SPIDIA4P

SPIDIA4P Newsletter 02/2021

SPIDIA4P GOALS REACHED – AND THE MISSION GOES ON!

KEEP MOVING FORWARD

Get the full project picture – review latest status an next steps

CONTENTS

EDITORIAL

Dear reader,

it is hard to believe how fast time flies. Our 4.5 years long EU HORIZON 2020 project SPIDIA4P has come to its funding end. Our journey will nevertheless continue. The Consortium and its website will stay active for improving diagnostics in healthcare. SPIDIA4P members will continue to develop, implement and train CEN and ISO standards for preanalytical workflows applied to in vitro diagnostics, biobanking and biomedical research. The new standards have also become key tools for in vitro diagnostic device manufacturers and health institutions to fulfill the pre-analytical requirements and related state-of-the-art requirements in the new EU In-vitro Diagnostics Regulation 2017/746 (IVDR). The External Quality Assurance (EQA) schemes program will be continued as well.

Securing good quality patient specimen and samples by well specified, developed, verified and validated pre-analytical workflows for all diagnostic applications remains a key task for further improving human diagnostics and therefrom resulting clinical decisions including therapies.

SPIDIA4P has achieved all main goals under its EU funding. 16 of our planned 22 pre-analytical ISO and CEN standard documents are developed and published. The remaining six are in final stages and will be published during the next few weeks and months. SPIDIA4P also developed the associated EQAs as planned. A deep EQA statistical analysis of the last years program at our partner IBBL is shown in this newsletter. Another continued focus during the last months was again dissemination including various invited congress talks as well as trainings on the new ISO and CEN standards and their implementation. A highlight was the Precision Diagnostics Europe 2021 Conference which was also SPIDIA4P's final conference during its funding period. The SPIDIA4P project achievements were prominently presented by 10 Consortium speakers.

I thank a wonderful SPIDIA4P consortium with always great team spirit and all collaboration partners for this success!

Please enjoy reading our latest main achievements and a short journey through the 4.5 years of the SPIDIA4P project.
Our next regular Newsletter is planned for early 2022.

Dr. Uwe Oelmueller, Coordinator, QIAGEN GmbH

HEADS UP:

Be sure to visit the SPIDIA website for important news and updates on the publications of new CEN/TS and ISO standards for pre-analytical workflows – www.spidia.eu will be continuously updated! Future SPIDIA4P Newsletters will follow!

WP1 UPDATE STANDARDS! // ULRIKE SCHRÖDER

ULRIKE SCHROEDER, M.SC.

DIN – Deutsches Institut
fuer Normung e.V.

ulrike.schroeder@din.de

While the EU funding end of SPIDIA4P is moving closer and closer, more and more standardization projects are being finalized within Work Package 1 (WP 1) to reach the goal of creating and implementing the portfolio of 22 pre-analytical CEN Technical Specifications and ISO International Standards (together with the existing standard documents initiated by SPIDIA) for selected pre-analytical workflows needed for personalized medicine.

The working group responsible for the development of the standard documents on European level, CEN/TC 140/WG 3 "*Quality management on the medical laboratory*", consisting of a high number of SPIDIA4P-partners as well as further pan-European experts, continued to hold all its meetings online in 2021. 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 Accepted PWI ISO/TS 7552-1
1.1	…for circulating tumour cells (CTCs) in venous whole blood – Part 2: Isolated DNA	Published as CEN/TS 17390-2 Accepted PWI ISO/TS 7552-2
1.2	…for circulating tumour cells (CTCs) in venous whole blood – Part 3: Preparation for analytical CTC staining	Published as CEN/TS 17390-3 Accepted PWI ISO/TS 7552-3
1.3	…for saliva – Isolated DNA	Published as CEN/TS 17305 Approved prEN ISO 4307
1.4	…for frozen tissue – Part 3: Isolated DNA (Former CEN/TS 16826-3)	Published as ISO 20184-3 EN ISO Publication will follow
1.5	…for exosomes and other extracellular vesicles in venous whole blood – Isolated RNA, DNA and proteins	Registered as CEN/TS 17747
1.5	…for venous whole blood – Isolated circulating cell free RNA from plasma	Registered as CEN/TS 17742
1.6	…for urine and other body fluids – Isolated cell free DNA	Preparatory Stage
1.7	…for Fine Needle Aspirates – Part 1: Isolated cellular RNA	Registered CEN/TS 17688-1 Final approval stage
1.7	…for Fine Needle Aspirates – Part 2: Isolated proteins	Registered CEN/TS 17688-2 Final approval stage
1.7	…for Fine Needle Aspirates – Part 3: Isolated genomic DNA	Registered CEN/TS 17688-3 Final approval stage
1.8	…for human specimen – Isolated microbiomes	Published as CEN/TS 17626:2021

1.9	...for metabolomics in urine, venous blood serum and plasma	Published as ISO 23118 EN ISO Publication will follow
1.10	...for formalin-fixed and paraffin-embedded (FFPE) tissue – Part 4: In situ detection techniques	Approved for publication as EN ISO 20166-4

Key: PWI – Preliminary 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) were published as CEN/TS-series 17390 in January 2020. Supported by a decision of CEN/TC 140, the documents have been proposed to ISO/TC 212 for development as ISO/TS documents and have been accepted there as Preliminary Work Items. Further actions on developing the documents will follow.

The saliva document (Task 1.3), published as CEN/TS 17305:2019, is already several steps further on ISO level and being developed as EN ISO 4307. The document has recently received 100% approval within the European and international enquiry stage and will soon go into the final approval stage.

CEN/TS 16826-3:2018, the frozen tissue document out of Task 1.4, is being developed on ISO-level as 20184-3. After receiving 100% approval in the international final approval stage, the document has been published on ISO-level in May 2021. As a project under the Vienna Agreement, the publication as EN ISO will follow soon.

Within the second wave of projects (Task 1.5 to Task 1.8), the documents on different FNA analytes (Task 1.7) are now registered as CEN/TC 17688-1,-2 and -3 and will soon go into the final European approval stage. The document on isolated microbiome DNA (Task 1.8) has already passed this stage and was published in May 2021 as CEN/TS 1762.

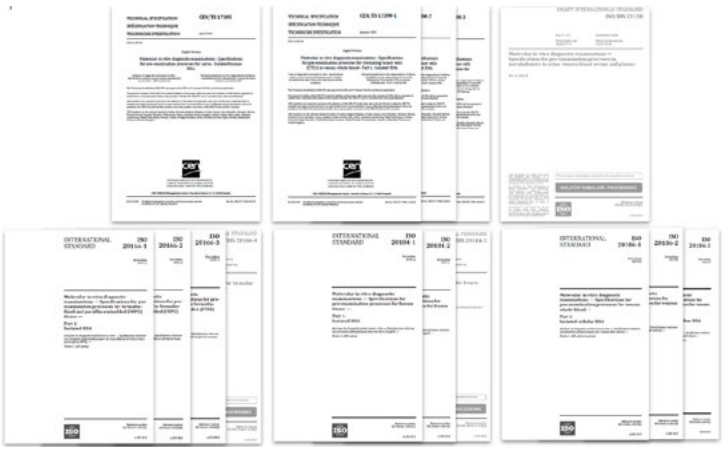
Work within CEN/TC 140/WG 3 now focuses on the three remaining documents on isolated RNA, DNA and proteins from extracellular vesicles (Task 1.5), on isolated circulating cell free RNA from plasma (Task 1.5) and on isolated cell free DNA (Task 1.6). While the document on isolated circulating cell free RNA from plasma (Task 1.5) has been submitted for the final European approval stage, its sister document on extracellular vesicles (Task 1.5) is close to being finalized and will follow soon. The last document missing (Task 1.6) will then be accordingly prepared and aligned to all previous work.

Further great progress has been made for EN ISO 23118 on metabolomics (Task 1.9) and for EN ISO 20166-4 on FFPE tissues in situ detection techniques (Task 1.10) on ISO level under the Vienna Agreement. After receiving 100% approval in the international final approval stage, ISO 23118 has been published on ISO-level in May 2021 (EN ISO publication to follow) and (EN) ISO 20166-4 in July 2021.

The goal of WP 1 is to develop 12 new CEN/TS and 2 new ISO standards – and we are almost there! So far 6 CEN/TS have been published, with the remaining 6 close to finalization, and both new ISO standards are published.

For some of the published CEN/TS documents, the journey however did not stop on the European level, but is successfully continued on the International level, leading to one further EN ISO publication and four more to be expected. Even with SPIDIA4P coming to an end, the standardization work within the standardization working groups will continue.

This great progress and unparalleled standardization[2] effort achieved within the project time of SPIDIA4P is only possible through the great effort, hard work and continuous engagement of all partners and experts within SPIDIA4P, CEN/TC 140/WG 3 and ISO/TC 212/WG 4. Once again, I would like to express my sincere thanks to everyone involved!



[2] 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!

SPIDIA

THE SPIDIA AND SPIDIA4P PROJECT HAS LED TO THE PUBLICATION OF THE FOLLOWING CEN/TS AND ISO STANDARDS IN 2018–2021

ISO-series 20166 – FFPE tissue	
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 20166-4:2021, Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue – Part 4: In situ detection techniques	https://www.iso.org/standard/75442.html NEW
ISO-series 20184 – Frozen tissue	
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 20184-3:2021, Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for frozen tissue - Part 3: Isolated DNA	https://www.iso.org/standard/78110.html NEW
ISO-series 20186 – Venous whole blood	
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
ISO 23118	
ISO 23118:2021, Molecular in vitro diagnostic examinations — Specifications for pre-examination processes in metabolomics in urine, venous blood serum and plasma	https://www.iso.org/standard/74605.html NEW

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

CEN/TS	
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
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=1B8E3EC3BB49D6FF8A6AA7684A31C1226
CEN/TS17390-3:2020: 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
CEN/TS 17626:2021, Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for human specimen – Isolated microbiome DNA	https://standards.cen.eu/dyn/www/f?p=204:110:0::::FSP_PROJECT:67446&cs=19BEA72D458CD2C9A464CD2018AB774D1 NEW

SPECIAL: IMPLEMENTATION OF STANDARDS

DANIEL GRÖLZ, PHD

Scientific Associate Director R&D
PreAnalytiX – Tissue & Liquid Biopsy Samples
QIAGEN GmbH

daniel.groelz@qiagen.com

Development of the PAXgene Blood ccfDNA and gDNA workflows in accordance with ISO 20186-2:2019 and ISO 20186-3:2019

There is overwhelming scientific evidence for use of circulating cell free DNA (ccfDNA) from plasma for different clinical applications in the fields of noninvasive prenatal testing, cancer treatment, organ disease and transplantation. But despite the high potential and large application spectrum, analysis of ccfDNA is only slowly becoming a part of standard health care. For instance, up to now, only a few assays for analysis of ccfDNA have received approval by the US Food and Drug Administration (FDA).

Concordantly, many authors of review articles point out that the main hurdle for broader clinical usage of ccfDNA analyses is the l**ack of pre-analytical workflow standardization and protocol harmonization.**

Many challenges are associated with isolation of ccfDNA. Usually ccfDNA is present in plasma in low concentrations (1–50 ng DNA/ml plasma) and is highly fragmented (<500 bp). After blood collection, outside their natural body environment, blood cells quickly release their genomic DNA (gDNA) via cell lysis and/or apoptosis and thereby increase the level of unwanted background DNA, thus impacting the performance of ccfDNA based analytical tests.

The SPIDIA4P partner PreAnalytiX (QIAGEN/BD Company) has addressed these challenges by development of a complete integrated preanalytical blood ccfDNA workflow covering all relevant steps including human venous blood collection, ccfDNA profile stabilization, transport, storage and isolation of ccfDNA. It consists of the PAXgene® **Blood ccfDNA Tube and purification kits for automated or manual extraction of ccfDNA from plasma and gDNA from the remaining cellular fraction.** The stabilization reagent in the blood collection tube prevents blood coagulation and apoptosis of white blood cells and is stabilizing the ccfDNA profile. It is free of crosslinking or crosslinker-releasing substances and hence does not chemically modify DNA.

For the development of the PAXgene Blood ccfDNA workflow, we implemented the respective ISO-Standards for pre-examination processes for venous whole blood genomic DNA (gDNA) and blood ccfDNA: ISO 20186-2:2019 and ISO 20186-3:2019, respectively. As the first step, the requirements and recommendations in the standards on specimen collection, handling, storage, transport, processing and documentation were transferred into standard operational procedures (SOPs) within our Global Design Control Process for diagnostic products developments under the ISO 13485 based Quality Management System. Working sheets are attached to the SOPs and guide all involved employees in their daily work through each step of the preanalytical workflow. This guarantees consistent and high quality samples and high quality isolated ccfDNA, which is a prerequisite for all kind of analytical performance studies, when the impact of a certain test condition is compared to a reference

In 2017, the new **European in vitro diagnostic regulation (IVDR 2017/746)** came into force and will replace the current directive (IVDD 98/79/EC) in May 2022. The pre-analytical workflow including variables, which have an impact on sample quality and analytical test performance, are prominently addressed in the IVDR. For example, in Annex II 6.1, it is explicitly stated that for product verification and validation, the description of the specimen type shall include "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". These are exactly preanalytical variables that are also covered in the pre-examination / pre-analytical ISO-Standards.

Therefore, for the development of the **PAXgene Blood ccfDNA CE-IVD workflow, the implementation of the relevant pre-analytical ISO-Standard did not only ensure high quality samples for analytical performance testing during development, verification and validation, but also compliance to the new EU IVD Regulation according to its pre-analytical and also state-of-the-art requirements.**

Christina Hartmann

Maike Remmel

Daniel Grölz

Franziska Heese

Katharina Brack

Lausra Sofie Witthaus

Carina Schaub

futher team members:
Nadine Burzlauer, Carina Mett, Larissa Kuhn, Tomasz Krenz

SPECIAL: IMPLEMENTATION OF STANDARDS

CHRISTINA HARTMANN

Senior Scientific Expert
PreAnalytiX – R&D Product Life Cycle Management

QIAGEN GmbH

christina.Hartmann@qiagen.com

Product Life Cycle Management activities in accordance with ISO 20186-1:2019 using the example of the PAXgene Blood RNA System verification on the new QIAcube Connect MDx

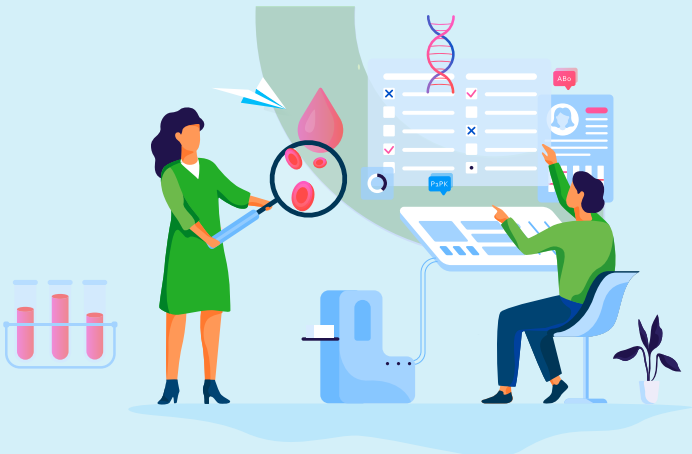
ISO-Standards for molecular in vitro diagnostic pre-examination processes are meanwhile at PreAnalytiX® and QIAGEN® routinely used in various areas including Product Life Cycle Management.

In order to maintain consistently high product quality, especially in the circumstance of targeted changes to a product, it is crucial to perform recurrent verification tests under standardized prerequisites. Any artificial and unrecognized impact on sample quality from specimen collection to processing might render verification results unusable or even lead to wrong conclusions with critical impact on the performance of diagnostic products.

A recent example is the verification of the established PAXgene® Blood RNA System in combination with the new QIAcube® Connect MDx instrument. As its predecessor, the QIAcube instrument, the QIAcube Connect MDx is designed to perform automated isolation and purification of nucleic acids in molecular diagnostic and molecular biology applications. Both instruments enable for automated use of the PAXgene Blood RNA Kit (FDA approved and CE-IVD) for purification of intracellular RNA from whole blood collected in the PAXgene Blood RNA Tube. The PAXgene Blood RNA System provides high-quality RNA from whole blood for RT-PCR used in molecular diagnostic testing.

The relevant ISO-Standard for RNA examination from whole blood, ISO 20186-1:2019 Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for venous whole blood — Part 1: Isolated cellular RNA, with its recommendations and requirements on specimen collection, handling, storage, processing and documentation was transferred into an SOP within QIAGEN's global design control process as part of the ISO 13485 based Quality Management System.

Performing the pe-analytical steps for the product performance verification of the PAXgene Blood RNA System in combination with the new QIAcube Connect MDx according to this ISO 20186-1 based SOP ensured reliable test conditions and results by use of high-quality test samples with comprehensive documentation of their course and characteristics. The results finally led to the successful release of the PAXgene Blood RNA protocol for the new QIAcube Connect MDx instrument.



Inspiring - Freepik.com

WP2 EQA // DR. OLGA KOFANOVA / DR. PAOLO VERDERIO / DR. CHIARA CINISELLI

DR. OLGA KOFANOVA
Integrated BioBank of Luxembourg
Olga.Kofanova@ibbl.lu
www.ibbl.lu

DR. PAOLO VERDERIO
Fondazione IRCCS
Istituto Nazionale dei Tumori, Italy
paolo.verderio@istitutotumori.mi.it
www.istitutotumori.mi.it

DR. CHIARA MAURA CINISELLI
Fondazione IRCCS
Istituto Nazionale dei Tumori, Italy
chiara.ciniselli@istitutotumori.mi.it

External Quality Assurance (EQA) program within SPIDIA4P and beyond: new features to come.

High quality biobank laboratories play a crucial role in the context of multi-center clinical trials, basic and applied research, by providing and enhancing the translational link within transversal and personalised medicine (PM) initiatives. These laboratories pursue the highest quality of collected biospecimens and associated annotated data that qualify their samples for downstream applications.

Irreproducible, unreliable experimental results have no scientific value, and could lead to wrong decisions later on, in the clinical decision making scenario.

Minimizing the number of sample processing errors and the number of irreproducible pre-clinical and clinical studies, biobank laboratories will also improve and speed up biomarker discovery and validation, thus strengthening the PM paradigm calling for standardized processes from the get-go .

As a part of biobank quality management system (QMS), EQA processing schemes, deployed in the context of EQA programs, have been introduced for biobank processing laboratories (Fig.1). The aim is to provide an independent assessment of a laboratory overall quality performance, on top of the pre-existing quality controls (QCs) that each laboratory has already established and internally implemented.

The annual Proficiency Testing (PT) program, developed by IBBL, supports the development of biobank quality assurance [1]. In parallel with the annual IBBL PT program, more EQA/PT schemes have been developed within SPIDIA4P and they correspond to pre-analytical CEN/Technical Specification documents (CEN/TS) developed under its own umbrella.

Get more information here.

Overall, the IBBL PT program includes the following processing EQA schemes for the pre-analytical phase. It includes, but it is not limited to:

- DNA extraction from whole blood
- RNA extraction from whole blood
- DNA extraction from FFPE material
- RNA extraction from FFPE material
- Microbial DNA extraction from saliva

- Microbial DNA extraction from stool
- DNA extraction from frozen tissue
- Total RNA extraction from frozen tissue
- Dual DNA/RNA Extraction from Frozen Tissue
- Cell-free DNA (cfDNA) extraction from whole blood
- Cell-free RNA (cfRNA) extraction from plasma
- Circulating Tumor Cells (CTC) detection and isolation
- Viable PBMC isolation

EQA of processing schemes provides information on laboratory processing methods by comparing the results of the PT participant/ laboratory within a group of similar methods, a so-called peer group. From this comparison, the performance of the each individual laboratory is determined with regard to imprecision, systematic error and human error. Different quality metrics, such as yield, purity, integrity, viability and biospecimen fitness for purpose are also evaluated.

The progression of the annual PT program in the context of SPIDIA4P has shown that the majority of participants was represented by EU countries , as shown at a glance in Figure 2, and more detailed in Table 1. It shows that some laboratories participated in PT program every two years. Despite the 2020 pandemic, the number of participants remained quite high. Also, while it is true the number did not go up, generally, the majority of those who were initially enrolled came back year after year. It confirms that the positive experience gathered under SPIDIA4P umbrella serves to pave the way for tighter adherence to QMS requirements, sensitizing biobanking laboratories to comply with the highest quality standards.

EQA over time

On average, more than 70% of participants successfully passed the proficiency tests, for all schemes. Laboratories that have participated in PT schemes over several years have seen global an improvement in their performance in terms of their z-scores [1]. Within the framework of SPIDIA4P WP2, an updated statistical analysis conducted on all data collected during the 6 years (2014-2019) of the annual IBBL PT program (Fig.3), provides evidence of the most critical preanalytical variables and the specificity of their impact on the applied processing methods. In details, we investigated the relationships between the performance measurements (i.e. z-scores) and the considered pre-analytical factors to highlight those mainly involved in the subsequent readouts. A scientific paper, summarizing these results, is actually in preparation [2].

All togheter these data are useful not only in the context of method development and validation by biobank laboratories, but also in the developement of standardized document reporting the most relevant processing information. According to ISO requirements [3] these documents should de facto accompany all samples entering the distribution process.

The EQA/PT program represents an essential part of a biobank laboratory's QMS: while it enables laboratory performance assessment, it provides useful insights into method performance characteristics, thus fulfilling accreditation authorities' demands [3].

References.

1. A. Gaignaux et al., *Biopreservation and Biobanking,* 2016, v.14, N5, 429-439.
2. 2. Verderio P., Ciniselli C.M., Gaignaux A., Pastori M., Saracino S., Kofanova O., Betsou F. "External Quality Assurance programs for processing methods provide evidence on impact of preanalytical variables", *Clin Chem Lab Med* [submitted].
3. ISO21899:2020 Biotechnology — Biobanking — General requirements for the validation and verification of processing methods for biological material in biobanks.

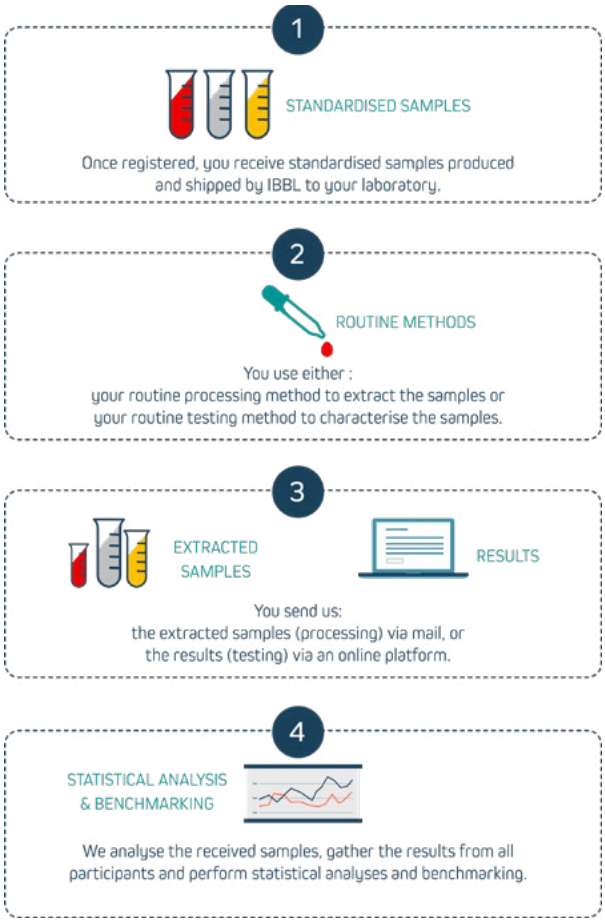


Fig.1. The annual IBBL PT programme design. The PT workflow as an external quality assessment tool.

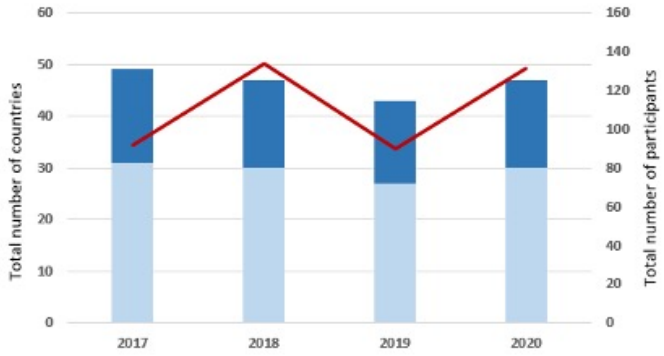


Fig.2. IBBL PT program development during the SPIDIA4P project. The red line describes the trend for the total number of program participants (right scale as a reference). The lower bar-chart part (light blue) depictsEU participants, while the upper one (dark blue)– is representative of the non-EU countries (left scale).

Year	Participant number	EU countries	Total countries
2017	92	18	31
2018	134	17	30
2019	90	16	27
2020	131	17	30

Table 1: Participant numbers and country breakdown per each year of the SPIDIA4P project.

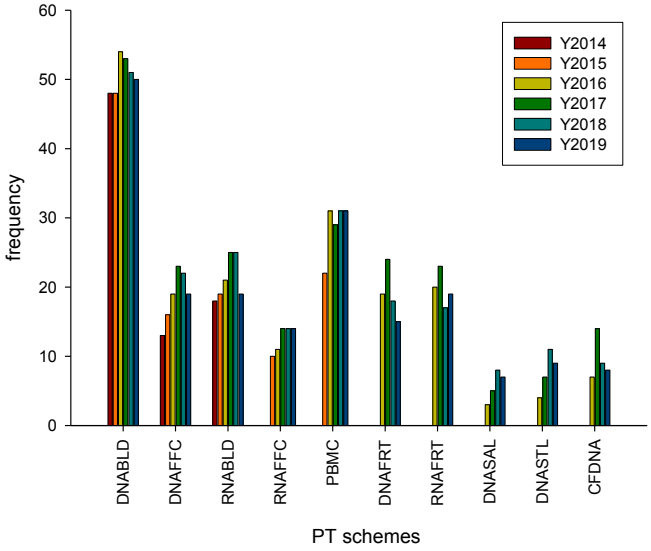


Fig.3. Number of attendances within each PT program among the 6-years annual IBBL PT program undergoing an updated statistical analysis.

WP3 – REVIEW // CORNELIA STUMPTNER

MAG. (FH) CORNELIA STUMPTNER
Project Manager BBMRI.at

Medical University of Graz, Austria

cornelia.stumptner @medunigraz.at

http://bbmri.at/

BBMRI-ERIC
Biobanking and BioMolecular resources Research Infrastructure

Putting the Spotlight on SPIDIA4P & Pre-Analytics

During the past four and a half years, SPIDIA4P partners have shown tremendous communication engagement and offered a huge portfolio of measures which helped to reach the goals of work package 3 "Implementation and Dissemination of (the pre-analytical CEN/TS and ISO) Standards & External Quality Assurance Schemes".

SPIDIA4P partners broadly reached out to various target groups, such as *in vitro* diagnostic developers and manufacturers, diagnostic laboratories, researchers, biobankers, and the respective professional societies as well as regulatory authorities. By launching the modern website www.spidia.eu as the central source of information, the general public was also addressed. In addition, SPIDIA4P members showed strong presence in many different fields such as biotechnology, biobanking, pathology, personalized medicine and clinical chemistry and laboratory medicine.

With hundreds of contributions to congresses plus live and virtual training courses, numerous personal discussions, newsletters and scientific publications, SPIDIA4P partners raised growing awareness on the necessity of using good quality patients'/donors' specimen and samples for diagnostics and research. SPIDIA4P successfully drew attention to the pre-analytical phase, critical pre-analytical variables, and the published CEN/TS and ISO standards for Molecular in vitro diagnostic examinations — Specifications for pre-examination processes. Indicators of communication performance like number of website visitors, newsletter readers and attendees at congresses and courses underline the interest of the audience in SPIDIA4P's dissemination activities.

SPIDIA4P has built up a broad European and global network with key stakeholder organisations including professional societies and opinion leaders, such as MedTech Europe, European Federation of Pharmaceutical Industries and Associations (EFPIA), European Medicines Agency (EMA), European Society of Pathology (ESP), Organisation of European Cancer Institutes (OECI), BBMRI Expert Centers such as CBmed, national accreditation agencies, and Notified Bodies.

This network helped and will help to further drive these subjects.

The topic was even brought into the EU Parliament. The event "Tackling issues on in vitro diagnostics for personalised medicine", organised by the SPIDIA4P consortium and BBMRI-ERIC, was hosted by members of parliament and was well attended by notable representatives of relevant stakeholder organizations. The well-organized and lively reporting around this event via social media before, during and after the event, an event brochure, a video as well as review reports, made this event a real highlight that raised a lot of attention and sustainable recognition.

Video:

https://www.youtube.com/watch?v=EPSNzGY2Yac

Many SPIDIA4P members were invited not only to public events like conferences and courses, but also to closed-door meetings of important stakeholder organizations.

The challenge to maintain the attention also during the COVID-19 pandemic was mastered perfectly well by the SPIDIA4P partners and even brought up more and sustainable digital training and educational material such as webinars, recorded presentations and videos. A list of these valuable materials can be found later in this newsletter.

All these communication and co-working activities led to a broader understanding that the pre-analytical phase is critical for specimen/sample quality and to the acceptance that specimens of high and defined quality are one important prerequisite for reliable and reproducible analytical test results. SPIDIA4P's activities invoked a broader awareness and acceptance that the CEN/TS and ISO standards represent the state-of-the-art of handling specimens

and samples during the pre-analytical phase. This was supported by the new EU *In vitro* diagnostics regulation (EU) 2017/746 (IVDR), which explicitly requires pre-analytical specimen/sample data to be provided, and by an increased recognition for accreditation needs (for example in biobanking, laboratory medicine).

The mission will go on

The topic of pre-analytics and the respective CEN/TS and ISO standards have been integrated in many international and national programmes, projects and initiatives and will therefore remain in focus. Also, its consortium members will continue even beyond the end of SPIDIA4P to include SPIDIA4P's messages in their communication and dissemination such as presentations at conferences, meetings, courses, and publications. Furthermore, the SPIDIA4P website and newsletters will persist. This continuation is extremely important, as new standards, which were generated within SPIDIA4P, are being published in 2021, and there is still a lot of effort and time required to broadly implement improvements in pre-analytical workflows in the different fields for the benefit of patients.

By regularly visiting the project website www.spidia.eu, you will stay up-to-date with regard to future progress, important events and the new standards in the area of pre-analytics that will support the improvement of global healthcare!

SPIDIA4P EVENTS // HIGHLIGHTS // 2017 / 2018 / 2019 / 2020 / 2021

JANUARY / FEBRUARY 2017

In the course of SPIDIA4P, we were glad to have some real event highlights – some of them were organized by the SPIDIA4P partners and as the popularity and awareness of our project and the importance of standards rose, our project members were more and more proactively invited by conference organizers to either present the latest project updates, spread the word, or to lead symposia and sessions.

On the next pages, you will find a list of event highlights since the project has started.

Kick off Meeting

From January 31 to February 2, 2017, all SPIDIA4P project members met at the coordinator´s QIAGEN site in Hilden, Germany, to kick off the project. As also all the thereafter following consortium meetings taking place twice a year, the kick off meeting was a very fruitful and effective meeting with important information exchange, goal setting and status updates that laid the basis for the upcoming activities.

SPIDIA4P EVENTS // HIGHLIGHTS // 2017 / 2018 / 2019 / 2020 / 2021

FEBRUARY 2017

International Biobanking Experts at "Pre-analytical Sample Processing" Course from BBMRI.at in Graz

International biobanking experts from six different countries met in Graz from 08th to 10th February 2017 in order to devote themselves to quality control of samples. The organizer of the course, Medical University of Graz (in context of the Austrian Biobanking and Biomolecular Research Infrastructure BBMRI.at) is a SPIDIA4P member and thus centrally involved in the development of ISO Standards and CEN Technical Specifications (CEN/TS) for Preexamination Processes.

Learning through hands-on, this 3-day laboratory course put this into practice. Participants learned about the CEN/TS requirements while practically working with samples and isolating RNA, which was then evaluated using different quality control methods. All steps were performed according to the CEN/TS documents. In addition to the BBMRI.at partner Institute of Pathology/Medical University Graz, which was responsible for the practical part, Andrea Wutte from BBMRI-ERIC, Ingrid Walter and Helmuth Haslacher from the BBMRI.at partners VetBioBank and MedUni Wien Biobank, respectively, contributed with lectures on blood pre-analytics and implementation of the CEN/TS.

Participants had also a chance to attend a presentation by Berthold Huppertz about Biobank Graz and a guided tour through Biobank Graz, which is one of Europe's largest biobanks.

SPIDIA4P EVENTS // HIGHLIGHTS // 2017 / 2018 / 2019 / 2020 / 2021

MAY 2018

May 16, 2018; Medical University of Graz

Course „CEN and ISO Standards for Pre-analytical Processes in Industrial Development and Medical Diagnostics"

Organized by Medical University of Graz in the context of BBMRI.at, this course introduced the European CEN/TS and ISO standards for the pre-analytical processing of human biospecimens.

Besides explaining common structures and specific differences of the various standards for different sample types and analytical techniques, the rationale and experimental evidence behind selected standards were presented. By participating in this course, the attendees obtained a solid understanding of purpose and aims of the standards, and learned how to implement them in their laboratories.

Review and presentations:

http://bbmri.at/news/-/asset_publisher/hbV7JGgJQAtz/content/successful-course-on-cen-and-iso-standards-for-pre-analytical-processes

SEPTEMBER 2018

Europe Biobank Week Antwerpen, Sep, 4-7, 2018

SPIDIA4P project members attended, chaired and presented different sessions as state-of-the-art speakers at the Europe Biobank Week in Antwerpen, Belgium

- Dr. Uwe Oelmueller – Standardized and Improved Pre-analytical Workflows: A Key for Reliable Diagnostics, Research and Biobanking
- Prof. Kurt Zatloukal – Role of Public-Private-Partnerships in Biobanking
- Andrea Wutte, M.Sc. – Session Chair for "Quality Assessment and Management of Samples and Data"
- Mag. Cornelia Stumptner BBMRI.at-Quality Management efforts; BBMRI Self Assessment Survey Tool: Test the quality of your pre-analytical procedures
- Prof. Peter Riegman – How biobanks can contribute to increase reproducibility of results
- Dr. Fay Betsou – Overview about the actual research in the field of preanalytics of liquid biospecimen
- Dr. Peter Abuja – Influence of dehydration protocol on residual humidity and quality of nucleic acids in fixed tissue

The participants also had the chance to test the BBMRI SelfAssessment Survey Tools for sample quality:

https://www.bbmri-eric.eu/services/self-assessment-survey/

SPIDIA4P EVENTS // HIGHLIGHTS // 2017 / 2018 / 2019 / 2020 / 2021

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 (CEN-CENELEC, Belgium), Uwe Zimmermann (DAkkS, national accreditation body of the Federal Republic of Germany) and Prof. Giorgio Stanta (OECI, ESP, Italy) 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 // HIGHLIGHTS // 2017 / 2018 / 2019 / 2020 / 2021

FEBRUARY 2019

ISBER Symposium,
February 5-6, 2019, Berlin, Germany

2nd Biospecimen Research Symposium: Focus on Quality and Standards

Besides presentations from invited SPIDIA4P project members Dr. Carole Foy (LGC) Dr. Uwe Oelmueller (QIAGEN) and Prof. Giorgio Stanta (UNITS), project member Dr. Fay Betsou (IBBL) chaired the dabate session on the CEN & ISO standards on Liquid Biopsies, being developed under SPIDIA4P. The session emphasized the importance of standards for pre-analytical worksflows applied to personalized medicine.

Recap of the ISBER symposium:

https://www.isber.org/news/505236/Recap-of-the-ISBERs-2nd-Biospecimen-Research-Symposium-in-Berlin.htm

Twitter Post IBBL during the event:

https://twitter.com/IBBLuxembourg/status/1093154157454860288

OCTOBER 2019

Europe Biobank Week 2019,
October 7–11 2019, Lübeck, Germany

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 Andrea Wutte, M.Sc., 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 Andrea Wutte, M.Sc., 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 Prof. Peter Riegman, Erasmus Medical Center, Rotterdam, NL (EMC)

SPIDIA4P EVENTS // HIGHLIGHTS // 2017 / 2018 / 2019 / 2020 / 2021

FEBRUARY 2020

Biotech Pharma Summit: Liquid Biopsy Conference
February 20-21, 2020, Lisbon, Portugal

Presentations and panel discussion by SPIDIA4P project partners

- Dr. Daniel Grölz (QIAGEN/ PreAnalytiX): "Circulating tumor DNA – pre-analytical considerations, international specimen improvement requirement, standards, legislation, technologies"

- Prof. Mikael Kubista (TATAA Biosciences): "Two-Tailed PCR for Precision Diagnostics"

Event brochure:

https://www.biotechpharmasummit.com/wp-content/uploads/2020/08/Liquid_Biopsy_Summit_PT_Lisbon_2020.pdf

Facebook posts by the organizer:

https://www.facebook.com/biotechpharmasummit/

MAY 2020

May 11-14, 2020 – Virtual Workshop

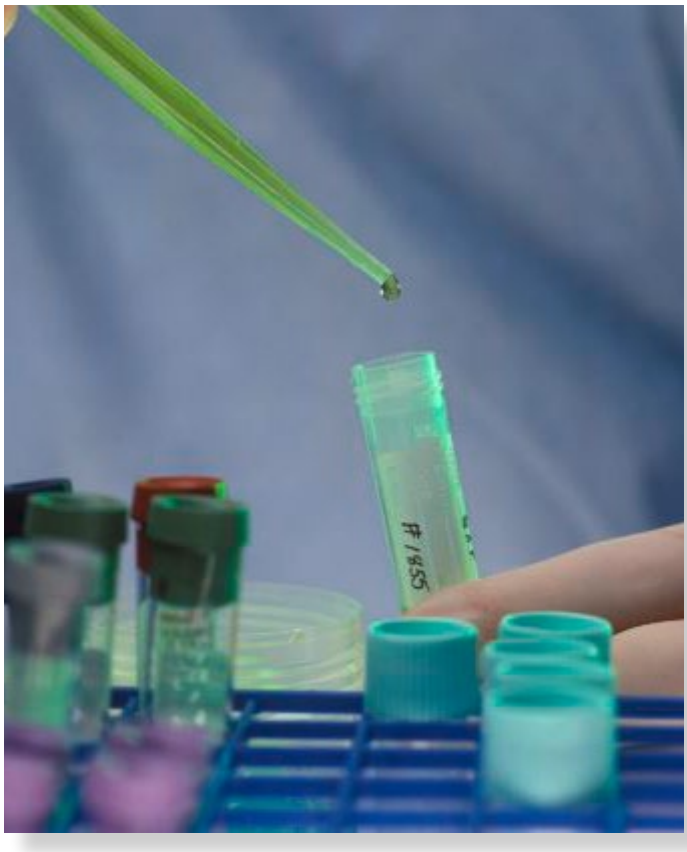
Implementing Biomedical Research Projects: the Complete Workflow from Concept, ELSI and Privacy Considerations to high-Quality Biobanking

Learning about relevant steps and associated ethical, privacy, sample quality and biobanking issues during the conception and implementation of biomedical research projects – this was the goal of the online workshop held May 11 – 14, 2020. With 39 international participants from 14 countries the workshop was well visited.

The course was organized by Medical University of Graz (Project EASI Genomics), BBMRI-ERIC (Project European Joint Programme Rare Diseases (EJP RD)) and jointly held with the partners BBMRI.at, QIAGEN and CBmed. Amongst many other interesting presentations, the SPIDIA4P members Mag. Cornelia Stumptner and Dr. Uwe Oelmueller were invited speakers.

Review and presentations:

http://bbmri.at/news/-/asset_publisher/hbV7JGgJQAtz/content/-implementing-biomedical-research-projects-



SPIDIA4P EVENTS // HIGHLIGHTS // 2017 / 2018 / 2019 / 2020 / 2021

SPIDIA4P partner Medical University of Graz jointly organized (in context of BBMRI.at – the Austrian Biobanking Research Infrastructure Node of BBMRI-ERIC) two events with the Austrian Life Science Cluster LISAvienna and the company en.co.tec.

Both events aimed at raising awareness of pre-analytical standards as state-of-the-art for IVD development and IVD use for selected molecular analyses. Second aim was to inform about the relevance of pre-analytics and corresponding standards in the context of IVDR. This also addressed the topic laboratory developed tests (LTD).

JUNE 2020

Webinar – (held in German), June 5, 2021

The CE Mark as a sufficient seal of approval for IVD tests?

This webinar was held in the context of the COVID-19 pandemic, which triggered a large number of Sars-CoV-2 IVD being developed and used.

Speakers from regulatory and notified bodies, from industry, diagnostics and academic research presented, one of them SPIDIA4P member Prof. Kurt Zatloukal (Medical University of Graz).

The 3 hours webinar was fully booked: 100 people from enterprices, universities and regulatory bodies all over Austria were able to attend.

More information and presentations for download:

http://bbmri.at/news/-/asset_publisher/hbV7JGgJQAtz/content/webinar-on-sars-cov-2-diagnostics-ce-certification

OCTOBER 2020

Virtual conference – (held in German, Oct 20–21, 2020)

LISAvienna Regulatory Conference for Medical Devices and In Vitro Diagnostics 2020

With this conference, the organizers contributed to the exchange of knowledge about the implementation of the Medical Devices Regulation (MDR) and the In Vitro Diagnostics Regulation (IVDR).

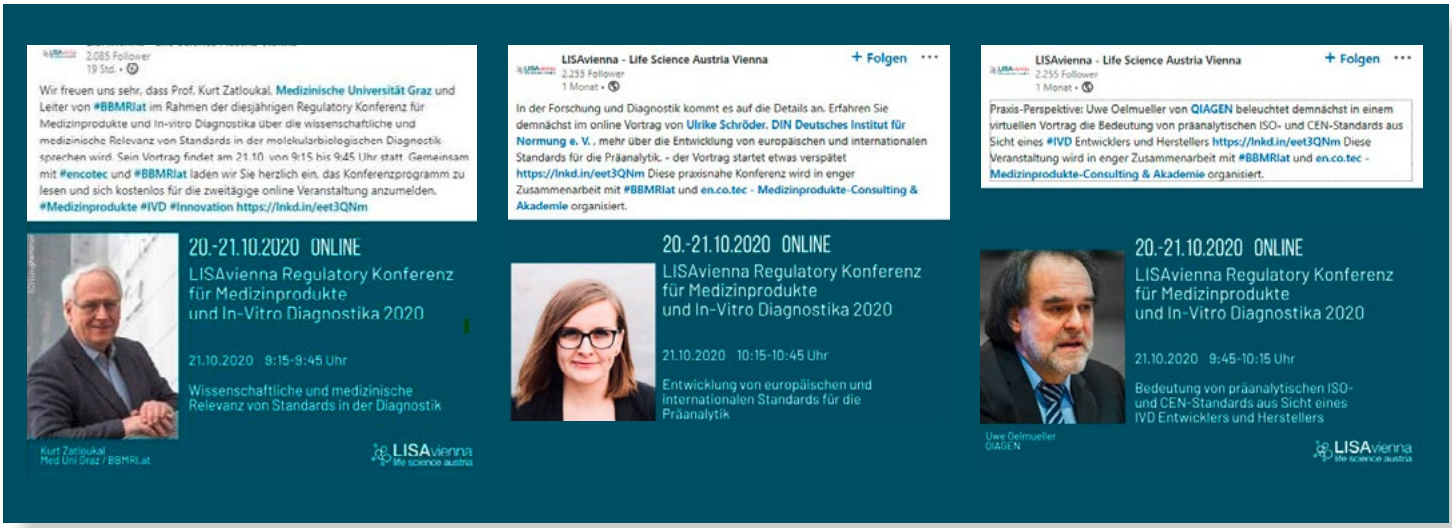
Over 520 persons from industry, regulatory bodies, funders and universities registered for the 2 day conference with 15 hours of virtual live lectures and discussions and asked about 200 questions.

Presentations for download:

http://bbmri.at/news/-/asset_publisher/hbV7JGgJQAtz/content/presentations-from-regulatory-conference-md-ivd-

Programme:

https://www.lisavienna.at/fileadmin/user_upload/LISAvienna/Files_Events/LISAvienna_Regulatory_Konferenz_fuer_Medizinprodukte_und_In_vitro_Diagnostika_2020.pdf



SPIDIA4P EVENTS // HIGHLIGHTS // 2017 / 2018 / 2019 / 2020 / 2021

OCTOBER 2020

BBMRI.QM In-Depth Training on ISO Standards
Web conference series on pre-analytical ISO standards 20184 / 20166 / 20186

In cooperation with SPIDIA4P, the BBMRI.QM team provided an in-depth training on the pre-analytical standards relevant for biomedical research and biobanking.

This BBMRI.QM training & education programme was presented as a virtual training, split into 16 sessions in which the individual chapters of the standards were discussed. Renowned experts gave comprehensive presentations on requirements, definitions and practical applications. The entire training program run from October 2020 to February 2021.

The webinars have been recorded and archived and can be accessed at any time for further study or for refreshing individual chapters. If you would like to have access to the recordings of our web conference series, please contact the QM Training & Education Manager: *Ulrike Rohrer: ulrike.rohrer@bbmri-eric.eu*

A prerequisite for active participation is the possession of the relevant ISO standards.

More information:

https://www.bbmri-eric.eu/services/bbmri-qm-training-education/

http://bbmri.at/news/-/asset_publisher/hbV7JGgJQAtz/content/bbmri-qm-training-session-on-tissue-blood-standards-rds

SPIDIA4P EVENTS // PAST EVENTS // 2017 / 2018 / 2019 / 2020 / 2021

November 2020

Europe Biobank Week
November 17-20, 2020
Virtual Format

Presentation by SPIDIA4P project partners
QIAGEN/PreAnalytiX
Dr. Tomasz Krenz, QIAGEN

Take a look at the presentation:

https://www.spidia.eu/fileadmin/Images/Download/Presentation/spidia4P/EBW_IndustryWorkshop_PAXgene_1120_EU.pdf

18.11.2020

10:00 AM – 10:45 AM
Preanalytical Considerations and Workflow Solutions for Liquid Biopsies
Industry Workshop
Tomasz Krenz · QIAGEN
BD Becton Dickinson

Session Chair on Nov. 17 and 20, 2020:

Prof. Riegman, Erasmus University Medical Center

17.11.2020:

9:30 AM – 10:45 AM
Global epidemic prevention strategies: the role of pathogen archives. Meet the experts
Session dedicated to epidemic threats, the situation caused by Sars-CoV-2. Strategies for strengthening research infrastructures and projects related t...
Live session
Peter Riegman · Erasmus MC
Rebecca Cox · University of Bergen
Neşe Atabey · Izmir Biomedicine and Genome Center ; BBMRI Turkey
HUMAN HEALTH: Medicine on the Move

10:30 AM – 11:30 AM
Global epidemic prevention strategies: the role of pathogen archives. Meet the experts
Session dedicated to epidemic threats, the situation caused by Sars-CoV-2. Strategies for strengthening research infrastructures and projects related t...
Live session
Neşe Atabey · Izmir Biomedicine and Genome Center ; BBMRI Turkey
Peter Riegman · Erasmus MC
Gualtiero Ricciardi · Università Cattolica del Sacro Cuore

SPIDIA4P EVENTS // HIGHLIGHTS // 2017 / 2018 / 2019 / 2020 / 2021

MARCH 2021

March 8-10, 2021– Virtual Conference

2nd IBCQ International Biobanking / Conference 2021

Invited Key Note Speaker: Dr. Uwe Oelmueller, QIAGEN and SPIDIA4P coordinator

Presentations by SPIDIA4P members Prof. Kurt Zatloukal, Medical University of Graz, and Prof. Peter Riegman, Erasmus MC

Programme:

https://usercontent.one/wp/www.ibcq2021.com/wp-content/uploads/2021/03/IBCQ2021_Event-Program-4.pdf

Presentation by Dr. Uwe Oelmueller:

https://www.spidia.eu/fileadmin/Images/Download/Presentation/spidia4P/IBCQ_2021_PPT_Uwe_Oelmueller_final_070321.pdf

MAY 2021

May 26-28, 2021 – Virtual format

SPIDIA4P presents: Precision Diagnostics Europe organized by SPIDIA4P project partner TATAA Biocenter

Review on page 27

http://precisiondiagnostics.eu/

SPIDIA4P PUBLICATIONS // ARTICLES

find all articles by SPIDIA4P members on *https://www.spidia.eu/publications/articles*

BBMRI-ERIC Magazine No. 6/2017 "Knowledge-Experience-Quality-Trust"

https://www.spidia.eu/fileadmin/Images/Download/magazines/2017_Newsletter6_7_WEB_BBMRI-ERIC.pdf

Brochure about the SPIDIA4P event on standards at the European Parliament in Brussels

Tackling issues on in vitro diagnostics for Personalised Medicine, SPIDIA4P

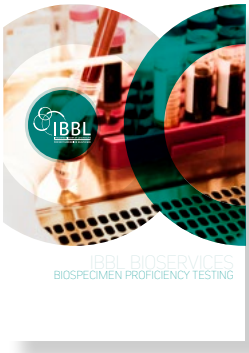
https://www.spidia.eu/fileadmin/Images/Download/Brochures/SPIDIA4P_Brochure.pdf

Highlight: Special Issue New Biotechnology

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

SPIDIA 4P Posters

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



Brochure IBBL Bioservices "Biospecimen Proficiency Testing"

https://www.spidia.eu/fileadmin/Images/Download/Brochures/IBBL-Biospecimen-Proficiency-testing-services_brochure.pdf

SPIDIA4P PARTNER // CONSORTIUM MEETINGS

During the runtime of the project, the SPIDIA4P partners had the chance to meet twice a year at the different partners´ sites for a lively and fruitful exchange of information and updates and to discuss and decide on further steps. During the lockdown due to the Corona pandemic, the format changed to virtual meetings - like for the final consortium meeting on May 25 and 26, 2021 – which enabled us to continue our usual intensive and effective exchange.

The SPIDIA4P project members during the 8th consortia meeting on May 25/26, 2021 in virtual format.

SPIDIA4P PARTNERS // PRECISION DIAGNOSTICS EUROPE

Precision Diagnostics Europe 2021 – a SPIDIA4P conference!

SPIDIA4P partner TATAA Biocenter organized the final SPIDIA4P conference „Precision Diagnostics Europe" which took place on May 26 to 28, 2021 in a virtual format. Due to the Corona pandemic, the originally planned „onsite" format in Prague in 2020 had to be shifted to 2021 – the transformation to the virtual format was set up very professionally and let to a very successful and fruitful event.

9 SPIDIA4P project members shared their expertise and many high-class external speakers took the opportunity to present at this well-perceived conference.

The conference attracted 120 unique registrations, where each registration could hold multiple participants. A total of 36 presentations was hosted with 60-70 viewers per presentation. 10 posters were shown with 463 reviews.

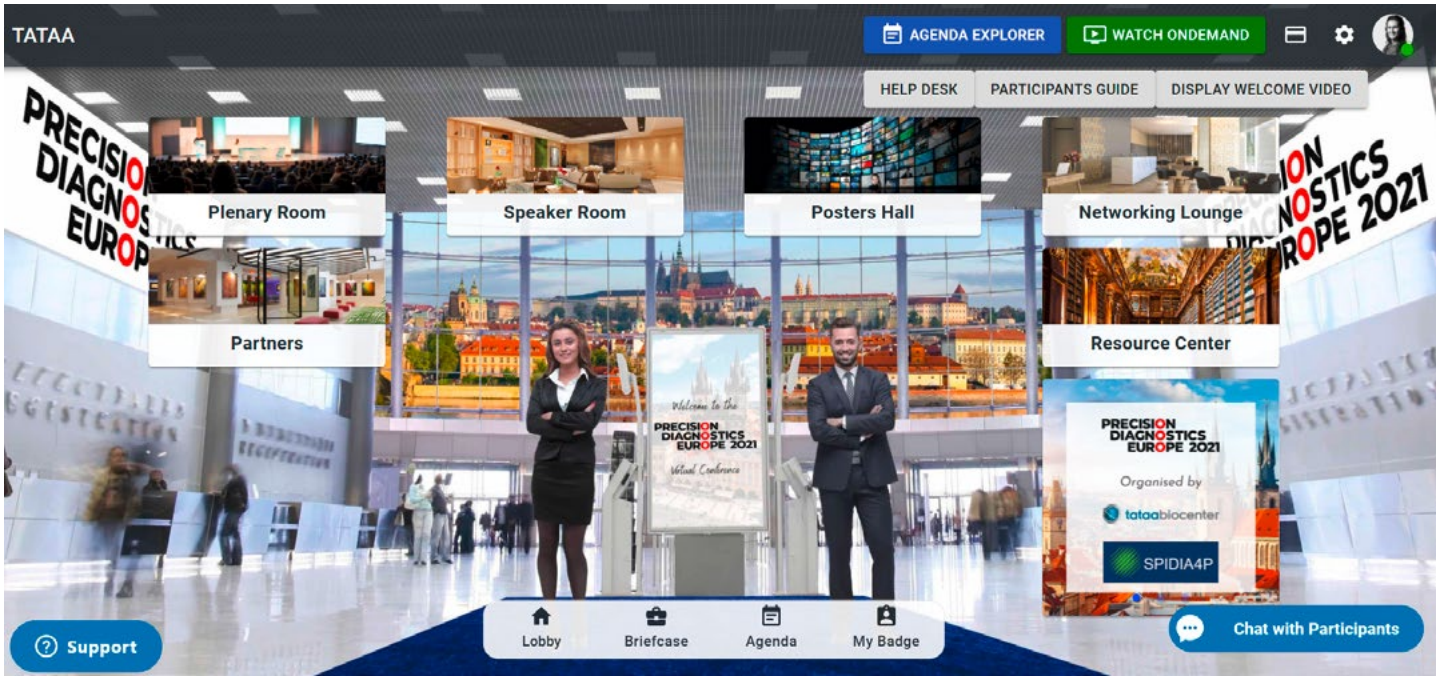
PRECISION DIAGNOSTICS EUROPE 2021

May 26-28, 2021

www.precisiondiagnostics.eu

The recorded presentations will be uploaded to the conference platform after the summer and will be available to the public – we recommend to check the SPIDIA Website www.spidia.eu for the final link to these recordings.

The „Virtual lobby" was the entry point for all participants:



INFORMATION, VIDEOS, WEBINARS

Gain more information and knowledge by looking at the various and many electronic education materials like videos, webinars, presentations etc., produced by SPIDIA4P members or collaboration partners

INFORMATION VIDEOS		
Dr. Uwe Oelmüller, Neue Standards für die Präanalytik	Video: Speaker Dr. Uwe Oelmueller on importance of pre-analytics and standards, role of SPIDIA4P (German language)	Video
Discussing Standards with SPIDIA4P at the European Parliament	Video report & interviews (e.g. with Dr. Uwe Oelmueller, M.Sc. Andrea Wutte and Members of the European Parliament) from the SPIDIA 4P event at EU Parliament on March 5, 2019, on the importance of pre-analytics and standards for precision medicine, role of biobanks, role of SPIDIA4P, organized by BBMRI-ERIC	Video
"Video RECAP: Boosting innovation through standards"	Video review on the conference "Boosting Innovation Through Standards" on Nov. 13, 2019, by CEN and CENELEC	Video
Video "A multi-analyte approach to Liquid Biopsy"	Video by CBmed, Graz, Austria, about their research of liquid biopsies for cancer treatment, stressing the need of sample quality and the implementation of standards, SPIDIA4P is mentioned (January 2021)	Video
Video by CEN & CENELEC "Standards + Innovation"	Very interesting crisp video (2 min.) by CEN & CENELEC, the European standardization organisations, about the connection between innovation and standards	Video
Video about background and goals of EU-STANDS4PM, one of SPIDIA4Ps Collaboration Consortium	Animated video about EU-STANDS4PM informing about why the rational of harmonized transnational standards, recommendations and guidelines are needed and helpful for personalized medicine	Video
"Misstand bei Bluttests (SWR)"	Documentation about what goes wrong during blood tests, analysis in different test laboratories (variability in the analyses, missing standards for IVDs) (German language)	Video
Blood Collection Tubes: Common Types	Video tutorial from AMBOSS, overview of the most commonly used blood collection tubes, one of the major pre-analytical variables (English language)	Video
Die Blutentnahmeröhrchen - AMBOSS Auditor	Video tutorial from AMBOSS, overview of the most commonly used blood collection tubes, one of the major pre-analytical variables (German language)	Video

INFORMATION, VIDEOS, WEBINARS

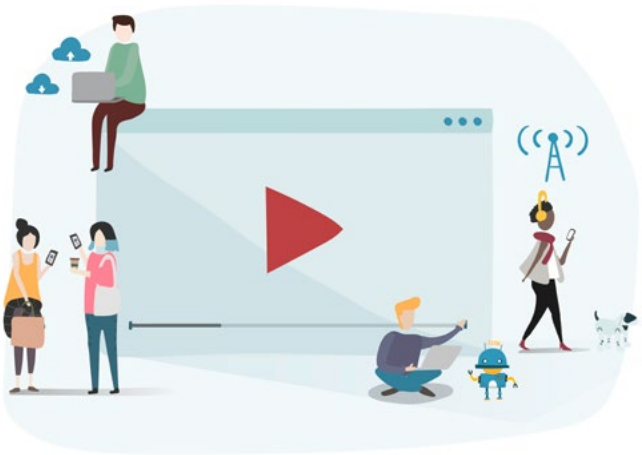
WEBINARS AND TRAININGS		
Personalized Medicine: SPIDIA4P Talk with Dr. Uwe Oelmueller Enhance the reliability of diagnostics with the support of standards	Webinar (video of recorded lecture) Dr. Uwe Oelmueller on the relevance of pre-analytics and ISO and CEN standards in industrial development and medical diagnostics and the work of SPIDIA4P given at the course "CEN and ISO Standards for Pre-analytical Processes" on July 6, 2018, organized by Medical University of Graz	*Webinar*
Relevance of Standards, IVD, Biobanks	Presentation (recorded) (German language) Prof. Kurt Zatloukal (Medical University of Graz) on the topic scientific and medical relevance of standards in diagnostics at a meeting of Medical University of Graz (in the context of BBMRI.at) with the management of the ▪ Austrian research society "Ludwig Boltzmann Gesellschaft" and the ▪ Austrian research funding organization "Christian Doppler" Gesellschaft"	*Information and video*
Standardized Preanalytics: The key for reliable Diagnostics, Research and Biobanking	Recorded presentation by Dr. Uwe Oelmueller in a QIAGEN Cancer Research Webinar (Nov. 5, 2020): Dr. Oelmueller informs about SPIDIA4P, importance of pre-analytics and standards in diagnostics, research and biobanking	*Webinar*
Managing preanalytical variables in Biobanking	Video (of a recorded presentation) given by Dr. Fay Betsou (IBBL) at the 5th EFLM Conference on Preanalytical Phase (Zagreb, 22–23 March, 2019)	*Video*
Pre-analytical considerations and workflow solutions for Liquid Biopsy	Webinar (recorded); QIAGEN Cancer Research Webinar Dr. Tomasz Krenz, QIAGEN, on pre-analytical factors, importance of pre-analytics and standards, and the liquid biopsy pre-analytical workflow (July 16, 2020)	*Webinar*
Preanalytical considerations – standards and how to implement in your laboratory	Webinar (recorded); QIAGEN Cancer Research Webinar "FFPE in focus series" by Dr. Daniel Groelz, QIAGEN, on August 18, 2020, about pre-analytical factors importance of pre-analytics and standards, and implementation of standards in the lab (free registration required)"	*Webinar*
Standardized Preanalytics: The Key for Reliable Diagnostics, Research and Biobanking	Webinar (recorded) Dr. Uwe Oelmueller, QIAGEN on the topics SPIDIA4P, importance of pre-analytics and standards in diagnostics, research and biobanking in an event organized by Frontline Genomics and PreAnalytiX (free access via registration)	*Webinar*
Quality Control and performance assessment of qPCR instruments	Webinar (recorded) Prof. Mikael Kubista (TATAA) on the topics importance of pre-analytical phase (demonstrated by examples mistakes happened), QC and QA methods; SPIDIA4P program mentioned	*Webinar*
Importance of Pipetting Accuracy for High-Sensitivity Techniques	Webinar (live) by Prof. Mikael Kubista (TATAA) on correct pipetting and the relevance of this pre-analytical issue for data reproducibility (free registration)	*Webinar*
Quality systems in biobanking & biomedical research	Webinar (recorded presentations) Speakers from IBBL and Andrea Wutte (BBMRI-ERIC) in an EATRIS webinar on „Quality and reproducibility" (Webinar #4, Dec 2019)	*Webinar*

INFORMATION, VIDEOS, WEBINARS

Relevanz von Standards in der Diagnostik	Webinar (recorded presentation) Prof. Kurt Zatloukal (Medical University of Graz) on the topic scientific and medical relevance of standards in diagnostics at the "LISAvienna Regulatory Konferenz für Medizinprodukte und In-vitro Diagnostik"" (Oct 21, 2021); coorganized by Medical University of Graz in the context of BBMRI.at) (German language)"	Webinar
Bedeutung von präanalytischen CEN und ISO Standards aus Sicht eines IVD Entwicklers und Herstellers	Webinar (recorded presentation) Dr. Uwe Oelmueller on the topic relevance of pre-analytical ISO and CEN standards from an IVD developer's and manufacturer's point of view at the "LISAvienna Regulatory Konferenz für Medizinprodukte und In-vitro Diagnostik" "(Oct 21, 2021); coorganized by Medical University of Graz in the context of BBMRI.at)(German language)"	Webinar
Entwicklung von Europäischen und Internationalen Standards für die Präanalytik	Webinar (recorded presentation) Ulrike Schroeder, M.Sc. (DIN) on the topic development of European and international standards for pre-analytics at the "LISAvienna Regulatory Konferenz für Medizinprodukte und In-vitro Diagnostik" (held 21 Oct 2021); coorganized by P15 Medical University of Graz in the context of BBMRI.at) (German language)"	Webinar
Tips and tricks for more accurate digital PCR	Webinar (recorded) given by Prof. Michael Kubista (TATAA) in the context of a QIAGEN webinar (free registration)	Webinar
European Technical Specifications for the pre-analytical phase become ISO International Standards: an update	Webinar (recorded presentation) Prof. Karl-Friedrich Becker (TUM) at the BBMRI-ERIC QM educational webinar series "ISO 20387:2018 "BIOTECHNOLOGY – BIOBANKING – GENERAL REQUIREMENTS FOR BIOBANKING" (free registration)	Webinar
The NEW standard for biobanks "ISO 20387 Biobanking – "General requirements for biobanking and how the BBMRI-ERIC Quality Management Service can help with implementation"	Webinar (recorded presentation) Andrea Wutte, M.Sc., (BBMRI-ERIC) on quality management requirements and ISO 20387 for biobanking at a BBMRI-ERIC QM webinar (Nov 13, 2018) (free registration, starting at 2:30 min))	Webinar
e-Training series about molecular in vitro diagnostic examinations – specifications for pre-examination processes organized by BBMRI-ERIC	Several Webinars (recorded) Speakers: Dr. Uwe Oelmueller (QIAGEN), Prof. Kurt Zatloukal (Medical University of Graz), Prof. Peter Riegman (EMC), Mag. Cornelia Stumptner (Medical University of Graz), M.Sc. Andrea Wutte (BBMRI-ERIC), Prof. Karl Friedrich Becker (TUM), Dr. Daniel Groelz (QIAGEN), Dr. Stefania Gelmini (UNIFI), Dr. Pamela Pinzani (UNIFI), Dr. Kalle Guenther (QIAGEN) – free registration needed; pre-requisite for the participance is the possession of the relevant ISO standards	Registration to Webinar series
Protocol for HER2 FISH Using a Non-cross-linking, Formalin-free Tissue Fixative to Combine Advantages of Cryo-preservation and Formalin Fixation, (Loibner et al., 2015)	Publication in video paper: publication with video demonstration of the major pre-analytical steps in this study (i.e. handling of tissue before HER2 in situ hybridization) – open access	Video paper
Presentation slides	Selected presentations are available on: https://www.spidia.eu/publications/presentations	

INFORMATION, VIDEOS, WEBINARS

MISCELLANEOUS		
Cell-Free DNA: A Diagnostic Revolution in the Works?	Article in Magazine Biocompare, Dec. 2019, by Angelo de Palma, containing information about pre-analytical considerations	*Article*
IBBL-Biospecimen-Proficiency-testing-services	Brochure IBBL on external quality assessment of biospecimens in form of proficiency-testing-services: Why to participate? How does it work?	*Brochure*
Tackling issues on in vitro diagnostics for Personalised Medicine, SPIDIA4P	Brochure "SPIDIA4P event on standards at the European Parliament in Brussels" on March 5, 2019	*Brochure*
Knowledge – Experience – Quality – Trust	BBMRI-ERIC Magazine, Issue No. 6/ 2017 – a special edition about the importance of sample quality, with severeal articles by SPIDIA4P members and information about the SPIDIA4P project	*Magazine*
Online Self-Assessment Survey Tool	Online Self-Assessment Survey Tool (SAS) i.e. an online tool that allows laboratories and biobanks to self-assess if their preanalytica procedures meet the requirements / recommendations of the pre-analytics standards. It thus supports them in their efforts to implement these standards.	*SAS tool*
Self-Assessment Tool for Molecular Pathology to Check Pre-analytical Workflows	Poster by SPIDIA4P members Prof. Kurt Zatoukal and Mag. Cornelia Stumptner et al about the Self-Assessment Tool (SAS) by BBMRI-ERIC	*Poster*
Upcoming Quality Requirements for Molecular Pathology	Poster by the SPIDIA4P consortium about the background and aim of the SPIDIA4P project and the pre-analytical sample quality standards by CEN and ISO	*Poster*
IBBL-Biospecimen-Proficiency-testing-services	Website section (with video) at IBBL on external quality assessment in form of biospecimen proficiency-testing-services: Why to participate? How does it work?	*Service information*



Rawpixel.com - Freepik.com

WP4 – ETHICS // PROF. PETER PIEGMAN

PROF. PETER RIEGMAN

SPIDIA4P WP4 leader, Head Erasmus MC Tissue Bank at the Pathology department, Erasmus MC Rotterdam, The Netherlands

p.riegman@erasmusmc.nl

Work package 4 (WP4) of the SPIDIA4P project was designed to safeguard that all project activities were performed within the existing rules and regulations. Around the start of the SPIDIA4P project, the GDPR was freshly implemented in the European countries. This was the moment the storm on how to exactly interpret this fairly new directive was just beginning to pick up in strength. The European Commission was also strongly involved for setting the stage for the project to follow the ethical and privacy rules correctly. An entire Work Package was added as WP6 before the project started that explained what the European Commission expected from WP4. A correct comprehensive and strict set of working rules were provided, like when to report what when you employ certain activities. From that basis the SPIDIA4P project set up the Ethics and Intellectual Property Committee (EIPC). It was composed of one member of each participant. In this way, the EIPC formed a web over the entire SPIDIA4P consortium that was able to monitor the local activities and at the same time monitor the activities reported to the EIPC from all the other participants.

From the start the activities of the project were properly planned and clear. There were activities planned involving trial and test performance data from other initiatives. It was relatively easy to get completely anonymized data from the other initiatives keeping the application of the GDPR simple. It was also not necessary to have coded or identifiable data, because the only thing SPIDIA4P wanted to do is check the data on pre-analytical influences on the test results.

It looked much more complicated to deal with the planned activities on animal and human biomaterials for developing reference materials within the project. For the human materials, the local ethics rules and regulations apply, because for the use of a human sample the country of origin determines the limitations. This means that the local law and regulations determine what requirements need to be met to allow use of human materials. The most important regulations are obtaining proper (informed) consent containing the option to share the biomaterials in international/ European cooperation as well as approval from the local Medical Ethics Committee (ME(T)C) or Internal Review Board (IRB).

For these SPIDIA4P studies, no personal data is used in the exchange and analysis of human biomaterials. The only data needed for proper analysis is no more than the disease state and tissue type of origin. Nonetheless, the European privacy legislation must be followed, which recognizes coded data as well as personal data. Luckily, this simple dataset could be used anonymized within the SPIDIA4P project.

Therefore, the registration, documentation and reporting to the European Commission of all local approvals from IRB's or METC's was sufficient to perform these activities within the consortium.

For using animal materials, the SPIDIA4P consortium needed to comply to the 3Rs (reduction, refinement and replacement) in relation to animal work. To spare animals from being needlessly sacrificed, mostly residual materials are used from animals sacrificed for other experiments or purposes than for SPIDIA4P. All institutes involved are following the local rules and regulations for use of animal materials. At the local institutes, an animal ethics committee is involved in approval of experiments concerning animals. Also here, the registration, documentation and reporting to the European commission was sufficient to perform these activities.

Copyrights and intellectual property rights:

The biggest workload for the EIPC in the end came from another angle. This concerned the copyrights and intellectual property rights. Since the main project objective was to produce ISO and CEN technical standards and disseminate the knowledge about these standards, a potential hazard exists that the copyrights of the ISO and CEN documents are violated or infringed. Therefore, the EIPC had to inspect all publications before they were released in the public domain. This concerns not only articles for scientific publications, but also all developed tools, presentations, lectures, material presented in workshops and webinars. All online activities are included and needed inspection. Since there is a very active work package on dissemination, this can be quite a busy task. On the SPIDIA4P website, you can find all dissemination activities and all of them were checked. The big advantage is that all members of the EIPC were all well aware of the project activities.

With the described methods of control, the SPIDIA-4P consortium is kept on track to comply to the sometimes complex rules and regulations that apply to the work done within the consortium.

Despite all the efforts of the EIPC, there were no incidents in SPIDIA4P of any violation of the rules and regulations.

We did have very lively discussions, certainly in the beginning of the project, on how to deal with copyright rules. In the beginning, I was a little too strict concerning the copyright rules. I remember, I recognized almost identical copies of a couple of sentences from a technical standard in development in a publication that was sent to the EIPC for approval. Upon recognition, I of course immediately responded to the author that this was not allowed. The author than used own wording to explain some of the requirements in another way. This point was discussed in the next annual project meeting where WP4 was a repetitive agenda item. Luckily, the secretariat of DIN and CEN was represented as consortium partner and could explain that as long as there is no complete overview of requirements and recommendations published and it is clear it is not a complete overview, it is no violation of copyrights. It even helps CEN and ISO, because if a laboratory wants to adhere to or become accredited for the standard they still need to buy the standard to find all the requirements and recommendations.

So far, I am happy to say that there were no incidents to report here. It seems dull, but in fact it is not dull at all. The conclusion is that all project activities were kept within all existing rules and regulations and therefore I of course thank the complete SPIDIA4P consortium for staying between the lines and the EIPC for checking all the disseminated work. It is an absolute delight to work with such a wonderful group of people all wanting the project to work. In fact, having all the public domain publications sent around before they are released, also gives a very good image on all the impressive SPIDIA4P dissemination activities.

© Pch.vector - Freepik.com

SPIDIA4P - AWARDS

These awards underline the growing acceptance and awareness about the importance of standards for pre-analytical workflows and innovation and shows the commitment of the SPIDIA4P project to expedite the development and implementation of the standards as well as drive targeted trainings and dissemination activities.

2017

DIN Golden Honorary Needle to Dr. Uwe Oelmueller for Merits on European and International Pre-analytical Workflow Standardisation

During the Global Biobank Week 2017 in Stockholm, Dr. Uwe Oelmueller, project coordinator of SPIDIA4P, was honoured for his comprehensive merits on European and International pre-analytivcal standardisation with the "DIN Golden Honorary Needle"

From 2008 to 2013, Dr. Oelmueller coordinated the SPIDIA project within the EU´s 7th research program.

This project led to a high success in the field of European and international pre-analytical workflow standardisation. He also is the convenor of the ISO/TC 212 Working Group (WG) 4 and the deputy convenor of the CEN/ TC 140 Working Group (WG) 3.

2019

Dr. Uwe Oelmueller received the STANDARDS + INNOVATION TECHNICAL BODY OFFICERS AWARD 2019 by the European Standards Organizations CEN & CENELEC

As the coordinator of both the highly successful FP7 project "SPIDIA - Standardisation and improvement of generic pre-analytical tools and procedures for in-vitro diagnostics" and its ongoing follow-up H2020 project "SPIDIA4P – Standardisation of generic Pre-analytical Procedures for In vitro Diagnostics for Personalised Medicine", Dr. Uwe OELMULLER, Convenor of CEN/ TC 140/WG 3 "Quality management in the medical laboratory" and of ISO/TC 212/WG 4 "Microbiology and molecular diagnostics" is the driving force behind translating research and industry needs in highly innovative fields into standard documents (CEN/TS, EN ISO, ISO) achieving significant impact in health care and diagnostics

Info:*Standards+Innovation Awards CEN and CENELEC launched the Standards+Innovation Awards to acknowledge the important contribution of research and innovation to standardization and celebrating the contributions of researchers, innovators and entrepreneurs to standardization*

More information:

https://www.standardsplusinnovation.eu/awards

https://www.cencenelec.eu/research/Standards_Innovation_Awards/Pages/default.aspx

SPIDIA4P // SUCCESS STORIES

2019

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 or pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue'.

Read more:

https://www.cencenelec.eu/News/Brief_News/Pages/TN-2019-015.aspx

2020

Standardization Fact Sheet –Great recognition by the European Commision!

On the occasion of the World Standards Day on October 14, 2020, the unit in charge of valorisation policies and intellectual property rights at the European Commission published a factsheet on standardisation demonstrating that standardisation is a crucial tool in the valorisation of knowledge & innovation.

The SPIDIA4P project was chosen to be one of the 3 success stories showcased in this factsheet – what a great recognition of the work and importance of the SPIDIA4P consortium and its efforts to initiate and develop 22 new pre-analytical ISO and European CEN standard documents to standardise the preanalytical phase and hence reducing the diagnostical errors!

Get the EU Standardization Fact Sheet:

https://ec.europa.eu/info/sites/default/files/research_and_innovation/strategy_on_research_and_innovation/documents/ec_rtd_valorisation-policies_factsheet.pdf

Press Release (German):

https://www.din.de/de/service-fuer-anwender/normungsportale/gesundheit/aktuelles/spidia4p-und-reach2020-erfolgsbeispiele-fuer-die-normung-und-standardisierung-in-forschungsprojekten-770822

SPIDIA4P NEWS // WEBSITE www.spidia.eu

KATRIN RODENKIRCHEN
QIAGEN / PreAnalytiX
Katrin.Rodenkirchen@qiagen.com

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

The SPIDIA project has received funding under the Seventh Research Framework Programme of the European Union, FP7-HEALTH-2007-1.2.5, under grant agreement no. 222916. The SPIDIA4P project receives funding from the European Union's Horizon 2020 research and innovation programme under grant agreement no. 733112.