

To minimise the risk of non-objective diagnoses and increase safety, CEN recently published the series of standards EN ISO 20166:2018 'Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue'. *https://standards.cen.eu/dyn/www/f?p=204:32:0::::FSP_ORG_ID,FSP_LANG_ID:6122,25&cs=1BCDC48EDC64C36351999CE550930A0C4*

Within its three parts on isolated RNA, isolated proteins and isolated DNA, this series covers the processes of analysis preparation, starting from sample collection to handling, documentation, storage and processing of specimens to the isolation of RNA, proteins and DNA.

The standards included in the 20166 series are specifically designed for molecular in vitro diagnostic examinations, including laboratory tests, performed by medical laboratories and molecular pathology laboratories. They are also applicable to other stakeholders, such as in vitro diagnostics developers and manufacturers, biobanks, institutions and commercial performing biomedical research and regulatory authorities.

The objective of this standard series is to reduce the impact of external factors on the results of examinations, thus ensuring that patients obtain diagnoses that are as objective as possible. Indeed, in research there is clear scientific evidence that several factors of the pre-examination phase influence the outcome of in situ detection and, thus, can have major impact on the diagnostic results. Since the reliability of analytical results in examinations is markedly dependent on the proper processing of the biospecimen during the pre-examination phase, a high level of standardization of the procedures of the pre-examination phase is required.

The EN ISO series 20166:2018 was developed in the framework of the SPIDIA project, a 4.5-year project funded by the European Union. Project partners, as well as representatives from a wider community of manufacturers, European and international research associations, users and researchers provided input on the content of the specifications. Its successor, the 48-month project SPIDIA4P (Standardization of generic Pre-analytical Procedures for In vitro DIAgnostics for Personalised Medicine), is taking up the work on standardization and improvement of pre-analytical procedures for in vitro diagnostics.

The standard series was developed by CEN/TC 140 'In vitro diagnostic medical devices', in close contact with ISO/TC 212 'Clinical laboratory testing and in vitro diagnostic test systems'. The Secretariat of CEN/TC 140 is held by DIN, Germany's National Standardization Body, who is one of the partners of the SPIDIA and SPIDIA4P projects.

WP2 EQA // DR. FAY BETSOU / DR. OLGA KOFANOVA

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Standardising biobanking practices:

The External Quality Assurance (EQA) programme in SPIDIA4P

Clinical biospecimens are the most commonly used sample-type for research purposes, but are often of poor quality given their susceptibility to uncontrolled and unrecorded pre-analytical variables. IBBL carries out biospecimen research and develops in-house quality control assays to guide researchers in their sample preparation, selection and processing decisions. To ensure that biological samples are suitable for their intended downstream applications and that their processing is fit for purpose, IBBL develops and implements external quality assurance (EQA) or proficiency testing (PT) schemes under Work Package 2 (WP2) of the SPIDIA4P project, with the aim of guaranteeing reproducible results and thus contributing to the standardisation of biobanking practices. The EQAs assess the efficiency of sample preparation methods in terms of the quality of the resulting samples, to be used for downstream diagnostic or research purposes.

As the only proficiency testing programme in the world that focuses on biospecimens, IBBL's PT programme acts as an External Quality Assessment (EQA) tool for laboratories working with biospecimens, biorepositories, research organisations and bioservice providers. Endorsed by the International Society for Biological and Environmental Repositories (ISBER), the PT programme allows these laboratories to validate their routine processing and analytical methods, compare their performance to that of others, comply with normative requirements, gain credibility and visibility, improve their performance and prove their consistency. IBBL's PT programme has become increasingly popular over the last years. In 2019, 91 participants from 29 countries registered for a total of 334 PT schemes.

The 2019 PT programme has been refined through the addition of one new combined processing and testing scheme, namely "Circulating Tumour Cells (CTC) Isolation and Detection", thus bringing the total offering to thirteen processing schemes:

- Circulating Tumour Cells (CTC) Isolation and Detection
- Cell Free RNA (cfRNA) Extraction from Plasma
- CSF Aliquoting
- Viable PBMC Isolation
- DNA Extraction from Whole Blood
- DNA Extraction from FFPE Material
- DNA Extraction from Frozen Tissue
- Microbial DNA Extraction from Saliva
- Microbial DNA Extraction from Stool
- Circulating Cell Free DNA (ccfDNA) Extraction from Whole Blood
- RNA Extraction from Whole Blood
- RNA Extraction from FFPE Material
- Total RNA Extraction from Frozen Tissue

Different partners have collaborated and supported these developments in various ways. The data from the above PT schemes over the past years are undergoing a global statistical data analysis by the Fundacio Centre De Regulacio Genomica Barcelona and Unit of Bioinformatics and Biostatistics, Department of Applied Research and Technological Development, Fondazione IRCCS Istituto Nazionale dei Tumori. This information and knowledge collected through the many years of IBBL PT programme history will also allow to contribute to the relevant ISO/TS documents.

In parallel, LGC have prepared new "in-process quality control materials" that are being tested through inter-laboratory evaluation in one of the PT schemes (ccfDNA extraction). This evaluation will allow us to quantify the variability between extraction methods and estimate the inter-laboratory reproducibility of the QC material quantification assay. This inter-laboratory exercise will provide additional data on the robustness of the ccfDNA extraction procedure when a variety of extraction kits, plasma input volumes and elution volumes are applied. The prototype LGC QC material is designed to monitor individual ccfDNA extractions as part of ongoing internal QC within a clinical or testing laboratory.

We are all very much looking forward to the conclusions from the EQA schemes described above and to a fruitful collaboration between the SPIDIA4P consortium partners.

SPIDIA4P EVENTS // HIGHLIGHT

March 2019

SPIDIA4P event on standards at the EU Parliament!

On March 5, 2019, the event "Tackling issues on in vitro diagnostics for personalised medicine", organised by the consortium SPIDIA4P and its partner, the European research infrastructure for biobanking, BBMRI-ERIC, took place at the European Parliament in Brussels.

Hosted by two Members of the European Partliament (MEP), Gesine Meissner (ALDE, Germany) and Lieve Wieverinck (ALDE, Belgium), the event was well attended and saw a panel of leading experts to address the important role of standards in facilitating innovation and the adoption of new technologies, together with improving the safety and performance of these products.

The room was filled with standards experts, scientists, industry representatives, and national regulators. MEPs Meissner and Wierinck set the tone, reminding everyone that industry and regulators have a responsibility to bring the safest and best diagnostics to the market as soon as possible.

Lively and fruitful discussions were held between the participants, amongst them Oliver Bisazza, Director Regulations and Industrial Policy at MedTech Europe, who started off the four keynote presentations by referring to the new Regulation on In Vitro Diagnostic Medical Devices (to be fully applied in 2022), which targets manufacturers and users of medical devices. He discussed the implications on notified bodies and on the use of IVDs in personalised medicine.

Dr. Uwe Oelmüller, SPIDIA4P Coordinator, revealed that persistent deficiencies exist in routine healthcare, leading to errors in diagnostics in the use of personalised medicine. He called for research to improve and stated that major improvements in technologies and standards are needed to overcome these persisting errors. The objective was set to establish 22 CEN & ISO Documents and EQAs for personalised medicine by 2020.

Prof. Kurt Zatloukal, SPIDIA4P partner and professor of Pathology at Medical University of Graz and Director of the Austrian biobanking node BBMRI.at, stressed the importance of biobanking, as it plays a key role in the implementation of standardised research conditions, stakeholder collaboration and security. In this regard, the development of standards, self-assessment tools, education programs and the promotion of biobanks reveal a number of possible paths for progress.

Jean-Luc Sanne, a Scientific Officer at the European Commission's Directorate-General for Research & Innovation, focused on Horizon 2020 and the proposal on Horizon Europe, which is expected to be launched soon. Within the framework, the second pillar will focus on personalised medicine. He stressed that standardisation involves patients, industry and research in order to guarantee patient safety, strengthen legal requirements for industry and reduce research errors in the field of personalised medicine.

Following the four keynote presentations, panellists Ashok Ganesh, Uwe Zimmermann and Prof. Giorgio Stanta provided their perspectives and animated a debate on the future of biomarkers development, personalised medicine and standardisation. Then the floor was opened for questions.

Read the full article here:

http://www.bbmri-eric.eu/news-events/academia-industry-research-partnership/

Watch the video-recap of the event here:

http://www.bbmri-eric.eu/news-events/video-discussing-standards-with-spidia4p-at-the-european-parliament/

Explore the event brochure here:

https://www.spidia.eu/publications/magazines

SPIDIA4P EVENTS // PAST EVENTS + COURSES / HIGHLIGHTS

To raise awareness about the importance of the quality of biological samples and standards for preanalytical workflows amongst targeted audiences, all SPIDIA4P project partners take part in congresses and conferences and share their expertise in specific courses. Please find some highlights in 2019 below.

January 2019

Workshop of the ACC (Alleanca Contro il Cancro/Alliance against Cancer) on January 18, 2019, Candiolo Italy, chaired by Prof. Anna Sapino. SPIDIA4P project member Prof. Caterina Marchiò, UNITO, IRCCS Candiolo, Torino, is the secretary of the Working Group „Pathology and Biobanking". Invited speakers / SPIDIA4P members:

- **Dr. Uwe Oelmueller** – New ISO and CEN Standards for Preanalytical Workflows to improve Diagnostics and Research
- **Prof. Kurt Zatloukal** – ISO for the pre-analytical phase in pathology The Participants also had the chance to test the BBMRI Self- Assessment Survey Tools for sample quality

Learn more about this highly important network that supports the implementation of standards under:

https://www.alleanzacontroilcancro.it/en/profilo/

February 2019

The ISBER 2nd Biospecimen Research Symposium 2019 Annual Meeting, February 5-6, 2019, Berlin, Germany with the subtitle Focus on Quality and Standards was an excellent platform for several SPIDIA4P project members who have been invited as speakers.

Dr. Fay Betsou, IBBL, Co-Chair of the Program Committee, chaired the session and led a plenary session on February 6, 2019, SPIDIA4P CEN and ISO Standards on Liquid Biopsy: Do we all agree?

Presentation Titles by SPIDIA4P representatives who participated on this debate:

SPIDIA4P Coordinator **Dr. Uwe Oelmueller** (QIAGEN):
New Standards for Liquid Biopsies Pre-analytical Workflows:
A Key for Reliable Diagnostics

Dr. Carole Foy (LGC Group):
Measurement Procedures and Materials to Support Standardisation of Liquid Biopsy Based Tests

Presentation in session **"Ex Vivo Preanalytics"**:
Prof. Giorgio Stanta, UNITS: Long-Term Storage of FFPE and INC

https://cdn.ymaws.com/www.isber.org/resource/resmgr/berlin_2019/isberberlinprogram_final.pdf

SPIDIA4P EVENTS // PAST EVENTS + COURSES / HIGHLIGHTS

March 2019

IFOM Conference (FIRC Institute of Molecular Oncology): "Cancer-Related Biobanks: a Value for Translational Research and Precision Oncology"
March 21, 2019, Milano, Italy

Presentations by:
- **Prof. Kurt Zatloukal BBMRI.at and Medical University of Graz (MUG),** "Relevance of sample quality in personalized medicine"
- **Dr. Peter Riegman Erasmus Tissue Bank Rotterdam, NL EMC):** "Standardization of sample collection for reproducible results and innovation of care"

https://www.ifom.eu/events/2019-cancer-related-biobanks/

5th EFLM Conference on Preanalytical Phase „Preanalytical Challenges – Time for Solutions" March 22-23, 2019, Zagreb, Croatia

Presentation by Dr. Fay Betsou:
Managing preanalytical variables in Biobanking

http://www.preanalytical-phase.org/2019/loadpage/info/programme

June 2019

OECI Oncology Days, June 19-21, 2019, Bari, Italy

Prof. Giorgio Stanta, UNITS, leader of the Working Group "Biobanks and Molecular Pathobiology", introduced the OECI Pathology Day "Molecular pathology in aggressive types of tumors",
Prof. Anna Sapino led the discussion at the end of this event

Presentation by:
Prof. Anna Sapino and Prof. Caterina Marchiò, UNITO:
"Molecular pathology of aggressive types of mammary cancer"

https://www.oeci.eu/Attachments/OECI_BARI_2019_SecondAnn_6.pdf

October 2019

SPIDIA4P project members organized, attended, chaired and presented at different sessions as state-of-the-art speakers at the Europe Biobank Week in Lübeck - Biobanking for a Healthier World, Germany, October 7-11, 2019:

The Workshop 4: Opportunities and Challenges to Implement the New Biobank Standard, organized by Dr. Andrea Wutte, BBMRI-ERIC

Session 3A: Pre-Analytic Impact on Sample Quality – Means & Measures

Presentation by Prof. Georges Dagher, INSERM, titled „Major Hurdles in the Development of Immuno-Oncology"

Session 5B: **"Quality Assessement and Management of Sample" –** chaired by Dr. Andrea Wutte, BBMRI-ERIC

Dr. Uwe Oelmueller was invited to take part in this session, presentation title:**"Pre-analytical Workflows Securing Good Quality Specimen – a Prerequisite for Reliable Diagnostics and Research"**

Session 8B: Novel Molecular & Medical Imaging Technologies in Biobanking was chaired by Dr. Peter Riegman, Erasmus Medical Center, Rotterdam, NL (EMC)

http://europebiobankweek.eu/

SPIDIA4P EVENTS // PAST EVENTS + COURSES

In total, the SPIDIA4P project members held more than 80 workshops and courses for different target groups so far – these are only some of them.

EU Research Infrastructures Workshop: Science and Society, EU Research Infrastructures: **Tackling Societal Changes**
January 14-15, 2019
Milano, Italy

http://www.bbmri-eric.eu/news-events/adopt-bbmri-eric-workshop-science-and-society/

Course/ Lecture **„Diagnostics in Medicine Course" at University of Manchester; Lecture: Role of International Diagnostic Workflow Standardization**
February 25, 2019
Manchester, UK

Course **„2 days NGS – Library Construction and Quality Control"** hosted by TATAA Biocenter and TUM
March 21-22, 2019
Freising, Germany

https://gene-quantification.de/qpcr-dpcr-ngs-2019/workshops-2019.html#analysis

Course **„Quality control and new guidelines in molecular analyses and biobanking hosted by TATAA Biocenter"**
March 28, 2019
Goteborg, Sweden

http://www.tataa.com/courses/

SiBioC (Italian Society of Clinical Biochemistry and Clinical Molecular Biology): **1 day event-Liquid biopsy as a source of potential biomarkers in the management and monitoring of the cancer patient**
April 16, 2019
Firenze, Italy

https://www.biomedia.net/corsi-convegni/evento-home/2652

EMBL Course „Liquid Biopsy" courses by TATAA and QIAGEN
September 23–28, 2019
Heidelberg, Germany

https://www.embl.de/training/events/2019/LIQ19-01/

SPANDIDOS 5th Pre-Conference Workshop **"Molecular biomarkers, SNP genotyping and rare mutation detection in cancer"** – course by TATAA Biocenter
October 5-9, 2019
Sparta , Greece

https://www.spandidos-publications.com/pages/Pre_congress_workshop_2019/

EXAMPLE OF A NEW POSTER BY SPIDIA4P PROJECT MEMBERS

SELF-ASSESSMENT TOOL FOR MOLECULAR DIAGNOSTICS TO CHECK PRE-ANALYTICAL WORKFLOWS

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BACKGROUND & AIM

A series of the CEN Technical Specification (CEN/TS) and ISO Standards for "In-Vitro Diagnostic examinations - Specifications for Pre-examination Processes" have been published and are in development.

The standards define requirements along the entire pre-analytical clinical workflow of samples. They are applicable to molecular diagnostics in personalized medicine.

METHOD

The BBMRI.at and BBMRI-ERIC Biobanking Infrastructures have developed an online Self-Assessment Survey Tool. It is based on standards and allows medical laboratories to evaluate if their pre-analytical procedures meet the requirements of the standards.

RESULTS

BBMRI Self-Assessment Survey Tool (SAS)
for assessing compliance of pre-analytical workflows of medical samples with CEN/TS & ISO Standards

1 What is the BBMRI SAS

The Self Assessment Tool set of IT-based questionnaires based on CEN and (upcoming) ISO standards for pre-analytical procedures*: i.e:

- FFPE tissue - RNA (CEN/TS 16827-1:2015)
- FFPE tissue - proteins (CEN/TS 16827-2:2015)
- FFPE tissue - DNA (CEN/TS 16827-3:2015)
- Snap frozen tissue - RNA (CEN/TS 16826-1:2015)
- Snap frozen tissue - proteins (CEN/TS 16826-2:2015)
- Venous whole blood - RNA (CEN/TS 16835-1:2015
- Venous whole blood - DNA; (CEN/TS 16835-2:2015)
- Venous whole blood - ccf DNA (CEN/TS 16835-3)
- Metabolomics in serum, plasma, urine (CEN/TS 16945:2016)

2 How to get access and use the BBMRI SAS

Access
- Go to: www.bbmri-eric.eu
- Fill out request form & fulfill pre-conditions
- Get started: receive link to SAS

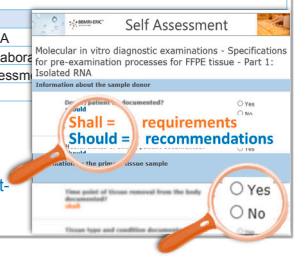
Evaluation
- Complete SAS survey
- Print report

OPTIONAL:
- Submit report to BBMRI-ERIC
- Be reviewed by BBMRI-ERIC

Quality Label
- Receive BBMRI-ERIC quality label for a sample collection
- Enhance visibility of your sample collection in the BBMRI-ERIC Directory

3 Look inside the BBMRI SAS

Inside the laboratory
• Primary tissue collection -
• Transport conditions
Outside the laboratory
• Primary tissue sample receipt at laboratory
• Evaluation of pathology of specimen and selection of sample
• Post-fixation of frozen samples
• Storage conditions
Isolation of total RNA
• General information for RNA
• Using a commercial kit / a labora
• RNA quantity & quality assessm
• Storage of isolated RNA



For details go to www.bbmri-eric.eu/services/self-assessment-survey/

SUMMARY

The Self-Assessment Survey Tool

- **is a supportive tool to be used in combination with CEN & ISO standards**
- **provides an interactive electronic check-list on pre-analytical quality requirements**
- **helps laboratories in implementation of standards**
- **enables structured evaluation of established pre-analytical processes and SOPs**
- **reveals deviations from standard requirements**
- **shows were optimization measures are needed**
- **allows principal investigators to display their quality-labeled collections in the BBMRI-ERIC Biobank Directory**

Funding:
BBMRI.at, BMBFW project (GZ 10.470/0016-II/3/2013)
SPIDIA4P, H2020 project (grant agreement no. 7331129)

SPIDIA4P EVENTS // UPCOMING CONFERENCE + EVENTS

2020

Get ready to meet the SPIDIA4P members at conferences and trainings in 2020! Upcoming courses can also be found on:

www.spidia.eu.

CONFERENCE

SPIDIA4P presents: Precision Diagnostics Europe
organized by SPIDIA4P project partner TATAA Biocenter
May 26-29, 2020
Prague, Czech Republic

Invitation notes by Prof. Mikael Kubista on page 18

Registration

http://precisiondiagnostics.eu/

The 10th Santorini Conference
September 18, 2020 – October 1, 2020
Santorini, Greece

Presentations by SPIDIA4P project members:
Dr. Uwe Oelmueller
Prof. Georges Dagher – Is there life between standards?

http://santoriniconference.org/

EVENTS

IFOM CONGRESS "CANCER-RELATED BIOBANKS: A VALUE FOR TRANSLATIONAL RESEARCH AND PRECISION ONCOLOGY"
March 21, 2020
Milan, Italy

PRESENTATIONS by Dr. Peter Riegman
Erasmus Medical Center, Rotterdam, NL

https://www.ifom.eu/en/cancer-research/research-labs/

„IVDR – STATE OF THE ART REQUIREMENTS FOR ANALYTICAL PERFORMANCE TESTING"
May 18, 2020
Vienna, Austria

SPEAKERS I.A.:
BBMRI.at: **Prof. Kurt Zatloukal**
CEN: **Ulrike Schröder**
Austrian Standard International (ASI): **Andrea Redelsteiner**
QIAGEN: **Dr. Uwe Oelmueller**

SPIDIA4P PUBLICATIONS // ARTICLES

Highlight: Special Issue New Biotechnology

The SPIDIA4P project members created a compilation of 9 exclusive scientific articles to be published in a very Special Issue of the renowned journal New Biotechnology – „Standardisation of generic Pre-Analytical Procedures for In vitro Diagnostics for Personalized Medicine – you can find them all on the website:

https://www.sciencedirect.com/journal/new-biotechnology/special-issue/10FDFZ1WK5J

and below:

Ghini V, Quaglio D, Luchinat C, Turano P, **NMR for sample quality assessment in metabolomics**, New Biotechnology, Vol. 52, 25 Sept. 2019, pages 25-34

https://doi.org/10.1016/j.nbt.2019.04.004 open access

Riegman PJH, Becker KF, Zatloukal K, Pazzagli M., Schroeder U., Oelmueller U. **How standardization of the pre-analytical phase of both research and diagnostic biomaterials can increase reproducibility of biomedical research and diagnostics**, New Biotechnology, Vol. 53, 25 Nov. 2019, pages 35-40

https://doi.org/10.1016/j.nbt.2019.06.007

Salvianti F, Gelmini S, Costanza F, Mancini I, ...Pinzani P **The pre-analytical phase of the liquid biopsy, New Biotechnology**, Vol 55, 25 March 2020, pages 19-29

https://doi.org/10.1016/j.nbt.2019.09.006

Kofanova O, Bellora C, Garcia Frasquilho S, Antunes L,....Betsou F, **Standardization of the pre-analytical phase of DNA extraction from fixed tissue for next-generation-sequencing analyses.** New Biotechnology, Vol. 45, 25 January 2020, pages 52-61

https://doi.org/10.1016/j.nbt.2019.07.005 open access

Bonin S, Stanta G, **Pre-analytics and tumor heterogeneity**, New Biotechnology, Vol. 55, 25 March 2020, pages 30-35

https://doi.org/10.1016/j.nbt.2019.09.007 open access

Verderio P, Pizzamiglio S, Ciniselli Ch, **Methodological and statistical issues in developing an External Quality Assessment scheme in laboratory medicone: Focus on biomarker research**, New Biotechnology, Vol. 52, 25 September 2019, pages 54-59

https://doi.org/10.1016/j.nbt.2019.05.001

Stumptner C, Pabst D, Loibner M, Viertler Ch, Zatloukal K, **The impact of crosslinking and non-crosslinking fixatives on antigen retrieval and immunohistochemistry**, New Biotechnology, Vol. 52, 25 September 2019, pages 69-83

https://www.sciencedirect.com/science/article/pii/S1871678419300792

Dagher G, Becker KF, Bonin S, Foy C,....Zatloukal K, **Pre-analytical processes in medical diagnostics: New regulatory requirements and standards**, New Biotechnology, Vol. 52, 25 September 2019, pages 121-125

https://doi.org/10.1016/j.nbt.2019.05.002

Annaratone L, Marchió C, Sapino A, **Tissues under-vacuum to overcome suboptimal preservation**, New Biotechnology, Vol. 52, 25 September 2019, pages 104-109

https://www.sciencedirect.com/science/article/pii/S1871678419301050?via%3Dihub open access

SPIDIA4P PUBLICATIONS // ARTICLES

find all articles by SPIDIA4P members on *www.spidia.eu*

In 2019, BBMRI.at has published numerous publications on the topics of pre-analytics standards, IVDR and quality management for biobanks under the title „Quality management for biobanks". Find all articles here:

http://bbmri.at/news/-/asset_publisher/vXLxX1e57Fqz/content/quality-management-for-bioban-1

Stumptner C., Sargsyan K., Kungl P., Zatloukal K.
Crucial Role of High Quality Biosamples in Biomarker Development Handbook for Biomarkers and Precision Medicine, 1st edition 2019

https://www.taylorfrancis.com/books/e/9780429202872

LIM M.S., BEYER T., BABAYAN A. ET AL.
Advancing Biomarker Development Through Convergent Engagement: Summary Report of the 2nd International Danube Symposium on Biomarker Development Molecular Imaging and Applied Diagnostics; online May 2019

https://link.springer.com/article/10.1007/s11307-019-01361-2 open access

Lampignano R., Neumann MHD, Weber S., Kloten V., Herdean A., Voss T., Groelz D., Babayan A. et al.
Multicenter Evaluation of Circulating Cell-Free DNA Extraction and Downstream Analyses for the Development of Standardized (Pre)analytical Work Flows.

Clin Chem 2019

https://www.ncbi.nlm.nih.gov/pubmed/31628139

Interview with Prof. Kurt Zatloukal, SPIDIA4P project member:

European biobanks: archives for future medicine Biobanks are the foundation of medical research. From Graz (Austria), the European biobanking research infrastructure BBMRI-ERIC is being set up and supervised. Digitalization and quality management plays essential roles, emphasized Kurt Zatloukal, director of the Austrian Node BBMRI.at and infrastructure initiator in the interview with the Austrian Press Agendy APA.

Read the full article (in German only)

https://www.wienerzeitung.at/nachrichten/wissen/forschung/2022574-Europaeische-Biobanken-Archiv-fuer-die-Medizin-der-Zukunft.html

On **December 12, 2019,** the online magazine Biocompare published an article which promotes the latest ISO standard that was created with the support of the SPIDIA4P project partners:

ISO 20186-3:2019, Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for venous whole blood – Part 3: Isolated circulating cell free DNA from plasma.

The author stresses the importance of pre-analytical workflows and points out that this "document specifically addresses how investigators should handle samples for ccfDNA analysis during the critical time between blood draw and assay".

https://www.biocompare.com/Editorial-Articles/558190-Cell-Free-DNA-A-Diagnostic-Revolution-in-the-Works/

SPIDIA4P PARTNER // CONSORTIUM MEETINGS 2019

Twice a year, all SPIDIA4P project partners meet at different partner sites to share information personally, discuss the current project status and upcoming activities.

The SPIDIA4P project members at the 5th Consortia Meeting on May 23/24, 2019 at the CNAG-CRG headquarter in Barcelona, Spain

The latest and 6th SPIDIA4P Consortia Meeting took place at the Fondazione IRCCS Istituto Nazionale dei Tumori (INT) in Milano from November 21–22, 2019

SPIDIA4P PARTNERS // ANNOUNCEMENT PRECISION DIAGNOSTICS EUROPE

Precision Diagnostics Europe 2020 – a SPIDIA4P conference!

European conference focusing on the new CEN and ISO guidelines in molecular diagnostics and the new CE-IVDR European directive resulting from the European efforts SPIDIA and the ongoing SPIDIA4P

www.spidia.eu

The conference is arranged at BIOCEV, which is the most recent research and development center in Czech Republic conveniently reached from the beautiful city of Prague.

www.biocev.eu

You will hear presentations from world leading experts in molecular analyses and biomarkers with focus on precision diagnostics, quality aspects and regulatory guidelines. You can also join hands-on training courses on various aspects of precision diagnostics held by experts.

Find more information on:

http://precisiondiagnostics.eu/

PROF. MIKAEL KUBISTA
Chairman of the Precision Diagnostics Europe 2020 conference

PRECISION DIAGNOSTICS EUROPE 2020

SPIDIA4P NEWS // WEBSITE www.spidia.eu

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Social Media

The SPIDIA4P project is continuously present on various Social Media channels, especially in conjunction with events and project news. Not only SPIDIA4P project partners post their latest news, but also interested professionals or involved institutions.

https://twitter.com/hashtag/spidia4p?lang=de

https://www.linkedin.com/search/results/content/?facetSortBy=date_posted&keywords=SPIDIA4P&origin=SORT_RESULTS

https://www.facebook.com/search/top/?q=SPIDIA4P&epa=SEARCH_BOX

Don´t miss

the central source for latest news and information about the project!

www.spidia.eu

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