SPIDIA4P Newsletter 01/2018

SPIDIA4P Homepage (www.SPIDIA.eu)

News about the SPIDIA4P project, including up-to-date lists of events where to meet us, downloads of SPIDIA4P posters and presentations, links to other organisations and related initiatives are posted regularly on our homepage. There you can also find more information about the background of the project and about the SPIDIA4P partners. If you have questions or ideas, you can also get into contact with us using the „Contact Us“ form. Feel free to visit us at www.SPIDIA.eu!

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About The Project

SPIDIA4P - Taking the Next Step!

Started on January 1st, 2017, the goal of the 48-month project SPIDIA4P (Standardisation of generic Pre-analytical Procedures for In vitro DIAgnostics for Personalised Medicine) is to go the next steps towards healthcare systems improvements with worldwide impact by developing and implementing a comprehensive portfolio of 20 European pre-analytical CEN/Technical Specifications and ISO/International Standards, addressing the important pre-analytical workflows applied to personalised medicine. These will also be applicable to research such as biomarker discovery, development, validation as well as to biobanks. Furthermore, corresponding External Quality Assurance (EQA) Schemes will be developed and implemented, aiming to survey the resulting diagnostic practice. SPIDIA4P will ensure training, education, and counselling as additional major foci of the project.

SPIDIA4P's highly successful predecessor SPIDIA laid the basis for developing and introducing the first 9 CEN Technical Specifications (CEN/TS) for pre-analytical workflows into European countries and initated their progress to ISO standards. Like SPIDIA, the current SPIDIA4P project is again bringing together key experts of numerous stakeholder organisations with deep knowledge on pre-analytical and analytical procedures, European and international standardisation organisations´ processes (CEN and ISO), external quality assurance, quality management, ethics and regulatory demands.

The SPIDIA4P consortium will closely coordinate with large European public research consortia to obtain access to research and validation studies data, serving as evidence for the new standards developments for achieving improvements of diagnosis, patient stratification and prognosis of disease outcome. It is funded by the European Union's Horizon 2020 research and innovation programme and consists of 19 highly experienced partners from private industry including SMEs, public institutions and the European Standards Organisation CEN.

Based on the success of SPIDIA coordination, QIAGEN has been renewed as Coordinator unanimously in SPIDIA4P.

SPIDIA4P Partners

- QIAGEN GmbH
- LGC Limited
- Technische Universität München, TUM
- DIN Deutsches Institut für Normung e.V.
- PreAnalytiX GmbH
- Inivata Ltd
- Cambridge Protein Arrays Ltd
- TATAA Biocenter AB
- Universita degli Studi di Firenze, UNIFI
- Consorzio Interuniversitario Risonanze Magnetiche di Metallo Proteine, CIRMMP
- Universita degli Studi di Trieste, UNITS
- Universita degli Studi di Torino, UNITO
- Biobanking and BioMolecular Resources Research Infrastructure Consortium, BBMRI-ERIC
- Luxembourg Institute of Health, IBBL
- Medizinische Universität Graz, MUG
- Institut National de la Santé et de la Recherche Médicale, INSERM
- Erasmus Universitair Medisch Centrum Rotterdam, EMC
- Fundacio Centre de Regulacio Genomica, CNAG-CRG
- Fondazione IRCCS Istituto Nazionale dei Tumori, INT

Award for SPIDIA and SPIDIA4P

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

During the Global Biobank Week 2017 in Stockholm (http://mailchi.mp/bbmri-eric/global-biobank-week-2017-as-it-happened-1928821?e=7171b79409), Dr. Uwe Oelmueller, project coordinator of SPIDIA4P, was honoured for his comprehensive merits on European and International pre-analytical standardisation with the "DIN Golden Honary Needle".

Dr. Oelmueller works since 1995 at QIAGEN, the leading provider of Sample-to-Insight solutions to transform clinical and biological samples into valuable molecular insights. As Vice President, he is heading the technology center for Diagnostic Sample Technologies within QIAGEN's global Molecular Diagnostics business area.

From 2008 to 2013, Dr. Oelmueller coordinated the SPIDIA project "Standardisation and improvement of generic pre-analytical tools and procedures for in-vitro diagnostics" 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 4 and the deputy convenor of the CEN/TC 140 Working Group 3.

SPIDIA4P´s Project Progress

Development of New pan-European and International Standards for Preanalytical Workflows Needed for Personalised Medicine

The SPIDIA4P Work Package 1 (WP1) is focused on the development of new pan-European and International Standards for selected high priority pre-analytical workflows needed for personalised medicine. These will be evidence based on research results provided by collaborating partners outside of SPIDIA4P, combined with expert knowledge on routine in vitro diagnostic laboratory practice and quality laboratory performance. In order to consider available relevant European research results, WP1 will incorporate data generated during the European FP7 project SPIDIA, by collaborating partners such as IMI CANCER-ID, UK STRATFix, CBmed Austria, CD-Laboratory Graz, EXCEMET, PhenoMeNal and EurocanPlatform as well as data generated during studies by different consortium members into standardisation. Thereby, SPIDIA4P aims to reduce the number of sample-based diagnostic errors, and non-reproducible pre-clinical and clinical studies. WP1 also targets to improve and speed up biomarker discoveries research, development and validations for reinforcing the era of personalised medicine and innovations in patient care.

To follow-up with our goals, SPIDIA4P identified the following 11 urgently needed pre-analytical workflows for molecular in vitro diagnostic examinations for:

- in venous whole blood circulating tumour cells – Isolated DNA / RNA
- in venous whole blood circulating tumour cells – preparation for analytical CTC staining
- saliva – Isolated DNA
- frozen tissue – Isolated DNA
- venous whole blood exosomes – Isolated cell-free circulating RNA
- urine and other body fluids – Isolated cell-free DNA
- fine needle aspirates – Isolated RNA / DNA / Proteins
- saliva and stool microbiomes – Isolated DNA

The development of 11 standard documents for these identified workflows will be handled on the European level within the European Committee for Standardisation (CEN). First, CEN Technical Specifications (CEN/TS) will be developed. These will be subsequently introduced into the international standardisation organisation ISO for further optimisation including addition of international requirements and recommendations. The envisioned end-results are EN ISO Standards.

SPIDIA4P is currently working on the first five CEN/TS documents on the list above within the CEN Technical Committee 140 "In vitro diagnostic medical devices". In 2019, the remaining six projects will be started.

Additionally, SPIDIA4P plans on developing a new EN ISO Standard based on the currently published CEN/TS 16945, "Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for metabolomics in urine, venous blood serum and plasma". The proposal has already been circulated for voting within ISO. The SPIDIA4P consortium also envisions preparing a new EN ISO Standard on "Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue for in situ detection techniques". This ISO document aims to give requirements for the sample collection, storage, transport, handling, processing and documentation during the pre-examination phase of formalin-fixed and paraffin-embedded (FFPE) tissue specimens intended for in situ examinations of the tissue morphology and for in situ analyses of biomolecules such as proteins, DNA and/or RNA, on FFPE tissue sections by using different in situ detection techniques. The work for both standardisation projects will start directly on the international level within ISO Technical Committee 212 "Clinical laboratory testing and in vitro diagnostic test systems".

External Quality Assurance (EQA) for Pre-analytical Workflows

As the only Biospecimen Proficiency Testing (PT) programme in the world that is focused on biospecimens, IBBL's (Integrated BioBank of Luxembourg) programme works as an External Quality Assessment (EQA) tool for laboratories working with biospecimens, biorepositories, research organisations and bioservice providers. Endorsed by the International Society for Biological and Environmental Repositories (ISBER), the PT programme allows these laboratories to validate their routine processing and analytical methods, compare their performance to that of others, comply with normative requirements, gain credibility & visibility, improve their performance and prove their consistency.

Within the SPIDIA4P Work Package 2, led by IBBL, the consortium develops and implements PT schemes for the pre-analytical phase. SPIDIA4P develops schemes for processing methods, covering the biomolecular extraction/isolation steps of the pre-analytical workflow. These schemes are built on IBBL's existing PT programme.

SPIDIA4P will enrich some of these existing processing EQA schemes with clinically relevant endpoints:

- DNA isolation from whole blood samples
- RNA isolation from whole blood samples
- Viable PBMC isolation from whole blood samples
- CSF processing
- DNA isolation from FFPE samples
- RNA isolation from FFPE samples

SPIDIA4P intends to develop the following new EQA schemes:

- ccfDNA isolation from whole blood samples
- Circulating Tumour Cells isolation from whole blood samples
- DNA isolation from saliva samples
- DNA isolation from stool samples
- ccfRNA isolation from whole blood samples
- DNA isolation from frozen tissue samples
- RNA isolation from frozen tissue samples
- Protein isolation from FFPE tissue samples

For some of the schemes, SPIDIA4P relies on the work previously performed by IBBL in collaboration with other consortia:

- JPND Biobanking Working Group for the CSF Processing scheme
- IMI CANCER-ID consortium for the schemes for isolation of ccfDNA, ccfRNA and circulating tumour cells from whole blood.

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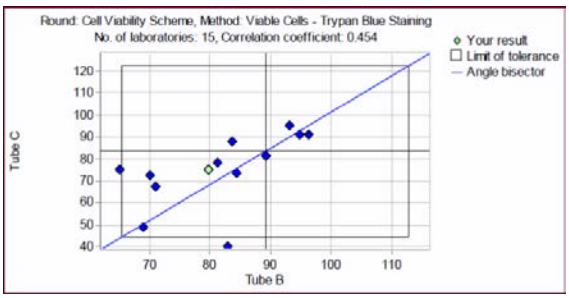

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Implementation and Dissemination of Standards & External Quality Assurance Schemes

The pre-analytical phase still accounts for the majority of errors in molecular diagnostics. Therefore, the need for standards to improve the pre-analytical processes when handling biological specimens became evident. The EU project SPIDIA laid the ground for the development of a series of CEN Technical Specifications for molecular in vitro diagnostic examinations – specifications for the pre-examination processes (CEN/TS), which address specific pre-analytical quality requirements for blood and tissue samples as well as the most relevant analytes (i.e., DNA, RNA, proteins and metabolites). The first 9 CEN/TS have already been published by the European Committee for Standardisation (CEN) and some will become International ISO Standards in 2019 or thereafter. In addition, more pre-analytical CEN/TS and ISO Standards are being developed in SPIDIA4P.

One of the main goals of SPIDIA4P is to increase the awareness about these CEN/TS and the EN ISO Standards among the relevant target groups (such as molecular in vitro diagnostic laboratories, biobanks and developers of diagnostics), achieve their acceptance, and foster their implementation.

This goal is addressed in Work Package 3 (WP3) "Implementation and Dissemination of Standards & External Quality Assurance Schemes" in which the following partners cooperate: Medical University of Graz, Austria (lead), QIAGEN, Inserm, TATAA, BBMRI-ERIC, Erasmus University Medical Center, PreAnalytiX, University of Florence, IBBL, INIVATA, LGC, DIN, Technical University of Munich, CIRMMP, University of Trieste, University of Torino.

In detail, WP3 aims to:

- Achieve broad acceptance of the CEN and ISO pre-analytical standard documents.
- Explore and elicit national and European funding programs to implement standards.
- Facilitate the implementation of CEN and ISO pre-analytical standardisation documents at accredited and nonaccredited laboratories in all personalized medicine related segments (diagnostics, biomedical/translational research, biobanking etc.).
- Communicate about the EQA schemes in the biobank, research laboratory and clinical laboratory communities.
- Develop training and education for diagnostic laboratories, diagnostic assay developers, researchers and biobanks.
- Reinforce by electronic and oral communication the awareness for the need to implement pre-analytical standards for improved sampling procedures in clinical routines as well as in translational schemas which is essential for improving health care.
- Offer the dissemination of standards in such a way that it complies with the confidentiality needs of the CEN and ISO standard documents to be protected through engagement with regulators.

Some steps towards the WP3 goals regarding education and training to support implementation have already been achieved. This includes developing and providing education & training for diagnostic laboratories, biobanks, researchers, or diagnostic assay developers, such as courses, webinars, videos etc.

SPIDIA4P Courses

Past Courses

- **"Introduction SPIDIA4P in the Work Programme for BBMRI"** BBMRI-ERIC WG web conference
  January 26, 2017
  http://www.bbmri-eric.eu/category/news-events/web-conferences/

- **"Introduction to Venous Whole Blood processes"** BBMRI-ERIC WG web conference
  February 7, 2017
  http://www.bbmri-eric.eu/category/news-events/web-conferences/

- **"Introduction to SF and FFPE Tissue processes, SPIDIA4P, ISO/TC 212"**, BBMRI-ERIC WG web conference
  February 7, 2017
  http://www.bbmri-eric.eu/category/news-events/web-conferences/

- **"Pre-Analytical Sample Processing in Biobanking": 3 Day Laboratory Course**
  Feb 8-10, 2017, Graz, Austria, given by BBMRI.at, Medical University of Graz, Austria (for details please see article below)
  http://www.bbmri-eric.eu/news-events/pre-analytical-sample-processing-in-biobanking-a-3-days-laboratory-course/

- **"Large Scale computing for metabolomics",** BBMRI-ERIC WG web conference
  March 16, 2017
  http://www.bbmri-eric.eu/category/news-events/web-conferences/

- **"SPIDIA4P Progress"**, BBMRI-ERIC WG meeting
  April 11, 2017
  http://www.bbmri-eric.eu/category/news-events/web-conferences/

- **"CEN/TS for venous whole blood",** BBMRI-ERIC WG web conference
  April 20, 2017
  http://www.bbmri-eric.eu/category/news-events/web-conferences/

- **"UNIFI activities and tasks in SPIDIA4P"**, BBMRI-ERIC WG web conference, May 19, 2017
  http://www.bbmri-eric.eu/category/news-events/web-conferences/

- **"Body fluid metabolomics by NMR, SPIDIA4P activities and tasks of CIRMMP"**, BBMRI-ERIC WG web conference
  June 6, 2017
  http://www.bbmri-eric.eu/category/news-events/web-conferences/

- **"EQA for biobanks and research labs"**, BBMRI-ERIC WG web conference
  June 8, 2017
  http://www.bbmri-eric.eu/category/news-events/web-conferences/

- **"SPIDIA4P and OECI"**, BBMRI-ERIC web conference
  July 7, 2017
  http://www.bbmri-eric.eu/category/news-events/web-conferences/

- **3rd qPCR & Digital PCR Congress**
  July 27-28, 2017, Philadelphia, USA by TATAA
  http://www.globaleventslist.elsevier.com/events/2017/07/qpcr-digital-pcr-congress-usa/

- **Liquid Biopsies course at the EMBL**
  Oct 09-13, 2017, Heidelberg, Germany, by TATAA
  https://www.embl.de/training/events/2017/LIQ17-01/index.html

- **"Digital Pathology"**, BBMRI-ERIC WG web conference
  November 23, 2017
  http://www.bbmri-eric.eu/category/news-events/web-conferences/

Next Courses

- **"Experimental design and statistical data analysis for qPCR"**
  April 16-20, 2018, Prague, Czech Republic
  www.ibt.cas.cz/sd/udalosti/kalendar/180416-qPCR-courses.html

- "**qPCR data analysis – implementation of the new CEN and ISO guidelines for the pre-analytical process in molecular diagnostics"**
  May 14-18, 2018, Göteborg, Sweden
  http://www.tataa.com/courses/course-descriptions/cen-iso-technical-specifications/

International Biobanking Experts at "Preanalytical 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 in samples. Avoiding errors in the pre-analytical phase of processing biological samples such as tissue or blood is a prerequisite for proper diagnoses and reliable research results and requires knowing the potential sources of error and establishing proper procedures for processing biological samples. Recently, 9 CEN Technical Specifications for molecular in vitro diagnostic examinations – specifications for the pre-examination processes (CEN/TS) – have been published that give guidance what to consider when collecting, processing, and storing samples for specific purposes. The organiser of the course, Medical University of Graz (coordinating the Austrian Biobanking and Biomolecular Research Infrastructure BBMRI.at) is SPIDIA4P member and thus centrally involved in the development of CEN/TS and EN ISO Standards.

Learning through hands-on, this 3-day laboratory course put this into practice. Participants learned about the CEN/TS requirement while practically working with a sample 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 /Med Uni Graz, who was responsible for the practical part, Andrea Wutte from BBMRI-ERIC, Ingrid Walter and Helmuth Haslacher from the BBMRI.at partners Vet Biobank and Med UniWien Biobank 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 one of Europe's largest biobank.

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Where to Meet Us

SPIDIA Partners give regularly presentations about the project and their results on various congresses. For more information on the events, please refer to the SPIDIA / SPIDIA4P homepage: www.spidia.eu.

Upcoming Events

- **ISBER Biospecimen Research Symposium: Quality Matters**

  February 27-28, 2018, Luxembourg

  https://isber.site-m.com/page/LuxeGeneralInfo

- "**qPCR data analysis – implementation of the new CEN and ISO guidelines for the pre-analytical process in molecular diagnostics"**

  May 14-18, 2018, Göteborg, Sweden
  http://www.tataa.com/courses/upcoming-courses/

- **Europe Biobank Week**
  September 4-7, 2018, Antwerp, Belgium
  http://europebiobankweek.eu

Past Events

- **Pre-analytical Sample Processing in Biobanking Course**
  Graz, Austria
  Feb 08-10, 2017
  http://bbmri.at/news/-/asset_publisher/xLKisOx4tBQH/content/international-biobanking-experts-at-bbmri-at-course-in-graz
  Oral presentations:
  - K. Zatloukal: Pre-analytical Sample Processing in Biobanking Course - Introduction & The Case for Pre-analytics
  - C. Stumptner: Conformity with CEN/TS and ISO Standards

- **qPCR dPCR NGS 2017 symposium**
  3-7 April, 2017, Freising, Germany
  http://www.qpcr-dpcr-ngs-2017.net/
  Oral presentation:
  - J. Björkman: How to monitor analytical and technical factors influencing qPCR

- **Inaugural Advances in Companion Diagnostics Congress**
  London, UK
  April 24-26, 2017
  http://www.rsc.org/events/detail/23167/Advances%20in%20Companion%20Diagnostics%20Congress%202017
  Oral presentation:
  - M. Kubista: "Quality Aspects And Tools In Molecular Diagnostics – Implications Of The New CEN And ISO Guidelines"

- **CORBEL meeting "How European Biological and Medical Sciences Research Infrastructures boost Innovation by Open Access"**
  Brussels, Belgium
  June 20, 2017
  http://www.corbel-project.eu/innovation-by-open-access-meeting.html
  Oral presentation:
  - U. Oelmueller: High Quality Clinical Samples: The Key for Reliable Diagnostics and Research

- **OECI Oncology Days 2017 – Pathology Day Conference**
  Brno, Czech Republic
  June 21-23, 2017
  https://www.esp-pathology.org/events-newsroom/events/congresses-events/unnamed-1.html
  Oral presentation:
  - S. Bonin: SPIDIA4P: Preanalytical Conditions of Tissues

- **Advanced Medicinal Therapy Products seminars, NLS days**
  Malmö, Sweden
  September 12, 2017
  https://www.nlsdays.com/about-the-event/
  Oral presentation:
    - M. Kubista: "Quality Aspects And Tools In Molecular Diagnostics – Implications Of The New CEN And ISO Guidelines"

- **Global Biobank Week**
  Stockholm, Sweden
  Sep 13-15, 2017
  http://www.globalbiobankweek.org/
  Chairs of Session 10C: Quality Assessment – A Key Factor for Successful Biobanks and Reproducible Science
  Oral presentations:
    - L. Krieger: SPIDIA4P - New International and European Standards for Biobanking in the making - Join us now!
    - P. Riegman: Technical Specifications for Collecting Diagnostic Samples: The Tool to Increase the Reproducibility of Results
    - P. Riegman: Opt out for residual materials preferred over signed informed consent (WMA declaration of Taipei)
    - G. Dagher: International Standards for Biobanks
    - Kurt Zatloukal: Innovative Technology and its Contribution to Biobanking
    - S. Neururer, C. Stumptner, K. Zatloukal: Implementation of Self-Assessment Surveys Based on the CEN/TS for Pre-Examination Processes
    - U. Oelmueller: High Quality Blood ccfDNA Specimen: The Key to reliable Analytical Test Results

- **49th National Congress of SIBioC– Laboratory Medicine (Italian Society of Clinical Biochemistry and Clinical Molecular Biology)**
  Florence, Italy
  Oct 16-18, 2017
  www.congresso.sibioc.it
  Poster:
    - P. Pinzani: SPIDIA4P: SPIDIA for Personalized Medicine - Standardisation of generic Pre-analytical procedures for In vitro DIAgnostics for Personalised Medicine

- **Summer School in Translational Cancer Research**
  Algarve, Portugal
  Oct 16-20, 2017
  http://www.cancercoreeurope.eu/events/summer-school-in-translational-cancer-research-2017.html
  Poster:
    - C. Ciniselli et al.: The European SPIDIA and SPIDIA4P Projects

- **Inauguration Event of the Austrian Platform of Personalised Medicine**
  Vienna, Austria
  Oct 19-20, 2017
  http://bbmri.at/news/-/asset_publisher/xLKisOx4tBQH/content/biobanks-in-personalized-medicine
  Oral presentation:
    - K. Zatloukal: The Role of Biobanks in Personalised Medicine

  Booth & Poster:
    - C- Stumptner: BBMRI.at – the Austrian National Node of BBMRI-ERIC

- **Standardisation in Life Sciences**
  Split, Croatia
  Oct 23-25, 2017
  One dedicated session on Biobanks
  http://www.hatz.hr/wp-content/uploads/2017/08/SPLIT.pdf
  Oral presentation:
    - G. Dagher: Quality really matters
    - G. Stanta: New developments in clinical research: standardisation as a basis for reproducibility of results

- **Biobanche nell'era della medicina personalizzata: obiettivi e sfide- Innovazione del sistema salute in Umbria**
  http://www.siadhealthcare.com/eventi/biobanche-nellera-della-medicina-personalizzata-obiettivi-sfide-innovazione-del-sistema-salute-umbria/
  Perugia, Italia
  October 27-28, 2017.
  Oral presentation:
    - S. Bonin: Condizioni preanalitiche dei tessuti (Preanalytical conditions of tissues)

- **OMICS 2017**
  Varadero, Cuba
  October 31, 2017
  http://biomed.cigb.edu.cu/omics17/omics17default.aspx
  Oral presentation:
    - M. Kubista: "Two-tailed PCR for ultrasensitive detection of microRNAs and some general quality concepts in molecular analyses"

- **Annual Biobank China 2017 & International Symposium on Precision Medicine**

  Changsha, China
  November 30-December 3, 2017
  Oral presentation:
    - G. Dagher: Quality of biological samples: A major issue

- **6th National Biobank Symposium**
  Berlin, Germany
  Dec 6-7, 2017
  http://www.biobanken.de/de-de/symposium/symposium2017_top/symposium2017.aspx
  Oral presentation:
    - U. Oelmueller: "Standardized Pre-analytical Workflows: The Key for Reliable Diagnostics, Research and Biobanking"

SPIDIA4P Publication

- **BBMRI-ERIC Magazine**
  Issue No.6/2017 "Knowledge-Experience-**Quality**-Trust"
  http://www.bbmri-eric.eu/wp-content/uploads/2017/02/2017_Newsletter6_7_WEB.pdf

SPIDIA4P Partners at the SPIDIA4P meeting in September 2017 in Florence, Italy

Colophon
SPIDIA4P, QIAGEN GmbH - QIAGEN Strasse 1 - 40724 Hilden - Germany

This project has received funding from the European Union's H2020 Framework Programme. CSA-Project H2020, Proposal # 733112