SPIDIA4P

SPIDIA4P Newsletter 01/2019

IN PROGRESS: NEW SPIDIA Website www.spidia.eu

New Design

New CEN and ISO standards published! See page 5

CONTENTS

EDITORIAL

Dear reader,

during the first 24 project months, SPIDIA4P has successfully started the project work for all intended 14 new CEN and ISO documents, addressing pre-analytical workflows for molecular analytical tests. (see page 4).

The new documents will complement the existing standard documents initiated by SPIDIA4P's predecessor SPIDIA. Those were first developed as CEN/Technical Specifications , but are now on their way to become ISO International Standards or were published as such in November and December 2018. Among the published documents are the ISO-series 20166, for formalin-fixed and paraffin-embedded (FFPE) tissue and the ISO-series 20184, for frozen tissue (see page 5).

SPIDIA4P has also achieved significant progress in the development, testing and implementation of External Quality Assurance (EQA) Schemes that accompany the standard documents (see page 6).

Furthermore, SPIDIA4P has started a quite huge portfolio of measures for the implementation and dissemination of standards and EQA Schemes. During the first 2 years, these included updates on the SPIDIA4P website *(www.spidia.eu)*, several social media campaigns, a first Newsletter sent to more than 16,000 recipients, development and release of a first wave of e-education and e-learning/teaching materials, several training courses, a digital self-assessment tool for the assessment of the compliance of preanalytical procedures with the published CEN/TS and the upcoming related ISO/IS documents, intensive presence at international conferences with more than 20 mostly invited talks, meetings with professional societies, and finally publications. More detailed information about the activities andpublications can be found on the new SPIDIA website which is currently in the process of being modernized and updated and will be available soon.

More details will be become public during the progression of the SPIDIA4P project.

Dr. Uwe Oelmueller, Coordinator, QIAGEN GmbH

SPIDIA4P event at the EU Parliament in Brussels on March 5, 2019!
SPIDIA4P partner BBMRI-ERIC and coordinator QIAGEN set the scene for a stakeholder workshop hosted by MEP Gesine Meissner and Lieve Wierinck with a panel of experts from all over Europe!

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WP1 GET THE NEW STANDARDS! // ULRIKE SCHRÖDER

ULRIKE SCHROEDER

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Work package 1 (WP1) in SPIDIA4P is developing new European and International Standards for selected high priority pre-analytical workflows needed for personalized medicine, evidence based on research results provided by collaborating partners outside from SPIDIA4P combined with expert knowledge on routine in vitro diagnostic laboratory practice and quality laboratory performance. WP1 also targets to improve and speed up biomarker discoveries and validations for reinforcing the era of personalized medicine and innovations in patient care.

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. As an overview, the stages for developing CEN/TS are depicted in **Figure 1**.

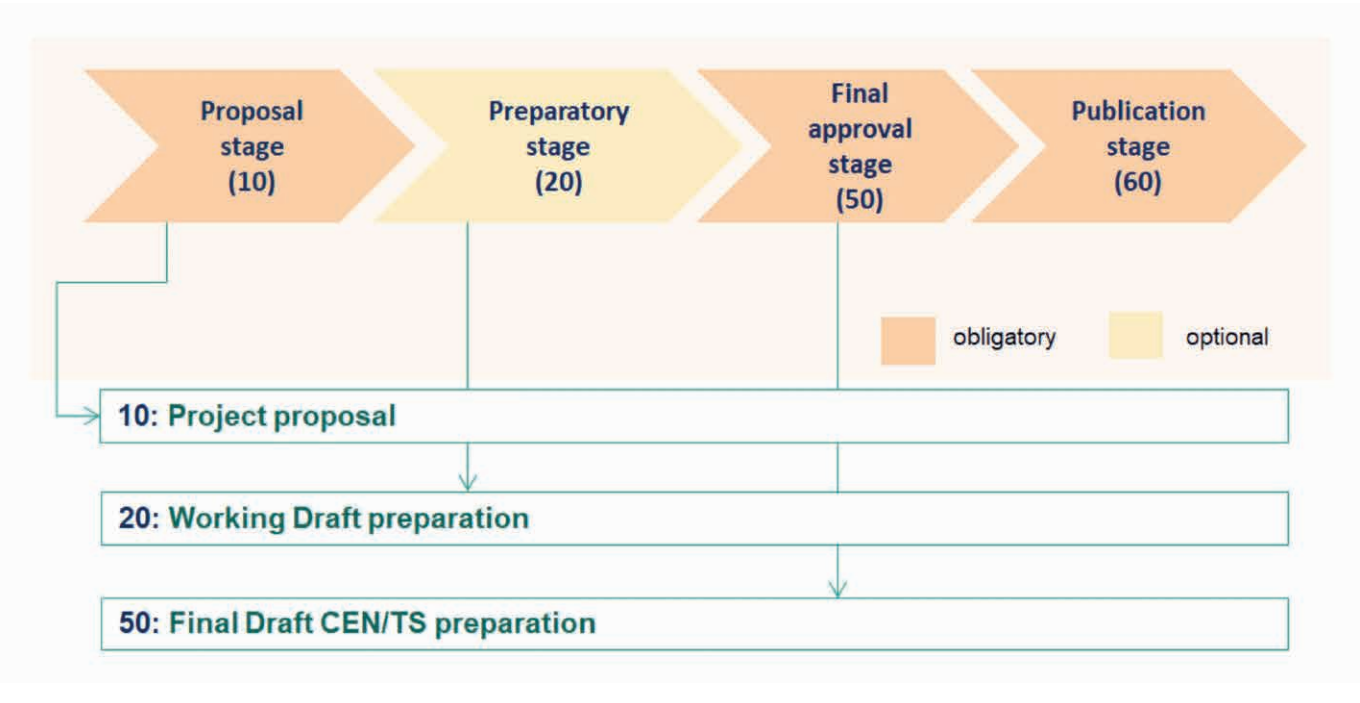

Figure 1: Stages for developing CEN Technical Specifications (CENT/TS)

According to the identified pre-analytical workflows, WP1 is split up into the following 10 tasks, resulting in a comprehensive portfolio of 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	Finalization of Working draft Stage 20
1.1	…for circulating tumour cells (CTCs) in venous whole blood – Part 2: Isolated DNA	Finalization of Working draft Stage 20
1.2	…for circulating tumour cells (CTCs) in venous whole blood – Part 3: Preparation for analytical CTC staining	Finalization of Working draft Stage 20
1.3	…for saliva – Isolated DNA	Final approval S tage 50
1.4	…for frozen tissue – Part 3: Isolated DNA	Published as CEN/TS 16826-3 Stage 60 NWI in proposal (ISO)
1.5	…for exosomes and other extracellular vesicles in venous whole blood – Isolated RNA, DNA and proteins	Accepted PWI Stage 10
1.5	…for venous whole blood – Isolated circulating cell free RNA from plasma	Accepted PWI Stage 10
1.6	…for urine and other body fluids – Isolated cell free DNA	Accepted PWI Stage 10
1.7	…for Fine Needle Aspirates – Part 1: Isolated cellular RNA	Accepted PWI Stage 10
1.7	…for Fine Needle Aspirates – Part 2: Isolated proteins	Accepted PWI Stage 10
1.7	…for Fine Needle Aspirates – Part 3: Isolated genomic DNA	Accepted PWI Stage 10
1.8	…for human specimen – Isolated microbiomes	Accepted PWI Stage 10
1.9	…for metabolomics in urine, venous blood serum and plasma	Accepted NWI (ISO)
1.10	…for formalin-fixed and paraffin-embedded (FFPE) tissue – Part 4: In situ detection techniques	NWI in proposal (ISO)
Key: PWI – Preliminary work item, NWI – New work item		

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) are currently being finalized to enter the final approval stage by 2019/Q1.

The saliva document (task 1.3) is now in the final approval stage and planned to be published as CEN/TS 17305 in 2019/Q2, while the frozen tissue document (task 1.4) has been published as CEN/TS 16826-3:2018 in July 2018. For further developing, the latter has additionally been brought into proposal stage as an ISO standard.

Next to the finalization of these projects, work on the second wave of projects (task 1.5 to task 1.8) has commenced. All projects have successfully entered the CEN proposal stage as preliminary work items (PWI) to be turned into new work items by 2019/Q1.

Both task 1.9 and task 1.10 are projects that start directly on ISO level. Task 1.9 has been accepted as a new project ISO/NP 23118 and work in the preparatory stage has begun.

Once finished, the documents created within WP 1 will complement the existing standard documents initiated by SPIDIA with the aim of creating and implementing a comprehensive portfolio of 22 pre-analytical CEN Technical Specifications and ISO International Standards, addressing the important pre-analytical workflows applied to personalized medicine.

An important milestone towards this goal is marked by the publication of the first 5 EN ISO standards on pre-analytical workflows by the end of 2018. These documents, first initiated as CEN Technical Specifications within SPIDIA and then developed as International Standards under the Vienna Agreement, have reached successful global recognition and are now available as 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.*

In 2019, this list will be even further extended by the soon-to-be published 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!

SPIDIA

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

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
In 2019, this list will be even further extended by the soon-to-be published documents **ISO 20186-1,** Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for venous whole blood – Part 1: Isolated cellular RNA and **ISO 20186-2,** Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for venous whole blood – Part 2: Isolated genomic DNA	

SPIDIA4P

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

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

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The External Quality Assurance (EQA) programme in SPIDIA4P

IBBL has continued supporting SPIDIA4P (Standardisation of generic Preanalytical Procedures for In vitro DIAgnostics for Personalised Medicine) as provider of EQAs.

Quality in pre-analytical workflows

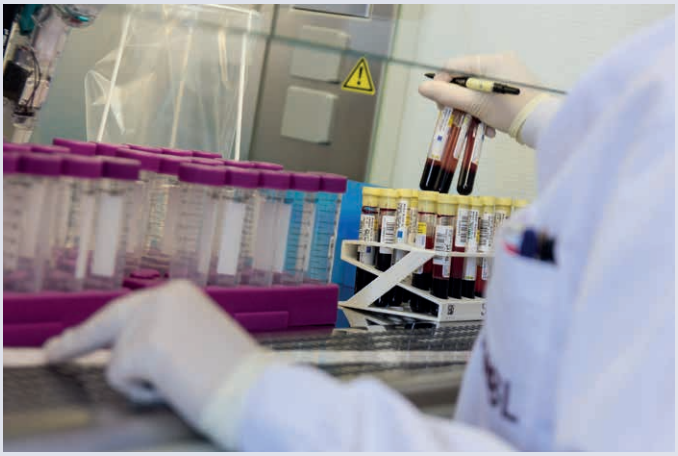
IBBL is one of the few biobanks that carries out biospecimen research and develops in-house quality control assays to ensure that biological samples are suitable for their intended downstream purposes. As such, one of its main matters of concern is the contribution to the standardisation of biobanking practices through the development of global technical standards that will guarantee reproducible results.

SPIDIA4P (Standardisation of generic Preanalytical Procedures for In vitro DIAgnostics for Personalised Medicine) seeks to initiate, develop and implement a comprehensive portfolio of 20 pan-European CEN Technical Specifications (CEN/TS) and ISO International Standards (ISO/IS) documents, as well as corresponding external quality assurance schemes (EQAs). These TS cover the pre-analytical workflows applied to personalised medicine, from documentation of patient information to sample collection, transport, processing and storage. They will also be applicable to research such as biomarker discovery, development, validation, as well as to biobanks, thus being a topic of particular interest and relevance for IBBL. SPIDIA4P is the follow-up of the earlier SPIDIA project, which set the foundation for the development and introduction of the first CEN/TS for pre-analytical workflows in Europe and for their progress to ISO standards.

As the leader of Work Package 2 (WP2), IBBL's role in SPIDIA4P focuses on the development and implementation of External Quality Assurance (EQA) schemes that accompany the pre-analytical procedures. 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. Specifically, IBBL's expertise as the sole provider of Proficiency Testing (PT) programmes entirely dedicated to biospecimens proves to be an asset for the activities of WP2. Indeed, IBBL's ISBER-endorsed PT programme acts as an EQA tool for a variety of institutions handling biological samples (laboratories, biorepositories, etc.), allowing them to validate their routine processing and analytical methods, compare their performance to that of others, comply with regulatory requirements and strengthen their credibility and visibility. Notably, IBBL has developed both a series of 'processing schemes', which allow the verification and benchmarking of the performance of biospecimen processing methods, as well as 'analytical schemes', focusing on the accuracy of the measurements. Given its proven effectiveness, IBBL's existing PT programme provides the basis for the development and deployment of new PT schemes for the pre-analytical processing methods.

In 2018, IBBL's existing EQA schemes have been enriched by the consortium and included DNA and RNA isolation from whole blood samples, DNA extractions from saliva and stool, DNA and RNA isolation from frozen and FFPE (formalin fixed and paraffin embedded) samples. Additionally, EQA schemes on protein isolation from FFPE and from tissue samples and on liquid biopsies have been developed – namely isolation of cfDNA, ccfRNA and circulating tumour cells from whole blood. Different partners have collaborated and supported these developments in various ways. Technical University of Munich have supported the protein extraction schemes by evaluating the homogeneity of the "processing items" and performing the downstream analyses. LGC are preparing new "in-process quality control materials" that are expected to be ready in the coming months. Fundacio Centre De Regulacio Genomica Barcelona and University of Florence have supported the evaluation of DNA and RNA respectively from both FFPE and frozen tissue items. The data from the above analyses have been analysed by the Unit of Bioinformatics and Biostatistics Milano. Last but not least, a collaboration agreement has been signed between SPIDIA4P and the IMI consortium CANCER-ID that will allow SPIDIA4P to benefit from the CANCER-ID experience and developments in terms of EQA schemes in the area of liquid biopsy (cell free DNA, circulating cell free RNA and circulating tumour cells), and that will also allow CANCER-ID to contribute to the relevant TS documents.

We are all looking forward to the conclusions from the EQA schemes described above and to a fruitful collaboration between the two consortia.



WP3 DISSEMINATION // DR. GIORGIO STANTA / DR. SERENA BONIN

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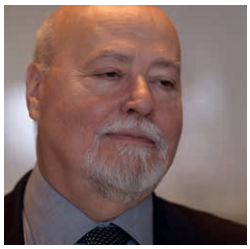

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UNIVERSITÀ DEGLI STUDI DI TRIESTE

THE IMPORTANCE OF NETWORKING AND TRAINING:

NEW DEVELOPMENTS IN PRACTICAL ONCOLOGY

Dr. Giorgio Stanta, Dr. Serena Bonin – Universita degli Studi di Trieste, Italy (UNITS)

One of the major problem in oncology today is to exchange reliable molecular analysis results among different oncologic institutions. To solve this, several networking initiatives have been established that ensure the exchange of latest results, findings and decisions.

One of these unions is **OECI**: the Organization of European Cancer Institutes involves over 90 cancer institutes in Europe with an important accreditation system. This accreditation is both for clinical part and also for clinical research and the organization is expanding also outside European borders. The exchangeability of molecular data reported on clinical records should be guarantee in all European institutions, it is connected to the problem of reproducibility of diagnostics and clinical research and mostly related to three major issues: 1. pre-analytical condition of biological material, 2. standardization of the methods and 3. careful evaluation of intra-tumour heterogeneity.

Also recently in the last OECI meeting in Poznan, Dr. Uwe Oelmueller, coordinator of the SPIDIA4P project, was invited to explain how CEN technical specifications could improve reproducibility of technical analysis.

We are working now to introduce CEN documents in the accreditation procedures. The Biobanking and Molecular Pathology working group of OECI has also started to prepare documents on methods standardization with the production of guidelines for whole exome sequencings (NGS) and for plasma-DNA analysis and is preparing new documents. A new type of standardized sampling of tumour tissues, taking into consideration the intra-tumour heterogeneity analysis, has been proposed.

Another important initiative, connected with OECI but also with European Society of Pathology and other European organizations, is a recent initiative related to the development of a **European Molecular Pathology Master**. The purpose is to prepare new professionals that have a common language. The master is open to molecular biologists, but also to pathologists and oncologists. The first year will be dedicated to oncological and infective diseases molecular diagnosis and the second one to clinical research. Also a wide practical training is planned. The new precision oncology should be also strictly related to bioinformatics and AI facilities, to accredited clinical research centers and reference laboratories. All this can be done only if a common language and knowledge is present in the new professionals acting in this field.

OECI Oncology Days 2018

https://www.esp-pathology.org/_Resources/Persistent/5afdc2602589aed418870b11d26c4b030d81055f/OECI%202018%20ONCOLOGY%20DAYS.pdf

WP4/6 / ETHICS // DR. PETER RIEGMAN

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Compliance to ethics rules and regulations within the SPIDIA4P consortium

In SPIDIA4P biomaterials, data and copyrighted material as well as publications that can contain intellectual property are used. The work done in the SPIDIA4P consortium must of course comply to the rules, regulations and ethics. Every participant is obliged to follow these. Therefore there needs to be adequate oversight if all the work is being done according to the rules, regulations and ethics, locally and in a European context. In general, when following the local rules, regulation and ethics the data and biomaterials can be used within the consortium.

Keeping control of compliance
To keep the oversight over the consortium SPIDIA4P has taken up an entire work package to deal with this challenge. It has according to the work package installed a committee called Ethics and Intellectual Property Committee (EIPC), that is the instrument forming the web to safeguard all the SPIDIA4P work is done according to the rules that apply to the work. The EIPC was constituted by the SPIDIA4P management. The management made sure the EIPC consists of all members from every participating institute. In addition, a chair was appointed who was also the work package leader of ethics of SPIDIA4P. The EIPC started with the development of a protocol for the EIPC already in the start of the project. In this protocol the duties of all members are described. One of them is, that every member has the obligation to report any non-compliance to rules and regulations related to SPIDIA4P activity. The later ensures that all participants send in their material for review.

The European Commission has also determined what the consortium must comply to before the project was given the green light to start. The later was defined in an extra work package. It describes what needs to be documented and send to the committee before the work described in the documents can start. This means before biomaterials and or data can be used in SPIDIA4P it must be documented how local rules and regulations are complied to. There must be arguments and proof submitted what rules apply including if consent was needed or not and if needed how it was obtained. Also how the new privacy laws are followed in case of using data. If consent was needed than it is important that within the consent European cooperation with other institutes is mentioned, which is one of the main differences with local use and use in a European consortium.

Human biomaterials used in SPIDIA4P:
The country of origin determines the limitations of use of a human sample. 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 the 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 and anonymous pre-analytical workflow parameters. Nonetheless, the European privacy legislation must be followed, which recognizes coded data as well as personal data.

Animal biomaterials used in SPIDIA4P:
The SPIDIA4P consortium need 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.

Copyrights and intellectual property rights:
Where it concerns copyrights and intellectual property rights the EIPC has to see all publications before it is being released in the public domain. This concerns not only articles for scientific publications, but also all developed tools, presentations, material presented in workshops and webinars. Also all on-line publications are included. Since there is an extensive work package on dissemination this can be quite a busy task. On the web site you can see all dissemination activities and all were checked.

With the described methods of control the SPIDIA4P consortium is kept on track to comply to the sometimes complex rules and regulations that apply to the work done within the consortium.

REPORTS FROM SPIDIA4P PROJECT MEMBERS // DR. TIM FORSHEW

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Inivata highlights the importance of standardization and pre-analytics

Inivata is a leader in the liquid biopsy field with a primary focus on circulating tumour DNA analysis. Their technology is based on pioneering research from the Cancer Research UK Cambridge Institute and The University of Cambridge and backed by multiple high calibre publications. They were invited to join the SPIDIA4P consortium in order to demonstrate that not only is a focus on both standardization and pre-analytics important to cancer patient care, but also to the success of SMEs working in the in vitro diagnostics space. Inivata's objective within SPIDIA4P is to monitor, then report back on the impact standardized pre-analytical workflows have on the success of the company. At the recent consortium meeting in Hilden, Dr Tim Forshew, a co-founder of Inivata gave a first update on their progress.

He described the completion of a US multi-centre prospective validation study of their InVisionFirst-Lung liquid biopsy test. The study recruited 264 patients with untreated advanced NSCLC at 41 US centres. Circulating tumour DNA was analysed in all patients. Tissue-based NGS testing was performed for the 178 patients where sufficient tissue was available. Not only did the InVisionFirst assay demonstrate excellent concordance with tissue profiling but in fact led to the detection of 26% more actionable alterations than standard of care tissue testing. Dr Forshew described how, a critical focus for Inivata over the four years since its inception have been on the pre-analytical phase of cell free DNA analysis. This included for example the standardisation of blood collection into stabilisation tubes and the optimisation and validation of cell free DNA extraction. Without such a focus, sensitivity would vary significantly from patient to patient meaning that regardless of the strengths of the analytical method, studies like this would not yield such exciting results. Although work is ongoing for Inivata this highlights the importance of the efforts of the SPIDIA4P consortium and beyond to improve and standardise pre-analytics globally and the impact this can have on SMEs.

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 2018 below.

May 2018

Successful Course "CEN and ISO Standards for Pre-analytical Processes"

The course organized by Institute of Pathology of the Medical University of Graz, SPIDIA4P, QIAGEN and BBMRI.at and held in Graz, Austria, raised awareness about the existence and relevance of the CEN Technical Specifications and ISO Standards and of standardizing pre-analytical processes in R&D and medical diagnostics. International participants learned about which CEN Technical Specifications (CEN/TS) "In-Vitro Diagnostic examinations – Specifications for Pre-examination Processes" have already been published and which pre-analytical CEN/TS and ISO Standards are under development.

The main focus of the course on May 16, 2018, was on demonstrating their relevance for medical diagnostics and research and development (R&D), particularly in the context of the new In-Vitro Diagnostic Regulation. The development process of standards was introduced and an overview on the structure and scope was presented.

The major pre-analytical factors and their influence on analyses results in pathology and human genetic laboratories were addressed and examples how to implement the standards were shown. Participants also had the opportunity to test the BBMRI-ERIC online Self-Assessment Tool. All participants rated the course 'excellent'.

Read the full article and get the presentations here

http://www.bbmri-eric.eu/news-events/pre-analytical-sample-processing-in-biobanking-a-3-days-laboratory-course

http://bbmri.at/news/-/asset_publisher/xLKisOx4tBQH/content/successful-course-on-cen-and-iso-standards-for-pre-analytical-processes

SPIDIA4P EVENTS // PAST EVENTS + COURSES / HIGHLIGHTS

September 2018

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

http://europebiobankweek.eu

- **Dr. Uwe Oelmueller** – Standardized and Improved Pre-analytical Workflows: A Key for Reliable Diagnostics, Research and Biobanking
- **Dr. Kurt Zatlouka**l – Role of Public-Private-Partnerships in Biobanking
- **Dr. Andrea Wutte** – Session Chair for "Quality Assessment and Management of Samples and Data"
- **Dr. Cornelia Stumptner**
- **Dr. 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 Self-Assessment Survey Tools for sample quality

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

The ISBER 2018 Annual Meeting, May 20-24, 2018 in Dallas, Texas, USA, with the subtitle Thinking BIG in TEXAS: Seizing BIG Opportunities in BIOBANKING Through Data, Collaboration and Innovation was an excellent platform for several SPIDIA4P project members who have been invited as speakers from IBBL- Dr. Fay Betsou and Dr. Olga Kofanova and QIAGEN – Dr. Uwe Oelmueller.

Presentation Titles: **Dr. Olga Kofanova:** PBMC Score: Gene Expression Ratio Indicates Peripheral Blood Mononuclear Cell (PBMC) Quality

Dr. Fay Betsou: Biospecimen Research in Clinical Fluid Specimens; A Summary from the 2018 ISBER Biospecimen Research Symposium

Dr. Uwe Oelmueller was invited to take part in the Symposium: Small Steps in in Quality Management leads to Big Results, presentation title: Standardized and Improved Pre-analytical Workflows: Crucial for Reliable Diagnostics, Research and Biobanking

http://meetings.isber.org/2018/

Austrian Society of Pathology | Autumn Meeting (Graz, AT) | Sep 27-28, 2018

- SPIDIA Consortium (presenter **C. Stumptner**, MUG); "Upcoming quality requirements for molecular pathology" (poster presentation)
- **C. Stumptner et al.** (MUG); "Self-assessment tool for molecular diagnostics to check pre-analytical workflows" (poster presentation)

Austrian Association of Molecular Life Sciences & Biotechnology Annual Meeting | Sep 17-20, 2018

- **C. Stumptner et al.** (MUG); "Austrian biobanking network BBMRI. at – a partner for research using biological samples"; (poster presentation); (Poster introducing BBMRI.at and highlights also the implementation of the CEN/TS & ISO standards in BBMRI.at partner biobanks and the work on the BBMRI Self-Assessment Survey Tools)

SPIDIA4P EVENTS // PAST EVENTS + COURSES

In total, the SPIDIA4P project members held more than 50 courses for different target groups – these are only some of the planned courses. Get ready to take part in the upcoming courses in 2019!

TATAA Biocenter, **Experimental design and statistical data analysis for qPCR**
April 16–20, 2018
Prague, Czech Republic

http://www.ibt.cas.cz/sd/udalosti/kalendar/180416-qPCR-courses.html

TATAA Biocenter, **qPCR data analysis – implementation of the new CEN and ISO guidelines for the pre-analytical process in molecular diagnostics**
May 14–18, 2018
Gothenburg, Sweden

http://www.tataa.com/courses/course-descriptions/cen-iso-technical-specifications/

BBMRI.QM Webinar, **Presentation of the upcoming new: "CEN technical standard for the pre-analytical phase of frozen tissue samples for DNA isolation"**
Peter Riegman, Head of Erasmus MC Tissue bank

http://www.bbmri-eric.eu/news-events/05a-bbmri-qm-webinar/

Erasmus Medical Center, **Summer School of Perzonalized Medicine**
June 19–22, 2018
Warsaw, Poland

http://teach2018.com/en/

TUM, **First BRoTHER Biobanking Summer School**
September 24–28, 2018
Regensburg, Germany

https://www.ukr.de/imperia/md/content/service/veranstaltungen/2018/bro-1809.pdf

Medical University of Graz, **Master of Science Biobanking**
October 1, 2018
Graz, Austria

https://postgraduate-school.medunigraz.at/universitaetslehrgaenge/masterlehrgaenge/master-of-science-biobanking/

Medical University of Graz / Biobank Graz, **Course "How to build a biobank"**
Nove,ber 28–30, 2018
Graz, Austria

http://bbmri.at/documents/10194/71587/Biobanking++Course_How+to+build+a+biobank.pdf/589f8127-8dc8-4221-9ef2-06d5a437c759

EXAMPLE OF A NEW POSTER BY SPIDIA4P PROJECT MEMBERS

UPCOMING QUALITY REQUIREMENTS FOR MOLECULAR PATHOLOGY

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BACKGROUND & AIM

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

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

METHOD

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

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

RESULTS

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

1 Why Standards?

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

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

2 Examples of Standards

Published:[5]

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

In development:

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

3 Content

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

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

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

4 Relevance for Molecular Pathology

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

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

Excerpt from IVDR Annex II

6. PRODUCT VERIFICATION AND VALIDATION

6.1. Information on analytical performance of the device

6.1.1. Specimen type

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

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

SUMMARY

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

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SPIDIA4P EVENTS // UPCOMING EVENTS + COURSES

2019

Get ready to meet the SPIDIA4P members at conferences and trainings in 2019! Upcoming courses can also be found on:

www.spidia.eu.

WORKSHOP

SPIDIA4P STAKEHOLDER WORKSHOP AT THE EUROPEAN PARLIAMENT hosted by MEP Gesine Meissner (ALDE, Germany) and MEP Lieve Wierinck (ALDE, Belgium)

March 5, 2019

Brussels, Belgium

REGISTRATION

http://www.bbmri-eric.eu/news-events/save-the-date-spidia4p-event/

EVENTS

IFOM CONGRESS "CANCER-RELATED BIOBANKS: A VALUE FOR TRANSLATIONAL RESEARCH AND PRECISION ONCOLOGY"

March 21, 2019

Milan, Italy

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

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

COURSES

March 9, 2019

3 courses at the 9th Gene Quantification Event qPCR dPCR & NGS 2019

https://gene-quantification.de/qpcr-dpcr-ngs-2019/main-2019.html

Freising, Germany (TATAA Biocenter in collaboration with Technical University of Munich)

March 21–22, 2019

Basic realtime qPCR Application Workshop 2 days

Analysis of Gene Expression data – qPCR, RNASeq, Microarray and Nanostring, 2 days

NGS – Library and construction quality control, 2 days

Freising, Germany (TATAA Biocenter in collaboration with Technical University of Munich)

March 28, 2019

In conjunction with Biobank Sweden Annual meeting

Quality control and new guidelines in Molecular analysis and Biobanking

REGISTRATION

Gothenburg, Sweden (TATAA Biocenter in conjunction with Biobank Sweden Annual Meeting)

SPIDIA4P PUBLICATIONS // ARTICLES

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https://www.sciencedirect.com/science/article/abs/pii/S0165993618302395

SPIDIA4P PARTNER // CONSORTIUM MEETING LUXEMBOURG

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

On April 10 and 11, 2018 IBBL hosted the SPIDIA consortium meeting in their new premises in Dudelange, Luxembourg, chaired by the project coordinator QIAGEN GmbH.

On the first day, the event provided an overview of the project and its advancement, before delving into the detailed progress report, status and action points specific to the various work packages (WP). In particular, day 1 focused on WP1 (Development of new pan-European and International Standards for pre-analytical workflows needed for Personalized Medicine), WP2 (Develop External Quality Assessment Schemes for the pre-analytical phase), WP4/6 (Project Ethics/data privacy and IP issues and IP management and Ethics requirements) and WP5 (Management). The session terminated with a dinner, where participants had the opportunity to exchange on the proceedings of the day.

The first half of the second day was entirely dedicated to discussions on the status of tasks, decisions and action points under WP3 (Implementation and Dissemination of Standards & External Quality Assurance Schemes). The session ended with the Governing Board meeting.

The SPIDIA4P project members at the 3rd Consortia Meeting in Dudelange, Luxembourg

SPIDIA4P PARTNER // CONSORTIUM MEETING HILDEN

On November 20 and 21, 2018, the Coordinator QIAGEN GmbH welcomed all SPIDIA4P project partners at the German headquarters in Hilden.

As always, this two-day meeting was an excellent opportunity for face-to-face exchange about the latest activities and status within the separate Work Packages, like already implemented CEN/TS and successful events and trainings, as well as discussions and decisions about the next steps and further plans.

All project members enjoyed and appreciated this very well-prepared and efficient meeting that laid the basis for the future project progress, and are looking forward to the next meeting in 2019, hosted by our project partner CNAG-CRG, Fundacio Centre De Regulacio Genomica, in Barcelona in May 2019.

The SPIDIA4P project members at the 4th consortium meeting at the QIAGEN headquarters in Hilden, Germany

SPIDIA4P NEWS // WEBSITE *www.spidia.eu*

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Coming soon!

In order to provide you with the latest news and information about the project, a comprehensive redesign is being made which includes:

- **new website structure** – find the requested information faster than before
- **new technical design** – compatible also for mobile devices
- **new modern layout** – state-of-the-art design

Currently planned for going online mid of March 2019 – stay tuned!

www.spidia.eu

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