Regions4PerMed

Interregional Coordination for a fast and deep uptake of Personalised Health

Regions4PerMed

Key Area 4: Innovation Flow in the Healthcare

Report

HORIZON 2020

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DESCRIPTION

This report summarizes the content elaborated within the Interregional Conference and Workshop which took place online in Santiago de Compostela in July 2021 and in November 2021

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1 Overview of the Key Area 4: Innovation Flow in the Healthcare

Research is the cornerstone of the development of new medical approaches leading to more knowledge and innovation advances thanks to omics technologies among others. The advances of genomics and other "omics" in recent years, have paved the way to a "new medicine", tailored to the patient and which is known as Personalised Medicine (PM).

In 2014, the Horizon 2020 Advisory Group has defined PM as a medical model using characterization of individuals' phenotypes and genotypes (e.g., molecular profiling, medical imaging and lifestyle data) to tailor the right therapeutic strategy to the right person at the right time, determine the predisposition to disease and deliver timely and targeted prevention. Personalised Medicine is not only based on adapted-patient diagnosis and treatments, but also envisages the prevention of diseases before their outset.

Research and Innovation are at the basis of personalised healthcare services, therapeutics, diagnostics for citizens and patients.[1]

Institutional awareness and the commitment of policy and decision makers in all member States and regions across Europe are crucial to facilitate the Research and Innovation flow into European healthcare systems, contributing to personalised and patient-centered healthcare and medicine.

Research and Innovation (R+I) should be supported by relevant policy strategies, including the creation of solid R+I infrastructure exploitation models, deployment of suitable financial instruments and the correct screening and assessment of the outcomes obtained with R+I initiatives. The application of the supportive strategy will lead to the desired outcomes and products from R+I projects.

[1] *The evolution of personalised healthcare and the pivotal role of European regions in its implementation, Future Medicine, 2021.*

European Local and Regional Authorities (LRAs) are a driving force of Health Research, Innovation and Healthcare modernization and need to be engaged in joint and coordinated policies in Europe to avoid fragmentation, ensure successful development of strategic initiatives and multiply benefits for citizen, industry academia and policy makers.

The main aim of the Key Thematic Area 4 (KA4), titled Innovation Flow in the Healthcare, was to address and tackle the main barriers that are holding back the adoption, at regional level, of health innovation for Personalised Medicine into healthcare systems, encompassing different stages, ranging financial tools to invest in R+I, regional infrastructures for development and clinical validation on new Personalised Medicine solutions and approaches.

2. Key Area 4 Conference

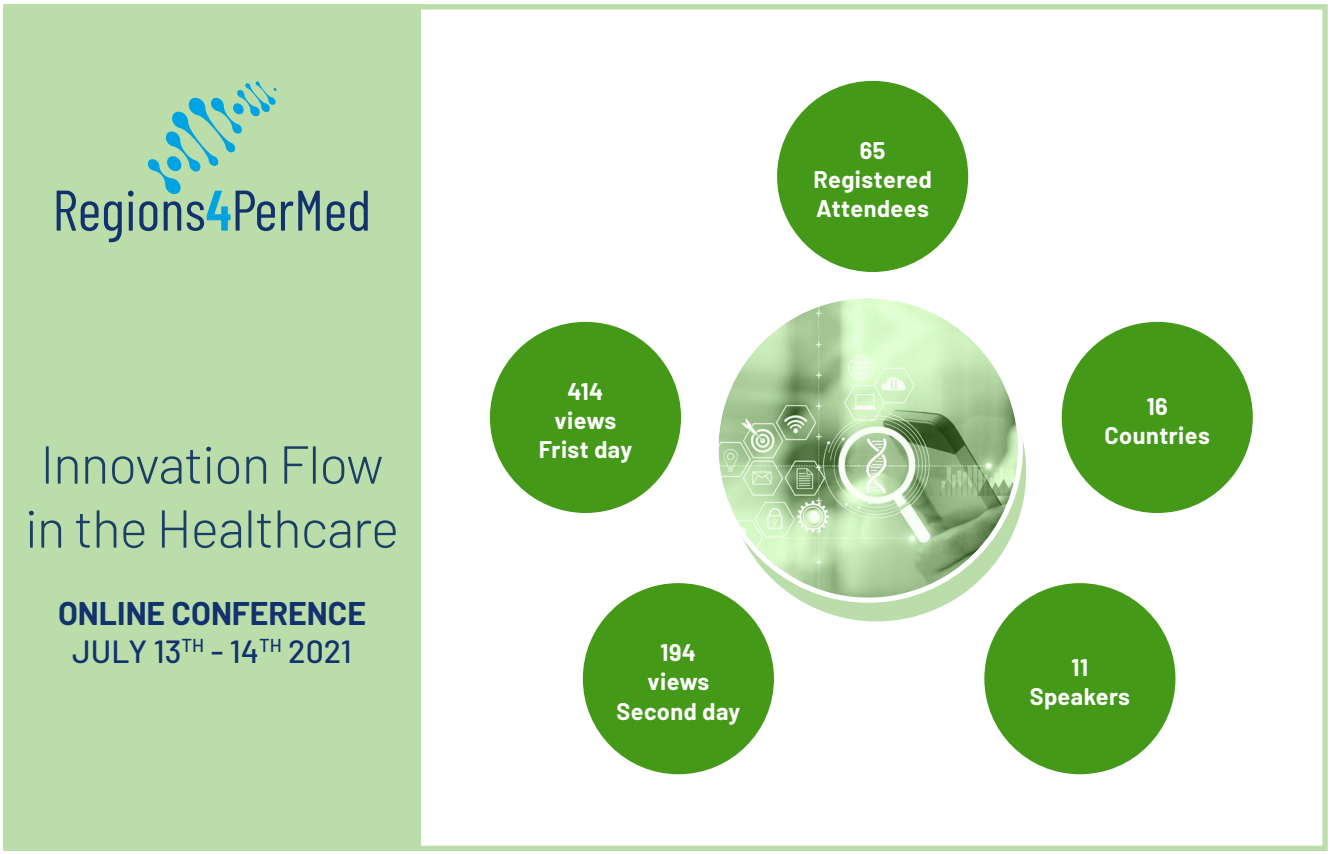


Figure 1. *KA4 Conference in a nutshell*

In July 2021 the fourth technical conference of the Regions4PerMed Project titled "Innovation Flow in the Healthcare" was organized by the Galician Health Knowledge Agency of the Galician Public Health System (SERGAS). The conference was held online due to the COVID-19 pandemic situation.

The Key Strategic Area 4 (KA4) focused on the main strategies to facilitate innovation flow into the healthcare system including the following aspects: R+I infrastructures (exploitation models such as by creating private-public partnerships or interregional networks for sharing data records), screening and prevention programs, financial instruments including innovative procurement tools such as Pre-Commercial Procurement (PCP) and Public Procurement of Innovation (PPI) as well as testing clinical outcomes from Personalised Medicine (PM) technologies (testing prototypes for further development in the future, performing validation

models for solutions and services before placing in the market, testing validated solutions and services...).

Within the conference we examined of the impact of the previously described strategies, and potential solutions and outcomes that can be implemented at a regional level:

- **Research and Innovation (R+I) models to boost innovation:** R+I infrastructures are the motor for the scientific and technical progress in healthcare and in Personalised Medicine in particular. Through these models the development of new technologies is possible, as well as services such as screening and prevention programs.
- **Financial instruments to support innovation:** The commitment and awareness of public institutions is crucial to boost innovation in healthcare. By employing proper supportive financial instruments, a public or private organization can facilitate innovative solutions for patient-centered new healthcare services.
- **Innovative Procurement Tools: Pre-Commercial Procurement (PCP) and Public Procurement of Innovation (PPI):** are prominent procurement and financial tools that enable the access from designing to testing to state-of-the art technologies, services, and prototypes in the healthcare system.

The speakers and the audience of the conference were experts in healthcare sector from academia, industry, public institutions and organizations as well as representatives from regional and governmental entities from different EU Member States. The numbers of the participation to the Conference are summarized in Fig.1.

2.1 OPENING SESSION

Healthcare quality is a crucial aspect that EU citizens are aware of. For this reason, legal and institutional organizations and stakeholders should consider the population's concerns for the implementation and enforcement of new policies focusing on building strong and efficient healthcare systems. In this sense, policies should prioritize the development on research and innovation related to Personalised Medicine.

The engagement of authorities will be crucial for the creation of sustainable healthcare systems. For this reason, the opening session of the conference was based on setting up the building blocks for the implementation of Personalised Medicine in regional health systems.

Antonio Fernández-Campa, **ACIS Managing Director from Galician Health Knowledge Agency (ACIS) – Spain**, presented the experience of the Galician Health Service (SERGAS) in innovative public procurement projects to obtain new advanced therapies (such as those obtained by Código100 project) as well as the recent implementation of the living lab model in Complexo Hospitalario de Ourense via the LABSAÚDE network, endorsing Galicia as a reference region in innovative projects on PM. He remarked the recognition of Galicia as a benchmark in the adoption of innovative practices for active and healthy ageing with 4 stars by the European Commission.

Jorge Aboal Viñas, **General Director of the Health Assistance Department from Galician Health Services (SERGAS) – Spain**, presented the SERGAS strategy to Personalised Medicine , from finished to ongoing projects related to PM. Through integrated electronic health records and an electronic prescription system, care and therapies are always adapted to all the information available on the patient, since health personnel have direct access to all the information available on the imaging and laboratory tests, pathologies and active medication of the patient. He highlighted the role of the Galician Public Foundation for Genomic Medicine that enables access to the genomic tests for required diagnosis and treatments, particularly prenatal diagnosis, pharmacogenomics, rare diseases and germline cancer. The Galician Public Foundation for Genomic Medicine is also enrolled in the IMPaCT (Precision Medicine Infrastructure related to Science and Technology) program and international initiatives such as the 1+Million Genomes (1+MG), the International Rare Diseases Research Consortium and the International Cancer Genome Consortium. Mr. Aboal remarked research initiatives like the Roche-CHUS Joint Unit and the SERGAS new strategy on advanced therapies, CART-T therapies. The roadmap of SERGAS PM and Cellular

Figure 2. *Host greetings from the headquarters of ACIS*

Therapies Strategies for Galicia is closely linked to the Galician Oncology Plan and the Galician Strategy for Rare Diseases. He highlighted the Galician translational medicine mechanisms increasing the co-operation between researchers and the biotechnology industry and guaranteeing access to key technologies such as proteomics for its introduction in clinical laboratories and creation of biobanks.

Following the opening session, the day continued with sessions dedicated to different topics.

2.2 SESSION I

Focused on "Research and Innovation (R+I) models to boost innovation". The session was chaired by **José María Romero Fidalgo** from the **Galician Health Knowledge Agency (ACIS).**

Gary Saunders, **Human Data Coordinator** from **ELIXIR Hub – United Kingdom**, introduced the role of regions and the use of genomic data in PM among jurisdictions across Europe.

ELIXIR is a research infrastructure that connects national bioinformatics centers with the European Bioinformatics Institute (EMBL-EBI) as a sustainable European wide infrastructure for biological research data by facilitating discoverability, access, sharing and analysis of genomics data, including rare diseases at large scale of participants. He introduced some initiatives that ELIXIR developed to move towards cross-border access to Beyond One Million human sequenced Genomes (B1MG) and the related healthcare data and how this data is applied to Personalised Medicine programs across the EU Member States.

Gary Saunders stressed that sustainable, in-place, stable and agile investments for infrastructures in a federated system are the ideal approach to maximize the opportunities for PM.

He also remarked the relevance of political willingness and the 1+ Million Genomes (1+MG) roadmap. 1+MG aims to define the requirements for accessing genomics and PM data, to translate requirements into technical specifications and implementation guidelines and to drive adoption and support to long-term operations.

Dr. Saunders explained some use cases from ELIXIR Hub, mostly rare diseases, infectious diseases, cancer or common complex diseases. He brought the attention of the audience over a key aspect which was citizens' trust who are the ultimate data owners.

Lastly, he explained the hurdles around infrastructures and data sharing during the COVID-19 crisis; however, the pandemic situation led to the identification of priorities to move forward and to redefine healthcare. It was shown that the most critical factors are interoperable standards that are needed to operate in an international federated system and networks of trust at all levels.

Take home messages:

- Regions must be involved in the construction of sustainable infrastructures for human genomics and translational data in Europe by facilitating discoverability, access, sharing and analysis of genomics data;
- The generation of an interregional federated system for human data management across jurisdictional access to data cannot disregard the regional dimension and the regional stakeholders;
- Citizens' trust is the key element of genomics data, since they are data owners;
- Healthcare systems should be redefined based on lessons learned in the COVID-19 pandemic.

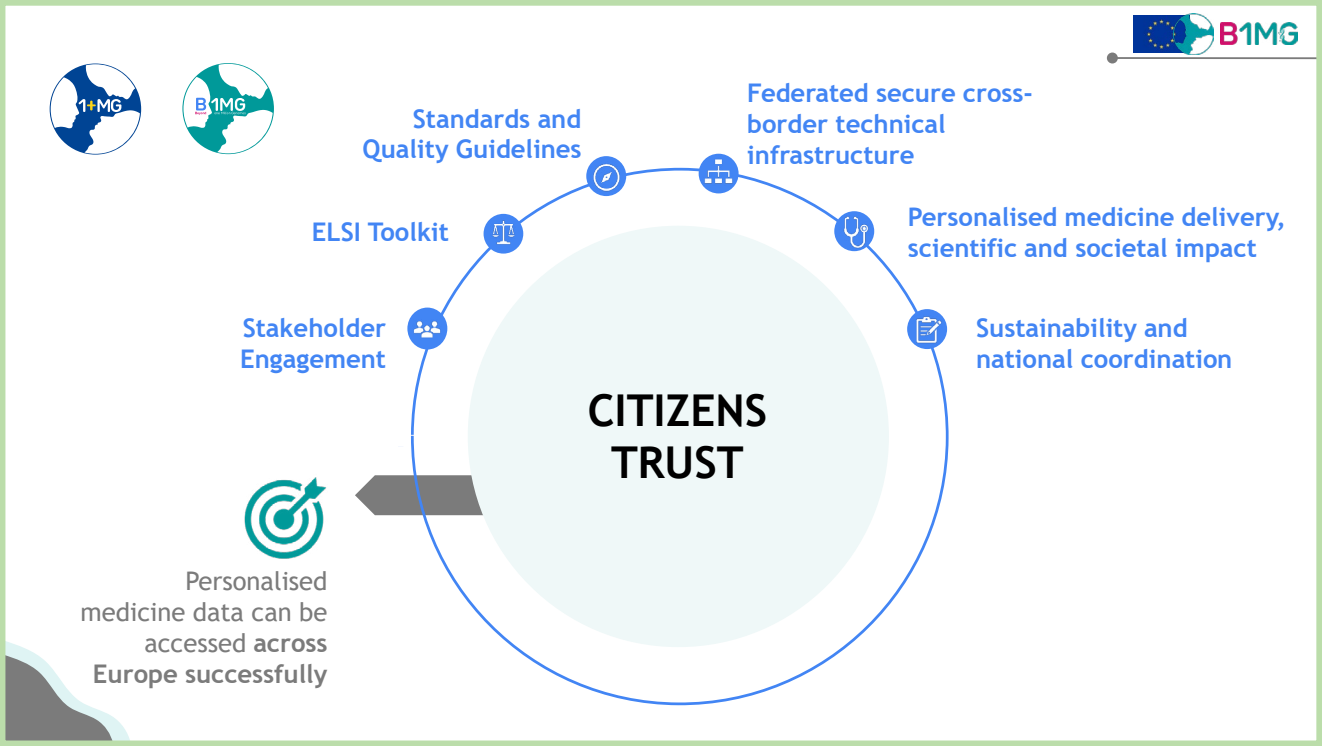


Figure 3. Citizens' Trust

Andrea Damiani, **Head of Artificial Intelligence R&D** from **Gemelli Generator - Italy**, presented the management and the application of real-world data to support hospital research centers. Different components are necessary to perform *in silico* clinical trials including synthetic cohorts, knowledge and data (epidemiology, biological, clinical trials and real-world patient data), disease model and therapeutic model.

He described five main problems to be addressed in the management of big data:

- velocity (obtaining results as quickly as possible);
- value (extracting multidimensional results);
- veracity (being confident on data and models);
- variety (using all available data sources) and
- volume (being able to count on a great number of data items by extent and time length).

Andrea Damiani presented the basis of the XAI (eXplainable Artificial Intelligence) framework whose objective is to show patients that the management of their data is ethical and leads to results in favor of patients, thus, ensuring patient trust.

Prof. Damiani highlighted the experience of integrating, storing and managing big data at Gemelli Generator. He described different collaborations among entities or healthcare facilities for innovative solutions always remaining proprietary during the data management.

Lastly, he presented an application of the XAI framework in colorectal surgery, easily understandable for doctors, called Colorectal Surgery Dashboard. Through this, doctors can comparatively analyze a patient's clinical parameters using the Gemelli system to provide statistics for reference subgroups, giving information on possible symptoms and the patient's potential evolution after surgery.

Take home messages:

- Regions need to invest to ensure the enhancement of Vs of big data: velocity, value, veracity, variety and volume;
- The establishment of PM and value based healthcare cannot disregard the local and regional dimension; the ethical management of big data for gaining patient trust is essential;
- Institutes that use big data should maintain and regions should enforce the compliance with the standards of proprietary information.

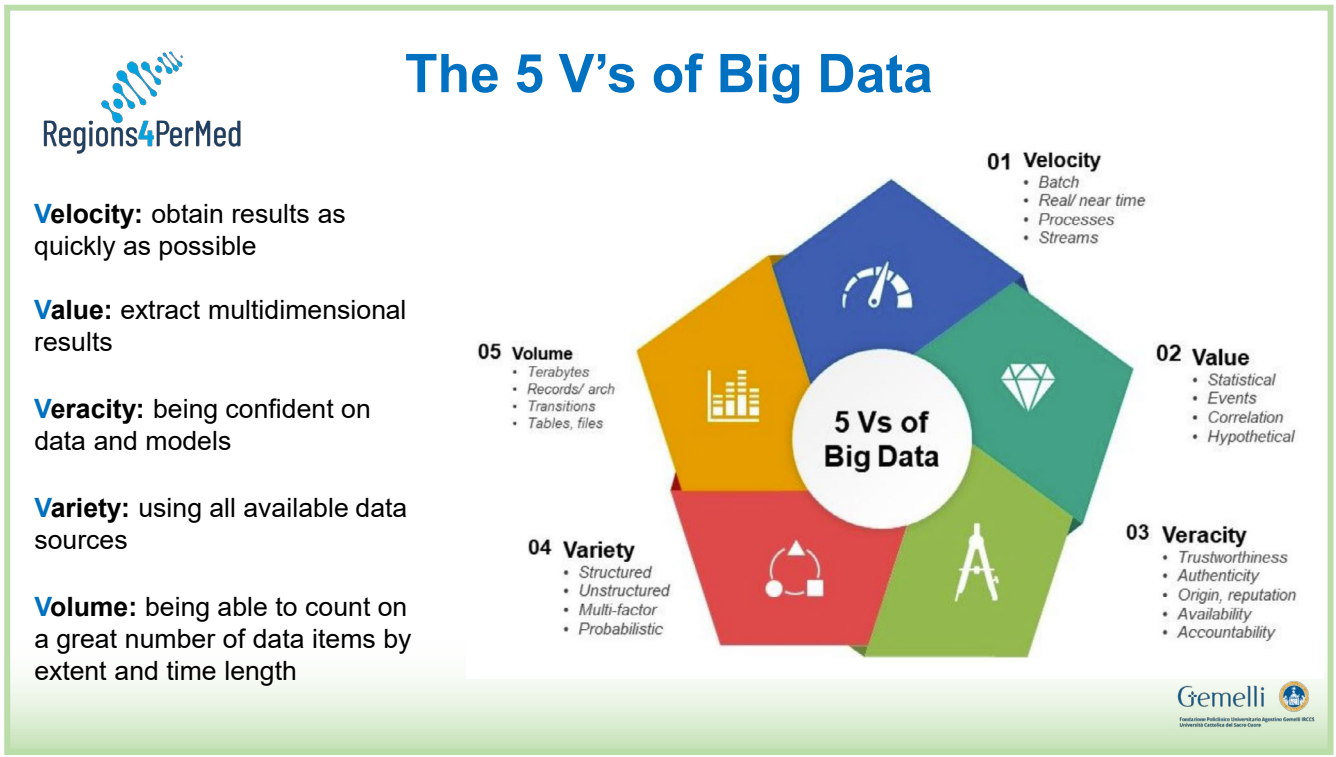


Figure 4. The 5 Vs of Big Data

Evdokimos Konstantinidis, **President of the European Network of Living Labs (ENoLL) - Greece**, introduced the European Network of Living Labs which has the mission to promote and enhance user-driven innovation ecosystems and who has coordinated the VITALISE project.

He highlighted the role of Living Labs as methodologies for developing and improving activities by co-creation, registration, multi-method approach, real-life settings, multi-stakeholder participation and active user involvement. Each new member of ENoLL should undergoa labeling and certification procedure for evaluating its organization, openness to co-creation and value creation for the involved stakeholders. For proper operation of ENoLL, the labeling and certification procedure should be harmonized.

The Virtual healTH Adn WeLlbeing Living Lab InfraStructurE (VITALISE) project is a methodology and approach on harmonizing the procedure of Living Lab (protocol, data collection, evaluation) and Information and Communication Technologies (ICT) tools (data sharing or data processing). VITALISE is a H2020 project with a duration of 36 months which aims to harmonize the Living Lab Health and Well-being Living Lab procedures and services. VITALISE offers researchers open access to more advanced research services guaranteeing the research community an exchange of knowledge and technologies. The methodology consists of three steps:

harmonization phase, the Joint Research Activities (JRA) phase and the invitation of external researchers for the evaluation of the effectiveness of the harmonized services and procedures.

Finally, he presented three research studies within the VITALISE project based on rehabilitation, transitional care and everyday living environment, involving 17 Living Lab infrastructures across seven countries with more than 300 researchers.

Take home messages:

- Harmonization is necessary to improve the labeling and certification procedure for Living Labs to become part of the European Network of Living Labs (ENoLL);
- Through examples such as VITALISE project research communities obtain access to existing health and well-being Living Lab infrastructures.

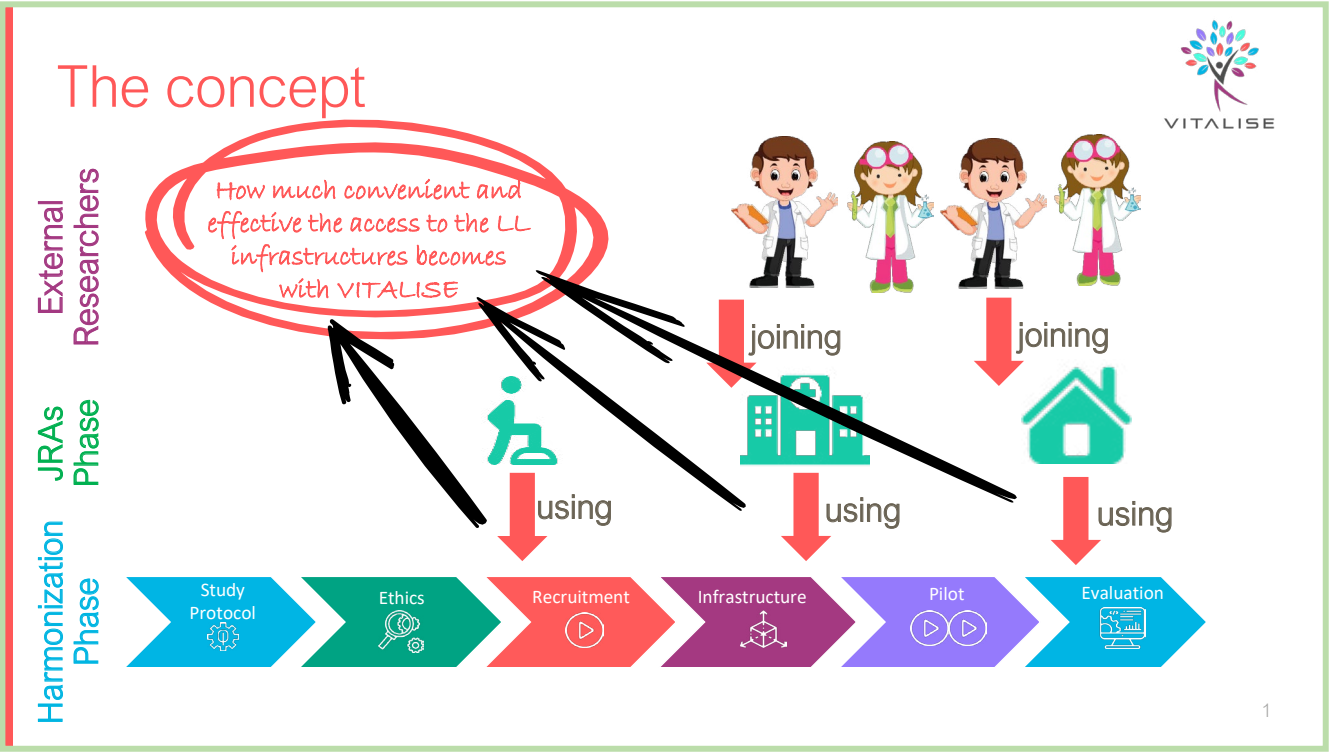


Figure 5. The methodology of VITALISE project

2.3 SESSION II

Focused on "Financial instruments to support innovation". The session was chaired by **José María Romero Fidalgo** from **Galician Health Knowledge Agency (ACIS).**

Cristina Bescos, Senior Director in Digital Health from European Institute of Innovation and Technology (EIT)- EIT Health Spain, presented the European Institute of Innovation and Technology and its financial programs to boost Research and Innovation developments in Personalised Medicine.

Dr. Bescos presented the main goals of EIT Health that are strengthening healthcare systems, promoting better health of citizens and contributing to a sustainable health economy in Europe. EIT Health is based on three pillars: accelerator (supporting entrepreneurs and star-ups), education (new capabilities in digital skills, working procedures and co-creation) and innovation (promoting collaborative projects very close to the market).

As an accelerator, EIT Health Spain supported start-ups that raised funds for almost € 67 million in 2020. Dr. Bescos also highlighted the relevant role of EIT Health in innovation which brought 55 products or services to market.

She summarized the financial instruments that EIT Health offers to start-ups through the following four programs:

1) Investor network: an international network of investors that selects and evaluates different start-ups. This network connects health-oriented investors and promising start-ups through cross-border financing and co-investments made by 80 investors from 17 countries.

2) An international crowdfunding platform: open for start-ups from across Europe in the areas of MedTech, Biotech and Digital Health. The first pan-European venture capital platform (MOWOOT) that is exclusively dedicated to foster and fund innovation in the health sector.

3) Venture Center of Excellence: an innovation program of EIT in collaboration with the European Investment Fund to connect investors and other key stakeholders from the life sciences and healthcare ecosystems to enable a highly qualified pan-European deal flow for later stage growth and upscaling funding.

4) A collaboration with Horizon Europe: EIT is fully integrated in the third pillar, innovation, through an agreement between the European Innovation Council (EIC) and EIT. Its objective is to align innovation with funding opportunities. The Collaboration Workstreams is a new program that started on the 9th of July 2021 that brought the opportunity to access and employ

the investment funding of the EIC into all the EIT as well as using the capacity of the network (bootcamp, mentoring, internationalization…) and of the organization of joint events. That pathway is an example of European financial instruments aligned in the terms of Horizon program, the EIC, EIT and the European Investment Fund (EIF).

Conclusions/ take home messages (some advice to the Regions):

- Innovation platforms such as the EIT Health act as an accelerator and enhance education and innovation;
- Innovation is supported by EIT Health through four programs: investor network, international crowdfunding, venture center of excellence and Horizon Europe;
- Collaboration between EIT Health and the European Innovation Council (EIC) is boosting innovation procurement across Europe;
- Innovation is fully integrated within the Collaboration Workstreams by cooperation among three main institutions: EIC, EIT Health and the European Investment Fund (EIF).

Orestis Kalliantzidis, **Policy Officer in DG Connect in eHealth, Well-being and Ageing, from European Commission-Belgium,** presented the European Commission commitment, approaches and funding opportunities for innovation procurement in healthcare through the Horizon program. Horizon program is a useful instrument for the promotion of personalised medicine by reaching the gap between innovation development and its actual deployment and use by patients and healthcare personnel. Horizon Europe consists of different call topics for policy coordination, research and the deployment of innovation. The coordination support action (CSA) tackles the policy part, pre-commercial procurement topic (PCP), research, Public Procurement of Innovation (PPI) and the deployment of innovative solutions.

Within the Horizon Europe program, he focused on Pillar II: Global challenges and European Industrial Competitiveness with the first cluster related to Health and the Pillar III: Innovative Europe. Horizon Europe defines the European Commission policy priorities at EU level translating them into key strategic orientations and expected impacts, particularly for the health cluster.

He remarked that the expected impacts for the healthcare and for the health innovation procurement topics are framed in Destination 4 within Horizon Europe. Destination 4 states some basic impact areas, comprising the promotion of good health and high-quality accessible healthcare as well as the resilience

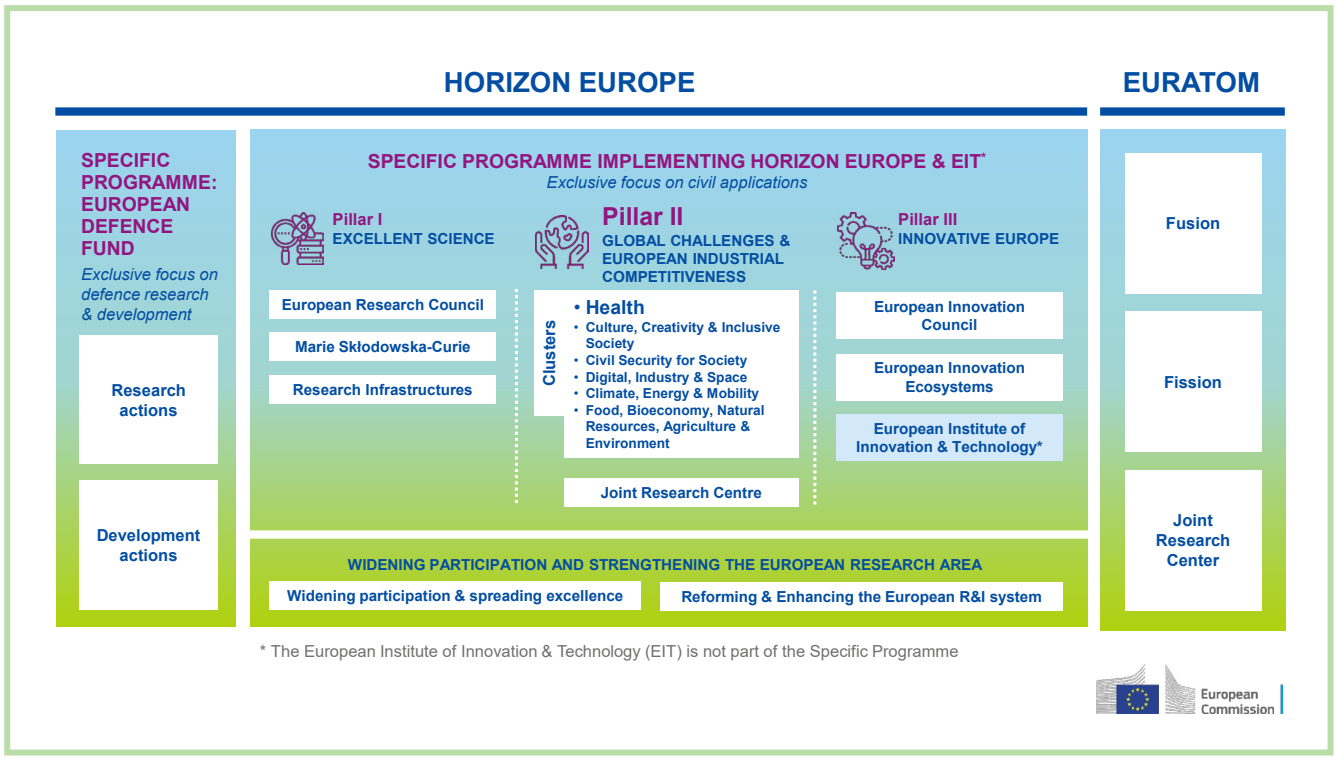


Figure 6. *Horizon Europe framework*

of healthcare systems and complementary impact areas like climate change mitigation and adaptation, high quality digital services and competitive and secure data economy.

He stressed the European Commission awareness of the relevance of public procurement of innovation in healthcare, in particular, as shown during the COVID-19 pandemic situation. The EU Commission carried out a benchmark study through DG Connect on innovation procurement which demonstrated that in Europe, investments and innovation procurement are two times lower compared to other leading global economies. This could be due to factors such as diverging policy and legal frameworks, language barriers, fragmentation of the European healthcare systems, different preferences of procurers and patients and risk aversion and lack of capacity to take advantage of opportunities.

Innovation procurement can increase the resilience of the supply chain by opening opportunities for European companies such as start-ups and SMEs, in particular, to access the public procurement markets, attract financial investment and scale up their business. These features are part of the expected outcomes under Destination 4.

He explained the work program, technical details and the key elements, activities and requirements of Horizon-HLTH-2021-CARE-05-04 (2021), which aims to create a healthcare innovation procurement network, including more and less experienced procurers from all sectors (clinical or procurement departments), to transfer knowledge and capacity-building.

Finally, Orestis Kalliantzidis presented two sister topics, PCP and PPI call topics for 2022 with the same expected impacts described in Destination 4 of the Horizon Europe Cluster 1 program, however, its mission is to increase the resilience of European healthcare systems in the context of the economic recovery. Through the PCP topic, the EU Commission would like to attract a consortium of procurers who aim to address needs that are not yet served by the market, such as research at the levels of solution design, prototype and development. With PPI, the needs can be addressed through solutions which are already close to the market, not requiring research but with the necessity to deploy in a real setting.

Destination 4: Topics in 2022

- HORIZON-HLTH-2022-CARE-08-02: **Pre-commercial research and innovation procurement (PCP) for building the resilience of health care systems in the context of recovery**
- Planned opening date: 06 October 2021
- Deadline date: **21 April 2022** 17:00:00 Brussels time
- Instrument: PCP
- Total budget: €25M
- Indicative proposal size: €5M

- HORIZON-HLTH-2022-CARE-08-03: **Public procurement of innovative solutions (PPI) for building the resilience of health care systems in the context of recovery**
- Planned opening date: 06 October 2021
- Deadline date: **21 April 2022** 17:00:00 Brussels time
- Instrument: PPI
- Total budget: 15M
- Indicative proposal size: €5M

European Commission

Figure 7. *PCP and PPI calls for 2022*

Take home messages:

- Destination 4 in Horizon Europe Cluster 1 program is about health and health innovation procurement. The regional authorities are expected to be the major beneficiaries of these measures;
- In Europe, investments and innovation procurement are two times lower compared to other global economies (i.e. US) due to factors like diverging policies or fragmentation of healthcare systems;
- Innovation procurement is crucial for modernizing the public sector and business growth, mainstreaming innovation procurement has the strategic importance to strengthen competitiveness;
- Healthcare innovation procurement network is necessary to ensure internal knowledge transfer and capacity-building;
- New calls of PCP and PPI are launched by the European Commission to increase the resilience of healthcare systems for economic recovery.

2.4 SESSION III

The session was chaired by **José María Romero Fidalgo**, Director **Health Development and Innovation Area (ACIS), Galicia, Spain.**

Rossana Alessandrello from the **Agency for Health Quality and Assessment (AQuAS), on behalf of Ramón Maspons Bosch - Spain,** presented the basics of public procurement of innovation (PPI) and the outcomes and benefits of PPI application in the healthcare system.

Public procurement of innovation is based on the statement "the needs must be defined by the demand", PPI investment starts with a clear definition of needs, which must be addressed by long-term and sustainable solutions via different approaches depending on geographic, economic and political settings of the respective regions.

Features such as strategy, innovation, citizens, analytics, evaluation and reimbursement are crucial for the correct implementation of public procurement of innovation (PPI).

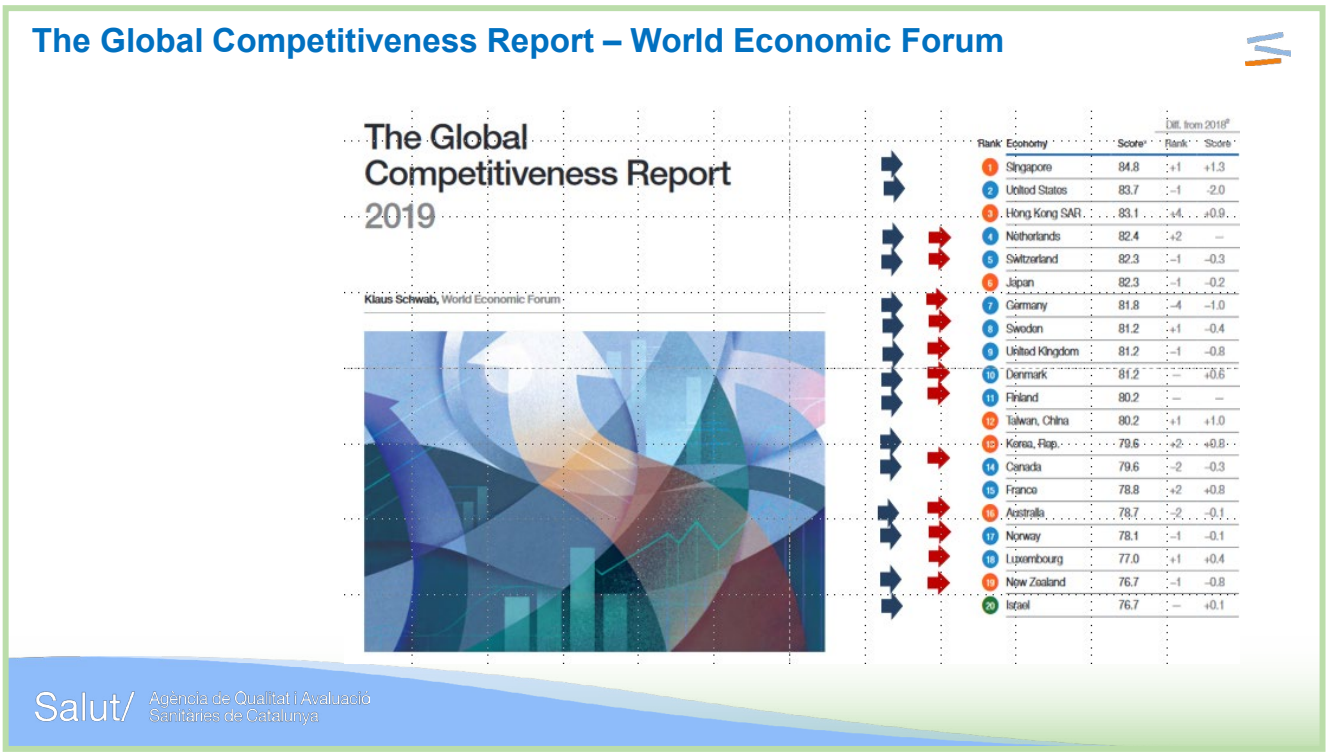


Figure 8. *Global Competitiveness Report 2019*

The **forces of attraction, information, interaction, rivalry and anticipation** that are common denominators in those 20 countries included in the Global Competitiveness Report of 2019, the combination of all forces leads those countries to be more competitive and become leaders in innovation worldwide. For this reason, all these forces **must be considered for the application of public procurement of innovation.**

Rossana Alessandrello highlighted that innovation in personalised medicine must reinforce prevention strategies for citizens from a long-term perspective. Besides previous forces, the value-based healthcare ensures step by step that investments have a direct effect on patient outcomes provided by using innovative technology deployed. Therefore, innovation, drivers (such as new technologies or value-based healthcare) and new business models are three key elements to be considered in public procurement of innovation.

Mrs. Alessandrello remarked that innovation brings the creation of knowledge, new agents, maybe dissemination models, business models establishing private-public partnerships and new tools for funding. All of them provide the creation and the adoption of innovation in sustainable way along the time in the healthcare systems.

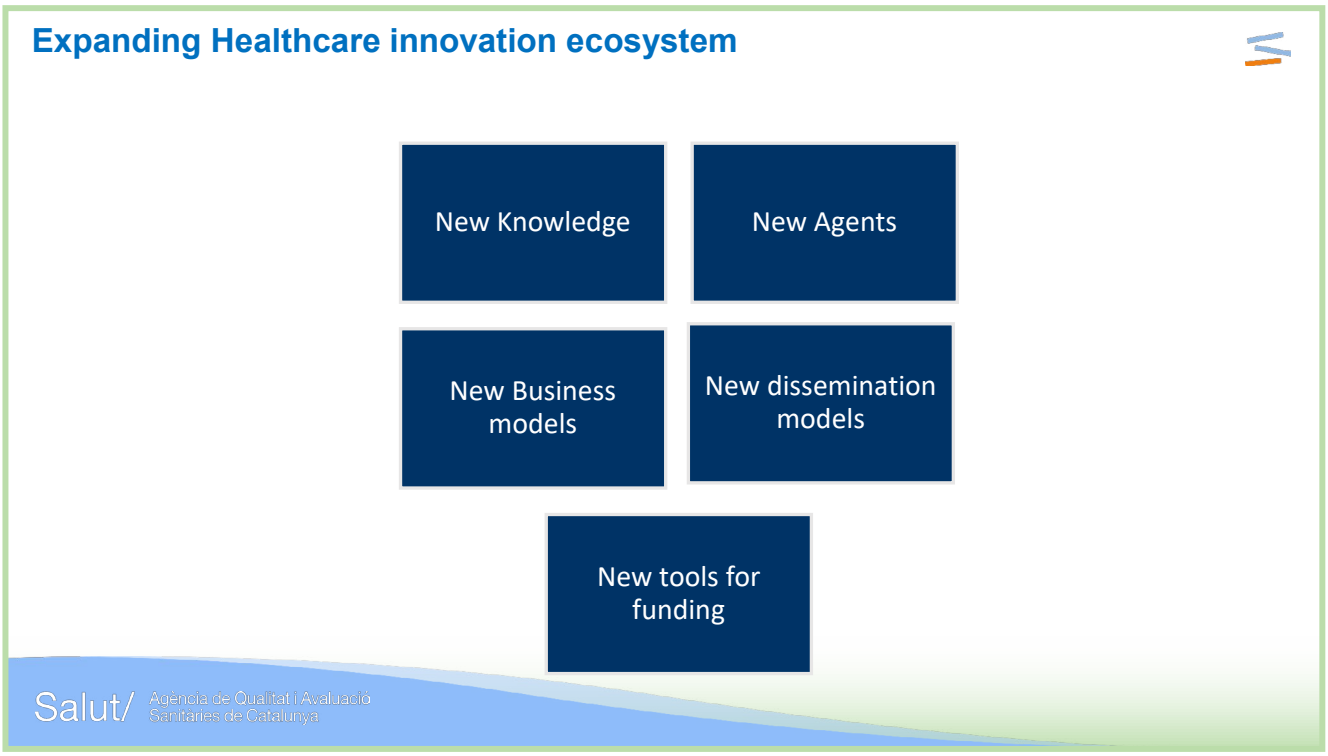


Figure 9. *Healthcare innovation ecosystem*

Take home messages:

- Public Procurement of Innovation (PPI) needs to be based on the identification of unmet needs and must be defined by the demand, because needs must be addressed by a possible solution. Stakeholders can use this instrument to obtain user-tailored solution. Therefore, innovation obtained by PPI addresses the needs with the resources in a sustainable and long-term way;
- Different PPI approaches should be considered when dealing with health technologies according to the different economic, geographical, and political environments across Europe. It should be noted that PPI encompasses from "nice to do" to "need to have";
- The key elements for Public Procurement of Innovation (PPI) are strategy, innovation, citizens, analytics, evaluation, reimbursement that should be considered by all interested procurers and buyers.

Rossana Alessandrello from the **Agency for Health Quality and Assessment (AQuAS)-Spain**, also presented the experience of AQuAS in public procurement of innovation (PPI) and Pre-Commercial Procurement (PCP) and the main barriers to overcome as shown in the application of these instruments for innovation in healthcare.

Different PCP and PPI projects such as DECIPHER, EURIPHI, INSPIRE and education programs like upRaise and iRaise were carried out by AQuAs during the last decade. AQuAs focuses on fostering the adoption of PCP and PPI instruments by launching a first call of € 30 Million and 18 projects were awarded and applied public procurement of innovation.

The first barrier in innovation is to know which procedure should be followed, mainly there are:

- Pre-Commercial Procurement (PCP): is an approach to public procurement of Research and Development (R+D) services without solution in the market, therefore, needs are unmet. The industry is sharing the risks and benefits with the market. At the same time, it is ensuring that industry will exploit these R+D services. It is exempted by the Directive on Public Procurement and the WTO agreements. During PCP, further application of public procurement is envisaged in a long-term vision.

- Public Procurement of Innovation (PPI): is a regular public procurement according to the Directive on Public Procurement. It is necessary to define the needs from a

technological perspective, why and how the needs should be addressed. The PPI needs are met when mature products and prototypes become commercialized services in an innovative way. By PPI, risk and benefits are also shared with the market. The economic operators of PCP are often aware of the extent of PPI, they design the solution with further application of PPI in long-term vision.

- Innovation Partnership is a new instrument designed under the new Directive on Public Procurement. It is one procedure comprising PCP and PPI instruments. Therefore, after the proof of concept of PCP (comprising Phase 0: curiosity driven research, Phase 1: solution design, Phase 2: prototype development and Phase 3: original development and testing of limited volume of products/services), the Phase 4 (deployment of commercial volumes of end-products) starts, which is the deployment of the successful solution from Phase 3.

Different aspects such as R&D agreements and pre-clinical & clinical investigations, individual healthcare provider, healthcare system, coverage, payer/health insurer and reimbursement must be considered to overcome innovative procurement barriers. It is important to take into account the level of ambition of healthcare systems and the reimbursement processes from the payer/health insurer, if the needs change (i.e. in-person visit solutions into virtual visit solutions).

PPI and PCP-based projects comprise the identification of needs, followed by verification of needs, feasibility analysis and market consultation in the expected period.

Finally, Rosanna Alessandrello remarked other main barriers of PPI and PCP-based projects that are the expected level of risk and skills for innovation adoption (through educational programs).

Take home messages:

- Two approaches for innovation: Pre-Commercial Procurement (PCP) is based on the identification of performance and functional needs meanwhile Public Procurement of Innovation (PPI) focuses on technological needs;
- Through PCP and PPI, risks and benefits are shared with the market;
- Innovation partnership is one procedure consisting of PCP and PPI instrument, the whole innovative chain is covered by innovation partnerships;
- One of the main barriers of PCP and PPI is to only focus on the need of individual healthcare provider or healthcare providers, to overcome it, all main actors and aspects must be considered and involved during the PCP and PPI.

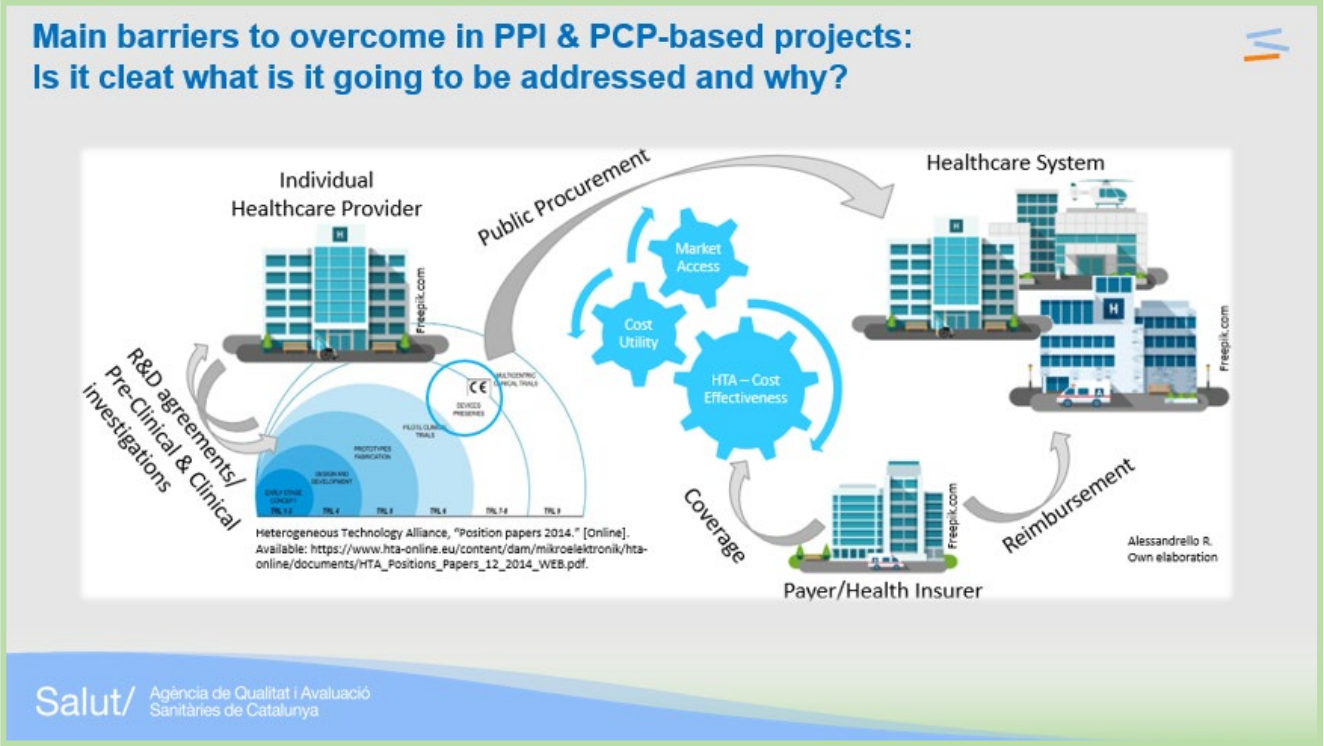


Figure 10. Main features of PCP & PPI -based projects

Ana Lucía Jaramillo from **Corvers Procurement Services B.V. - The Netherlands**, described the PCP and PPI approaches and the tools provided by the European Assistance for Innovation Procurement (EAFIP), focusing on the EAFIP methodology.

EAFIP is an initiative of the European Commission of DG Connect that started in 2015 to support public procurers in the implementation of PCP and PPI projects. EAFIP offers a toolbox for policymakers, procurers and legal advisors, webinars, conferences and workshops and provides local assistance to public procurers through a legal network across EU.

She complemented the presentation of Rosanna Alessandrello, summarizing the definition of the innovation procurement that occurs when public buyers acquire the development or deployment of pioneering innovative solutions to address specific mid- to long-term public sector needs. The whole cycle of innovation procurement starts with the curiosity driven research until the actual deployment of the solutions.

Ana Lucía Jaramillo detailed the full-blown application of the EAFIP methodology. She highlighted the importance of five preparatory steps that comprise the business case methodology, before launching a procurement:

1. Needs identification and assessment: the first step consists of identifying and scoping unmet needs with the specific requests from the end users and using different tools (e.g., functional analysis system

techniques). This early assessment allows time for an effective understanding of the need; it paves the way to the second step.

2. Prior art analysis and Intellectual Property Rights (IPR) search: once the needs are identified, desk research in the public domain will help identifying existing technological solutions and the room for new developments. The IPR search provides additional information to the state-of-the-art and the possibility to develop innovative solutions. It also enables the determination of the technological readiness level of possible solutions based on the defined unmet needs and thus, the procurement method to apply (i.e. PCP for R&D or PPI). One intelligent tool for IPR search is the IPlytics platform.
3. Analysis of the standards' landscape: is performed to evaluate the degree of consensus on solutions with minimum quality safety requirements that are available based on needs analysis.
4. Open market consultation: this step aims to inform the market on the needs and the SOTA (State-Of-The-Art) findings as well as the key contractual setup and the conditions of the procurement in order to verify whether the project is feasible and know the capabilities of the market in terms of time and maturity of the solutions. This provides the legal justification for the application of PCP, PPI or a Commercial Off-the-Shelf Procurement.
5. Value calculations: to build the business case and support investment decisions during the life-cycle of the project, a cost and benefit analysis based on different scenarios is needed.

Procurers can define their procurement strategy based on results of the five preparatory steps described above. Based on the determined Technology Readiness Level (TRL), a PCP is preferred for TRL < 8 and PPI for TRL 8 and 9. After defining the procurement, the award procedures must be chosen. In PPI, procurers can choose award procedures within the scope of the Directives, such as competitive dialogue, a competitive procedure with competitive negotiations, an open procedure with framework agreements and with multiple suppliers or innovation partnership. Although PCP does not fall under the Directives, it must be compliant with the principles of transparency, equal treatment, non-discrimination, proportionality and competition.

All these six steps will be translated into the tender documents and the procurement procedure steps for the award of a public contract, in the next step (7).

Step 8 consists of the contract management and is based on the definition of the procurement strategy translated into the procurement documents which establishes the milestones that must be monitored, the type of deliverables and performance clauses like value engineering. Step 9 consists of post-contract management, which includes standardization and monitoring IPR obligations. Finally, the evaluation of lessons learned takes place in a tenth step, aiming to apply best practices in the next procurement.

Take home messages:

- Apply a step-by-step wise methodology for the strategic use of procurement to steer in innovation;
- Strengthen the relation and engagement with the market;
- The five preparatory steps: needs identification and assessment, prior art analysis and Intellectual Property Rights (IPR) search, analysis of the standards' landscape, open market consultation and value calculations, are essential to define the procurement strategy and the award procedure of a public contract.

Javier Quiles del Río from **Galician Health Service (SERGAS) - Spain**, presented the Galician experience in Information and Communication Technologies (ICT) projects deployed by PPI instrument, particularly, electronic health record system along the regional healthcare service (SERGAS).

The first application of PPI-based initiative in Galicia was the Hospital2050 and Innovasaude in 2011. Within this initiative, 16 projects were based on ICT solutions. The rationale of the projects is based on the same previous described step-by-step strategy, starting with the identification of ICT unmet needs of SERGAS for the development of new solutions and the state-of-the-art analysis by market consultation (85% companies provided positive feedback for the evaluation of the type of solutions). Specific clauses for innovation (i.e. IPR belonged to the company or progression measurement and funding along the project) were included in the open public tender. The companies that were awarded include one SME and multinational companies.

He explained TELEA as an example of a PPI-project, which is a home monitoring solution. After development of a PPI-tender, SERGAS as a public service launched a tender to deploy these solutions. At the end of 2019, TELEA was available for

every healthcare professional and every patient in Galicia. He stressed the final goal of innovation is to obtain a large deployment of the solutions at the end of development stages. Another example was the platform for patients, E-saude, through which more than 150.000 users can access their own data. This proved very beneficial during the COVID-19 pandemic situation. He presented a third project, HEXIN-Big Data, that enables the secondary use of electronic healthcare record system data for analysis and research of diseases.

In 2016, the second major project on PPI was developed in SERGAS. Código 100 encompassed three main areas related to patient empowerment, therapies and professional solutions. Different ICT projects were developed by Código 100 and some aspects were improved, particularly association for innovation and the negotiation for innovation introduced by the new EU Regulation on public procurement. As a result of Código100, Javier Quiles presented SIPAD, a mobile APP for diabetes patients and CADIA, a technology that applies artificial intelligence for image analysis. Finally, he presented SHARE which is a large platform containing all kinds of multimedia content to provide patient clinical information. The SHARE platform also analyses the patient profile and detects the main areas that patients are interested in when looking for information, creating personalised content for each patient.

Finally, he concluded that the success of regional initiatives is due to regional EU alignment supporting e-health main lines. He remarked the importance of ICT in health governance at regional level and combining funding for innovation and deployment of solutions.

Take home messages:

- The final purpose of innovation is to largely deploy the solutions, leading a creation of regional cost-efficient healthcare system;
- Association and negotiation for innovation enables to know the market readiness for innovative solutions before awarding the contract to successfully steer the public procurement tool;
- The success of Information and Communication Technologies (ICT) initiatives based on Public Procurement of Innovation (PPI) are due to regional-EU alignment to support e-health lines;
- Regional authority involvement in fostering ICT initiatives in combination of funding by PPI can support innovation and enrich healthcare systems through the use different platforms and e-health systems by healthcare personnel and citizens.

Alicia Piñeiro Redondo from **Galaria (SERGAS) - Spain**, explained the Galician experience procurement of innovation from InnovaSaude with InnovaSuMMA, a PCP project of new biotechnological products for Personalised Medicine, EMPATTICS project for new ICT solutions for patient empowerment, Código100 and finally Innovatrial and InnovaMicroLab projects.

Código100 is a PPI plan aiming to improve the quality of life of patients through enabling developments in the biotechnology and biomedical fields to accelerate the implementation of Personalised Medicine within SERGAS. Through Código100, SERGAS launched four calls for tenders: CADIA project, 1 PCP and 2 Innovation Partnerships. The PCP call included three challenges (not specific for a product but for a category of products) focusing on pathology and aiming to develop and test new devices based on liquid biopsy accessible biomarkers for early diagnosis, prediction of responses or monitoring of patients with neurological or rheumatologic disorders or cancer.

The development of biotechnological and pharmacological solutions is complex due to regulatory constraints and the need of sampling by recruiting patients or using biobanking samples. The PCP design comprised only two phases: phase 1 consisted of definition, prototyping and technical validation of solutions and phase 2 encompassed the proof of concept in a clinical setting with patients or using biobanking samples.

During the tendering stage, 50% of the applicants were excluded, mainly because these SMEs and startups lacked a strong legal department. Therefore, it is necessary to develop dedicated measures to support companies with such administrative documents and processes for a suitable PCP proposal.

Alicia Piñeiro showed the final PCP solutions for Código100 in the area of therapies:

- e4Quant: a quantitative test of apolipoprotein E4 detection in human plasma designed by Biocross for prediction of Alzheimer disease progression;

- PharmaHIC-ReTER Test by Healthincode: a Next Generation Sequencing approach for genetic biomarkers related to the response to biological drugs for rheumatology;

- PQreader+Promonitor Test by Progenika Biopharma: an integrated point of care solution for quantitative monitoring of biological drugs and qualitative monitoring of anti-drug antibodies in human blood for rheumatology uses;

- OMTX100 by Oncomatrix: a non-invasive diagnosis of solid tumor (colon and lung cancer) in blood exosomes using a novel

combination of genes expressed in tumor epithelial cells and in tumor microenvironment cells.

She also presented the innovation partnership procurement (IPP) experience of Galician Health Service (SERGAS). Two unmet needs for R+D were clearly defined to be purchased and introduced in SERGAS clinical processes. Two innovation partnership calls were carried out: one for development and validation of a multi-marker test for molecular characterization of tumor and the second for development and clinical testing of a multichannel device for advanced resection of rectal tumors. The IPP design was similar to PCP but including the selection phase as the first step and the tendering stage was a complex process. Alicia Piñeiro Redondo presented the results obtained by innovation partnership procurement: a solution for a multi-marker test to molecular characterization of tumors was IMPUL 20 for NSCLC by Agilent and a solution for a multichannel device for advanced resection of rectal tumors were a pre-prototype developed by SERGAS surgeons based on the removal of rectal lesions during endoscopy; and UNI VEC by Vecmedical is a device for advanced resection of rectal tumor by flexible endoscopy and transanal endoscopic surgery.

Take home messages and lessons that other regions may benefit:

- The development of biotech and pharma solutions present regulatory constraints and need of sampling by recruiting patients or using biobanking samples, therefore, a public procurement should be perfectly framed and defined to overcome these barriers;
- Previous experience in Pre-Commercial Procurement (PCP) showed the need of strong legal department for obtaining successful proposals during the tendering stage, thus, regional authorities should develop measures to support companies with the administrative workload.

2.5 Main outcomes of the conference

Research and Innovation is needed for the integration of new techniques, technologies and services for clinical prevention and diagnosis into healthcare. In this context, research infrastructures that manage human data, including genomics, should do this in compliance with ethical and proprietary standards to gain patient and partners' trust. Additionally, these infrastructures should exchange interoperable data in a federated system considering all different jurisdictional legislation. The construction of research networks combining biological data together with citizen's information enables the access and analysis to high-value molecular profiling data that should be in accordance with regional and European legislation.

Public and private investments/ funding are essential to sustain the development and deployment of innovative prototypes, solutions and technologies in Personalised Medicine. As first step in innovation procurement procedures, the unmet needs must be clearly identified and defined before performing any procurement. Depending on the identified unmet needs, different degrees of Technology Readiness Level (TRL) solutions should be demanded. Pre-Commercial Procurement (PCP) contributes and supports innovative research by procuring the research and development of solutions presenting TRL < 8. Meanwhile, public procurement of innovation or innovation partnership offer solutions presenting high TRL. Likewise, prototypes, solutions and services acquired by these innovative procurement tools must be foreseen for short and long-term applications. These innovative instruments lead an interactive dialogue between payer/ health insurer and procurer, enhancing their commitment and increasing efficiency of the outcomes.

All solutions, prototypes or developments obtained by PCP, PPI or innovation partnership should be implemented and exploited for their expected duration in research or clinical settings. Therefore, authorities should support and assign laboratory, or real hospital or healthcare installations to test and use these novelties to pave the way to a sustainable and efficient healthcare system.

Personalised Medicine is based, among others, on technological development in omics. Collaboration among regional research institutes, academia, industry and public institutions is necessary to create an environment for accelerating and sharing new knowledge and advances.

Construction of a federated sustainable infrastructure for human genomics and translational data in Europe enables discoverability, access, sharing and analysis of genomics data.

Developing and validating solutions for citizens and healthcare personnel to access to e-health records and telemonitoring.

Research & Innovation are key for achieving sustainable healthcare systems.

Harmonization is necessary for labeling and certification procedure for Living Labs.

Procedures, standards and platforms should be required to facilitate application of public procurement tools for innovation.

Technological solutions support medical and healthcare personnel to prevent and diagnose diseases.

Artificial Intelligence is becoming ubiquitous in our daily life. Healthcare professionals and patients are continuously accessing to their e-health records (such as image processing or laboratory test results).

Citizen's trust is fundamental for deployment of genomic and health data.

3. Key Area 4 Interregional Workshop

The Workshop was held on 16th and 17th of November 2021 in an online format in the Galician Health Knowledge Agency (ACIS) headquarters due to the COVID-19 pandemic situation and represented a follow-up of the 4th KA Conference.

The aim of the Workshop was to trigger regional exchanges and discussions with regionally embedded stakeholders on innovation in Personalised Medicine, sharing opportunities and best practices that emerged in their professional experience. All speakers were selected in accordance with their expertise in innovation in the field of Personalised Medicine. As in the conference, the audience was composed of regional and governmental entities involved in health policies coming from different EU Member States and beyond.

The main roles during the sessions are described below:

- **The Chairs** were José María Romero Fidalgo and Ana Cajaraville Leiro, whose role was to open the discussion, introduce the topic, give the floor to the speakers, manage the Q&A session and time, and raise questions to orientate the debate. They also summarized the main points of the presented topics.
- **The Speakers** were experts/policy makers/representatives of the public or private sector that explained best practices or lessons learned in the context of the session.

All speakers and chairs as well as Regions4PerMed partners have been actively involved in the organization of the workshop. Zoom connections were organized with speakers of each session, to define the structure of the session and to discuss challenging issues, with the aim to trigger the debate among participants. The main purpose of the workshop was to exchange and share experiences with all participants to explore healthcare solutions. The plan was to discuss "Best Practices" and lessons learned examples, as well as capacity building activities and policy co-creation with all Regions4PerMed partners.

The Workshop focused on three Policy Intervention Areas:

1. Research and Innovation (R+I) infrastructure models to foster innovation;
2. Financial instruments to support innovation. Innovation procurement tools: Pre-commercial Procurement (PCP) and Public Procurement of Innovation (PPI);
3. Smart and future hospitals.

The organizer and host of the event was the Galician Health

Knowledge Agency (ACIS), Spain. Although, the workshop was first designed to take place in a hybrid format, all presentations and discussions of the event were conducted remotely via Zoom platform and broadcasted through a YouTube channel.

The preparation of the agenda for the workshop was based on the experience of the experts from the conference and the feedback and recommendations gathered from an *ad-hoc* expert group, the Advisory Board and Regions4PerMed partners.

The main outcomes of the conference and workshop are collected and summarized in this report.

Draft plan of the Workshop

Due to the pandemic situation, the Workshop consisted of two days in a virtual format:

The first day included an opening session with an introduction to the topic and project by José María Romero Fidalgo and Gianni D'Errico, project coordinator at the Fondazione Toscana Life Sciences, followed by the panel sessions where speakers and partners shared with the audience their lessons learned and best practices related to the previous defined policy intervention areas.

The second day was based around the elaboration and prioritization of recommendations on Personalised Medicine within Regions4PerMed Consortium. The day started with a virtual visit to the Living Lab of Ourense, followed by a capacity-building and co-creation meeting.

3.1 Panel sessions

3.1.1 POLICY INTERVENTION AREA 1: Research and Innovation (R+I) infrastructure models to foster innovation

Rationale: *Collaboration between public and private research institutes represents a solution-making model providing innovative technologies and services in PM. Encouraging synergic interactions is necessary to develop and deploy innovative solutions on Personalised Medicine within healthcare systems. Exchanging and sharing new approaches and methodologies among European regions will allow a quantitative improvement of knowledge and procedures for establishment of coordinated and valuable Research and Innovation (R+I) networks for further scientific, technical and technological advances.*

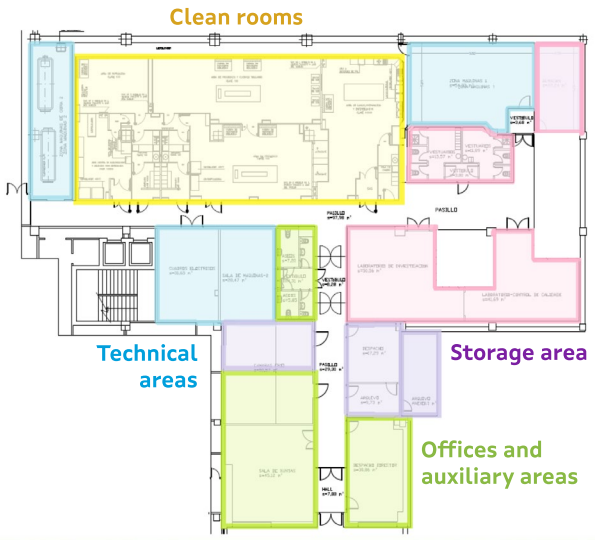
The main purpose of the panel session was to learn new models to boost innovation by creating robust and competitive Research and Innovation (R+I) infrastructures at regional, national and international level.

The workshop was opened by **Mariona Baliu-Piqué** from **Galaria (SERGAS) - Spain**, who presented the centralized manufacturing center for cellular immunotherapy for Galicia located in Santiago de Compostela.

The Galician immunotherapy manufacturing center is going to be part of the Galician Health Services, of 100% public nature and with an initial investment of more than € 3 Millions. She presented the facilities, which include clean rooms for immunotherapy manufacturing center and the main activities of the center, which consists of clinical and research activity. The clinical activity focuses on the production of Advanced Therapy Medicinal Products (ATMPs), for the promotion and development of new clinical trials. The main aim of clinical activity is to facilitate the population access to these novel therapies by enabling local production in the center. Currently ATMP production includes complicated logistics, which may increase the cost of these therapies. Own laboratories and equipment are available for researchers in the center with the participation of hospitals, universities, research foundations and institutes, to promote the development of cutting-edge technology in Galicia. The main objective of research activity is to create a Cellular Immunotherapy Research Unit in Galicia.

Facilities:

- 200 m2 of clean rooms
- 150m2 of laboratories
- 100m2 of warehouses
- 100m2 of offices
- 400m2 of technical areas



Clean rooms:

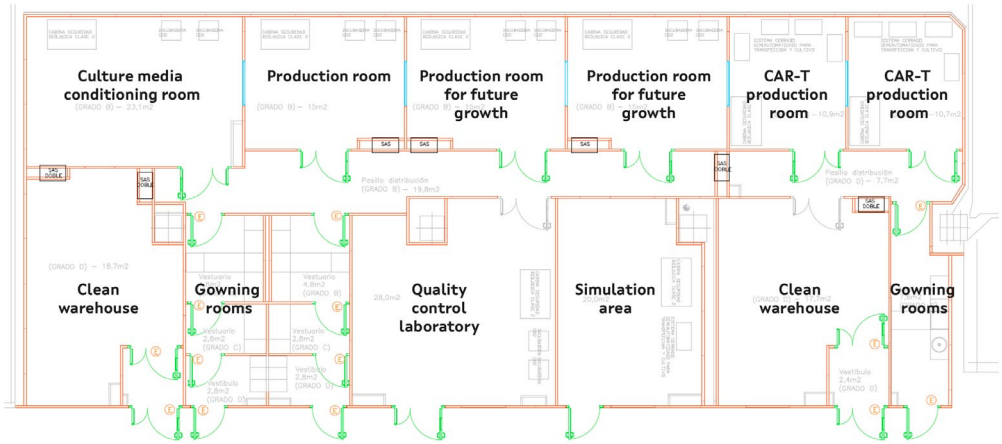


Figure 11. Galician immunotherapy manufacturing center settings

As clinical activity, it is expected to produce 1 or 2 academic Chimeric Antigen Receptor T-cell (CAR-T) drugs in the framework of clinical trials designed by other organizations through collaboration and knowledge transfer agreements. According to this, the first step was the production of a new CAR-T cell drug for hematologic cancer treatment with the Hospital Clínic de Barcelona and IDIBAPS. In the medium/ long term, it is expected to produce academic CAR-T and other advanced cellular immunotherapies of own design by a Research Unit in Galicia.

Dr. Baliu-Piqué commented the mission of research activity, which is the mobilization of development of research projects, union of research groups, and lines to concurrence in competitive calls, increase the funding opportunities and enhance the execution, testing and validation of new drugs at research stage. She remarked the importance of collaboration with other centers within research activity.

Prof. Angel Alonso Sánchez (Chief Scientific Officer Navarra Government Strategy on Personalised Medicine) has presented "The NAGEN Scheme of Navarra".

Prof. Alonso pointed out the great importance of genomic medicine applications such as in the diagnosis, development of new therapies and technological capacities for storing and processing genomic information.

NAGEN 1000 project brings together all advantages of the genomic medicine into healthcare. Navarre healthcare system considered all barriers related to being a small region with about 650.000 inhabitants such as low throughput genome sequencing facility, lack of bioinformatics platforms and at the beginning of the project there was no adequate infrastructure to store genomic data and no ethical/legal framework and a lack of computing and processing capabilities for genomic data processing.

The first aim of the NAGEN 1000 Project was the implementation of the use of the whole genome sequencing information as a clinical tool for Personalised Medicine in Navarra Public Health Service. It implies using the highest technology in sequencing for Navarra healthcare workforce. NAGEN 1000 selected 1000 patients with rare diseases. He explained that NAGEN 1000 operated with the following methodology: starting with the whole genome sequence analysis and all the information from the phenotypic of the patient a diagnosis of the genetic condition of the patient was obtained and additional research was conducted to obtain a diagnosis. The available genomic information is also explored or identifying reproductive as well as pharmacogenetics risk.

The main results of NAGEN 1000 were the identification of the cause of the condition in 36% of the patients and strong candidates for the cause in 26% of the patients. He highlighted that all patients had been subject to several rounds of genetic testing during prior years without obtaining any result. Regarding secondary results, more than 2% of the participants were predisposed to suffer a severe genetic condition; therefore, clinical actions were performed to improve the conditions of those patients.

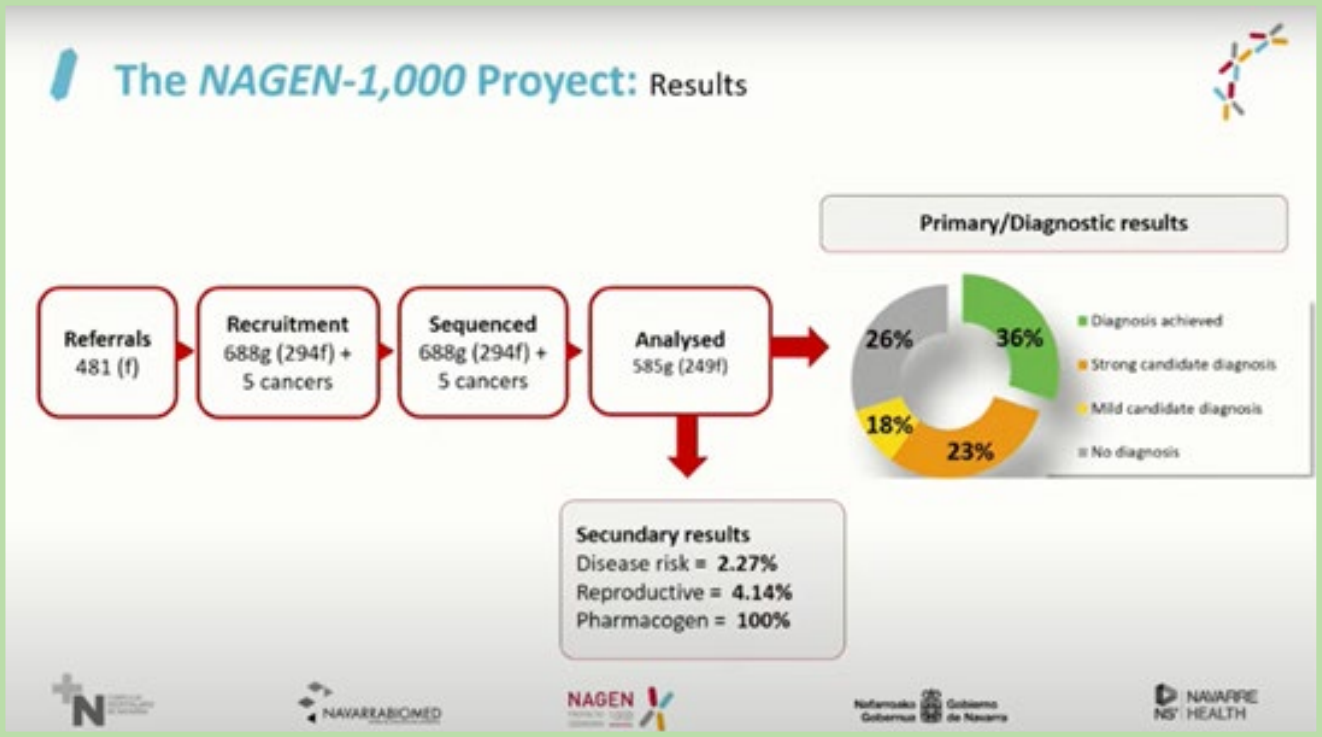


Figure 12. Results of NAGEN-1000 Project

With Nagen 1000 the time for diagnosis and its cost were reduced significantly. The diagnosis results were obtained in 6 months instead of more than 10 years for standard genetic approaches and the cost of the genetic analysis process was reduced by 25%.

He explained the NAGEN scheme comprises five additional pilot projects on different applications of genomic medicine such as pharmacogenomic driven prescriptions, hypercholesterolemia genomic personalised management, pediatric and neonatal intensive care units and population breast cancer screening.

Prof. Alonso also presented the Navarra Strategy on Personalised Medicine based on real data collected and produced in the clinic and in the research to provide new drugs, treatments and diagnosis. The Navarra Strategy on PM integrates three strategic areas: health, research and innovation, and economic development. The NAGEN Scheme and Navarra PM strategy are part of the Spanish Strategy on Personalised Medicine launched in 2020 and of the 1+ Million Genome (1+MG) project.

Dr. Thomas Tradler (Head of the Executive Department Business Development of Fraunhofer Institute for Cell Therapy and Immunology (IZI), Leipzig, Germany) has introduced Fraunhofer society and Fraunhofer IZI. He has also shown an overview about strategies to regional innovation.

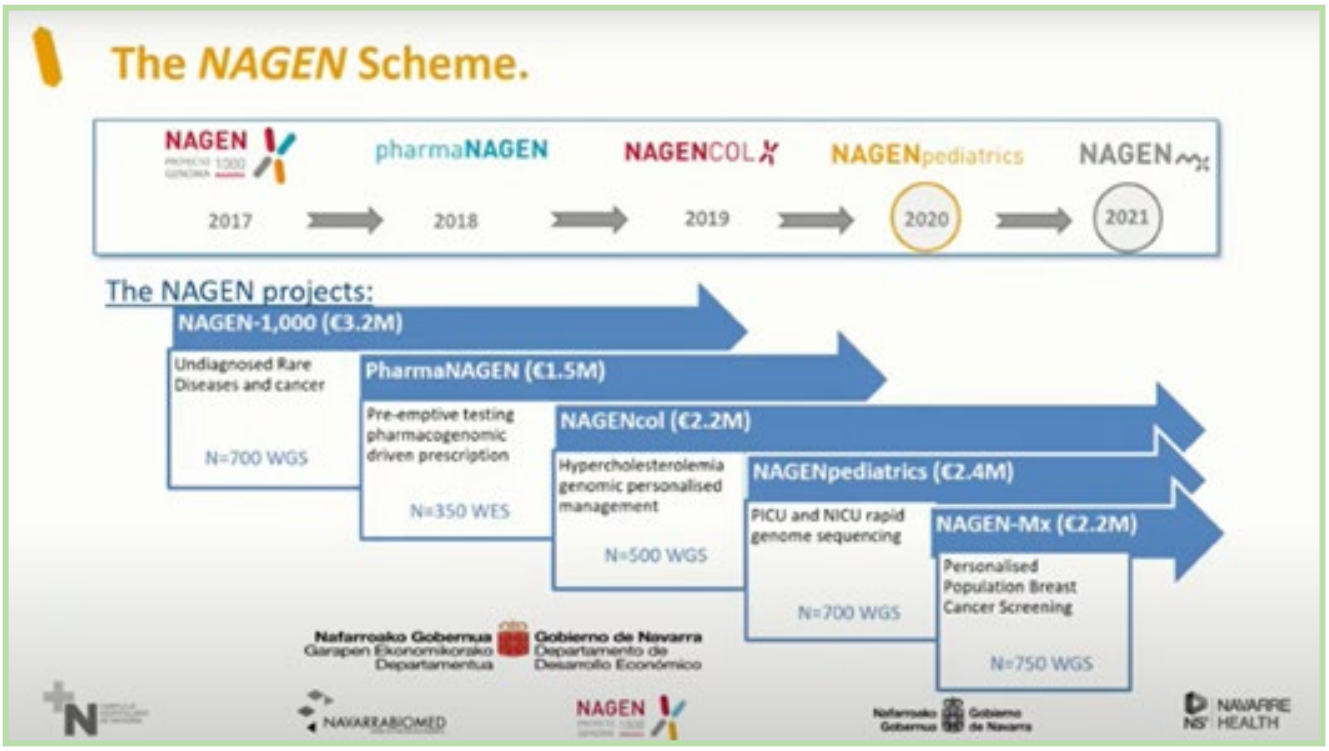


Figure 13. The NAGEN Scheme

The Fraunhofer-Gesellschaft (FhG) is a German research organization. It is Europe's largest society for applied research in life sciences, information technology, microelectronics, light & surfaces, production & energy, materials & components, and defense & security. With 75 institutes, almost 30.000 employees and an annual budget of € 2,8 Billion, Fraunhofer Society's main activities and business models are contract research, joint development, licensing and consulting.

The Fraunhofer Institute for Cell Therapy and Immunology (IZI) is one of the largest institutes of Fraunhofer in the life sciences and has its headquarters in Leipzig. Its main business unit is cell and gene therapies; the second is drug and vaccine R&D by developing small organic molecules, antibodies and vaccines for human and veterinary medicine; the third business unit focuses on DNA and RNA diagnostics and biomarkers their discovery and clinical validation; and the fourth business unit is extracorporeal therapies focusing on developing new dialyzers.

The cell and gene therapy unit covers the entire value chain from early development to clinical trials. Dr. Tradler stressed that the business is based on two pillars: performing research and capabilities as well as conducting and pursuing internal and joint R&D projects together with industry or academic partners.

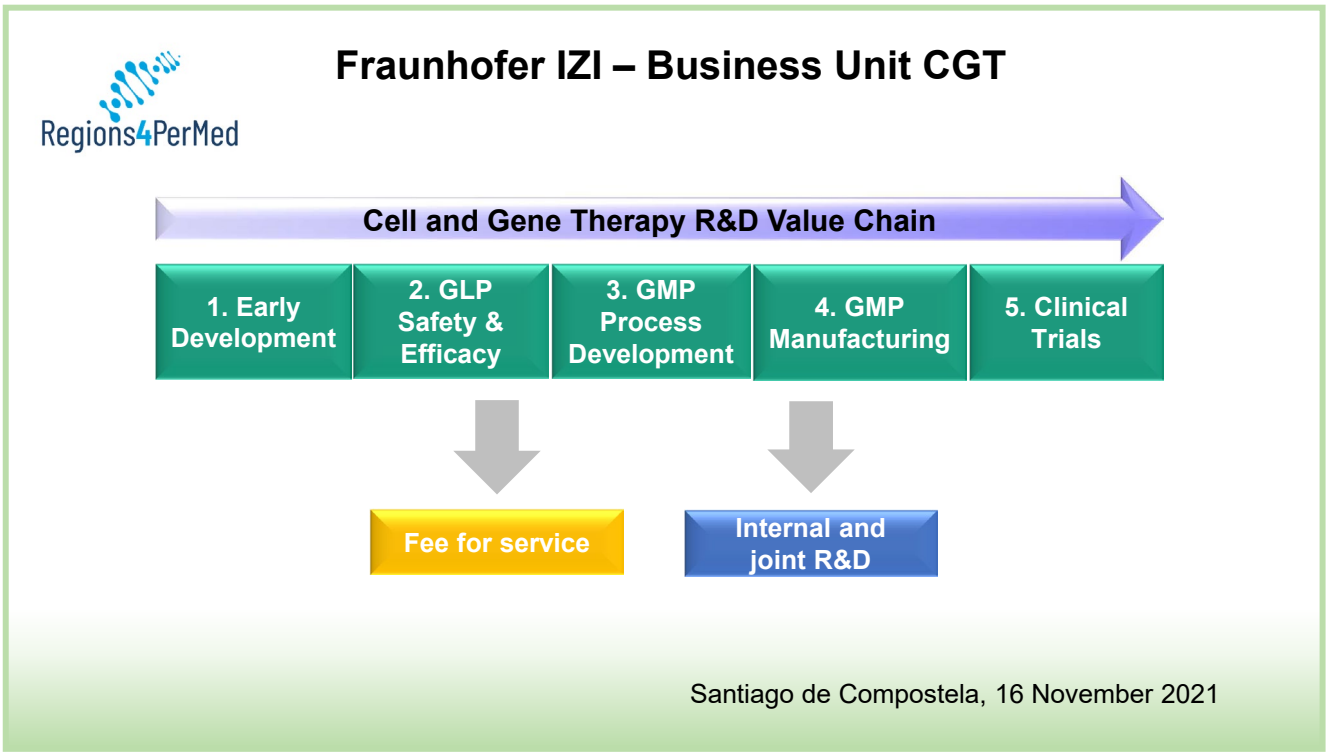


Figure 14.Cell and Gene Therapy value chain

He described three ways how Fraunhofer IZI impacts the innovation flow into the region. The strategy of facilitating the innovation flow starts with applied joint research activities with industry and academic partners to promote knowledge and innovation. The second step is the excellence research partnerships with national and international partners to develop innovative technologies and products and the third part of the strategy is the creation of spin-off companies and the creation of subsidiaries of international companies in Germany. Related to the third part, Saxocell® is a novel cluster initiative in the field of ATMP aiming to create so-called "living therapies" with € 5 Million dedicated for the next three years that can be expanded to € 15 Million up to nine years in total to create a European lighthouse for cell and gene therapy.

Key Recommendations:

- *Regional investment in innovative therapies development facilities are proven to be sustainable and beneficial for the local healthcare systems. Similar initiatives should be pursued and linked in other regions and other Countries;*
- *Collaboration of multidisciplinary research groups in competitive calls, increase the funding received and enhance the development, testing and validation and market placement of new therapies. Regional Authorities should further enhance these dynamic within their territories;*
- *Planning and implementation of approaches including the application of new validated omics, i.e. genomic technologies, in their local, regional and national healthcare systems introduce relevant benefits in a wide range of socio-economic areas such as medicine, healthcare, education or Research and Development (R+I). Regions should work together to foster the research and innovation in omics to be applied directly in real clinical settings;*
- *Institutes on applied research come forth the development of techniques, technologies, products, formation of enterprises and subsidiaries in their Member States. Additionally, joint research with companies leads to continuous learning, innovation, and creation of expertise within the region. Thus, regions should support and invest the creation of this type of infrastructures oriented to R+I industry applications.*

3.1.2 The POLICY INTERVENTION AREA 2: innovation supported by two procurement tools, Pre-commercial Procurement (PCP) and Public Procurement of Innovation (PPI) for novel health care services.

> ***Rationale:*** *The deployment of different financial instruments can offer to interested stakeholders the opportunity to develop projects, services, technologies and prototypes to improve the healthcare system. Through these financial tools, the creation of a cost-efficient and sustainable system can be realized, providing high-quality healthcare services to citizens. It should be mentioned that innovative procurement tools, consisting of Pre-Commercial Procurement (PCP) and Public Procurement of Innovation (PPI), have been successfully employed in different regions. Both instruments have become straightforward and robust pathways to obtain beyond state-of-the-art solutions, technological and technical prototypes, or services at different stages of maturity.*

Prof. Adrián Llerena, **Scientific Director of the MedeA Project at Extremadura University Hospital** presented the Clinical Implementation of an e-Health based Pharmacogenetics and Personalised Prescription System in a European Regional Health Service (MedeA).

The use of genetic biomarker during the clinical drug prescription process is frequently recommended since 34% of the drugs contain the reference to a biomarker.

Prof. Llerena explained the Spanish strategy on PM framed by policy makers. The Spanish Senate created a committee to evaluate the potential clinical implementation of genetic and genomics in 2017, with the mandate that all gathered information on genetic and genomics must be implemented in the public healthcare system. In 2020, the Spanish Government introduced a national strategy for the implementation of clinical pharmacogenetics in the public healthcare service, called IMPaCT (Precision Medicine Infrastructure related to Science and Technology). IMPaCT consists of three branches: epidemiology, data science, and genomics. The genomics branch includes a work package for pharmacogenomics lead by Prof. Angel Carracedo. Prof. Llerena is the leader of the pharmacogenetics implementation part.

Extremadura is one example for the implementation of pharmacogenetics due to its size, location, the uniform healthcare data collected (ethnically homogeneous population)

and an existing electronic health record system. The direct drug cost of Extremadura amounts to € 478 million of a total healthcare system budget of € 1876 million. Apart from measurable direct cost, drug use also encompasses indirect costs, e.g. related to the (unwanted) side effects of drug use. Taking this into account, the MedeA approach is based on identifying major factors in drug response specific to the individual patient. Those major factors are their genetic and genomic information, their clinical data (liver function, renal clearance, etc) and drug-drug interactions/proper dosage in order to predict and prevent Adverse Drug Reactions (ADR). Extremadura Healthcare System is implementing a program, including genetic and genomics, for the prediction of inter-individual variability considering that patients are in polytherapy.

With a budget of € 5,3 million the MedeA project shall develop a personalised prescription program that will be integrated in the electronic medical data records to release this a PPI process was initiated. The PPI first challenge for the companies, during the competitive call, was to develop a clinical decision support system with a clinical visualization supporting tool, named Personalised Oriented Prescription System (PoPS). PoPS is based on three databases: genetic biomarkers, the drug-drug interactions, and the electronic medical record data. The first challenge for the companies, during the competitive call, is to develop a clinical decision support system with a clinical

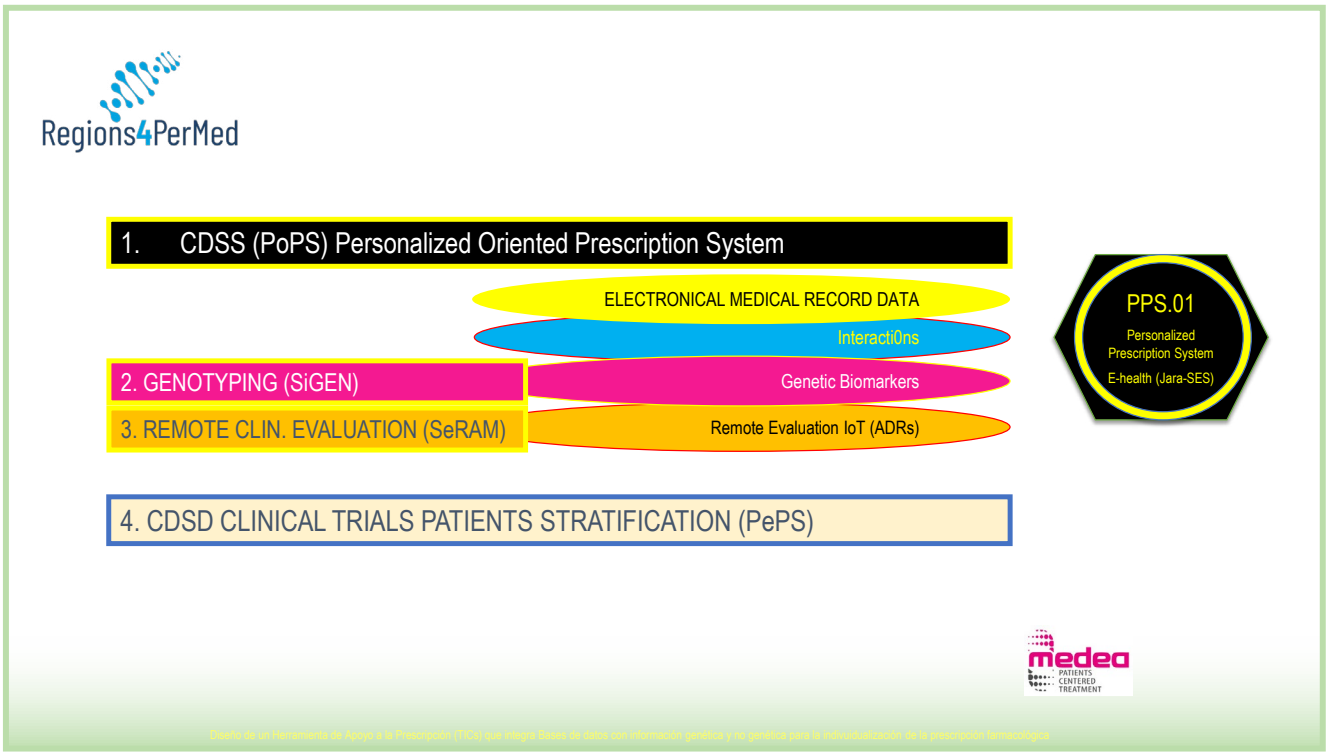


Figure 15. Challenges of MedeA project

visualization supporting tool, named Personalised Oriented Prescription System (PoPS). The second challenge is the genotyping, and the third challenge is the evaluation of the adverse drug reaction. The last challenge for the companies is to develop a tool for clinical trials.

Prof. Llerena explained the procedure followed during the application of association for innovation and public procurement of innovation: exploration of the market (with 83 proposals), selection of companies, 3 stages for negotiation (projects, negotiations and final project), phase I for contract execution (model, prototype and pilot) and finally implementation in the whole healthcare system. In 2020, the selection of the companies began, and in 2022 it is expected to proceed to the development of the pilot and prototype and the deployment of this prototype in the healthcare system is expected in 2023.

Nevertheless, the validation of the program by companies was changed due to the COVID-19 pandemic, and from the MedeA project launched a clinical validation. He has remarked the problem that was faced during the validation process, shown as inequality and biotechnological gap. The implementation of pharmacogenetics should be for the whole population.

Finally, Prof. Llerena showed the preliminary data of adverse drug reactions data, highlighting that 28.6% of patients suffered a severe adverse drug reaction and 21% of them were in the hospital due to this severe adverse drug reaction.

The modernization of healthcare through PCP in Lombardy region was presented by **Matteo Pozzetti** on behalf of **Gabriele Busti** (Head of the office Investment for Research Innovation and Technology Transfer, **Lombardy - Italy**) and **Marco Penco**, Research and new products manager, presented the **Info Solution S.P.A** experience in PCP.

The speaker explained the legal framework of PCP in EU and in Italy (Italian Legislative Decree 50/2016), its principles and applications. PCP is applied when the public contract involves services of research and development, and the benefits are exclusively assigned to the contracting authority for its use. He compared the conditions of a regular procurement and PCP. PCP is a competitive procedure that follows three phases: solution design, prototype development and experimentation. Matteo Pozzetti also explained the main requirements of PCP to exclude the configuration of State-aid.

Matteo Pozzetti showed the tenders launched by the Lombardy region funded under ERDF 2014-2020. In 2013, the first pilot

PCP was launched for the benefit of a Public Hospital to purchase a smart system for moving beds. PCP was concluded and one company started the commercialization in 2021. In 2018, two PCPs were launched for the evaluation of the fragility of the coronary atherosclerotic plaque. The development of a robotic exoskeleton for motor rehabilitation in neurological patients with upper limb motor deficit was launched in 2018. During 2020, the technological development of the imaging in surgical assistance and support system was also launched.

Mr. Pozzetti presented the lessons learned in PCP application by Lombardy region. The phase 0 is essential to identify needs in the market. It is very important to create opportunities of communication between stakeholders. It is necessary to ensure more time for suppliers to design prototypes and experiments and reduce the administrative time of evaluation. Lastly, it is essential to make the tenders more attractive without limiting profits.

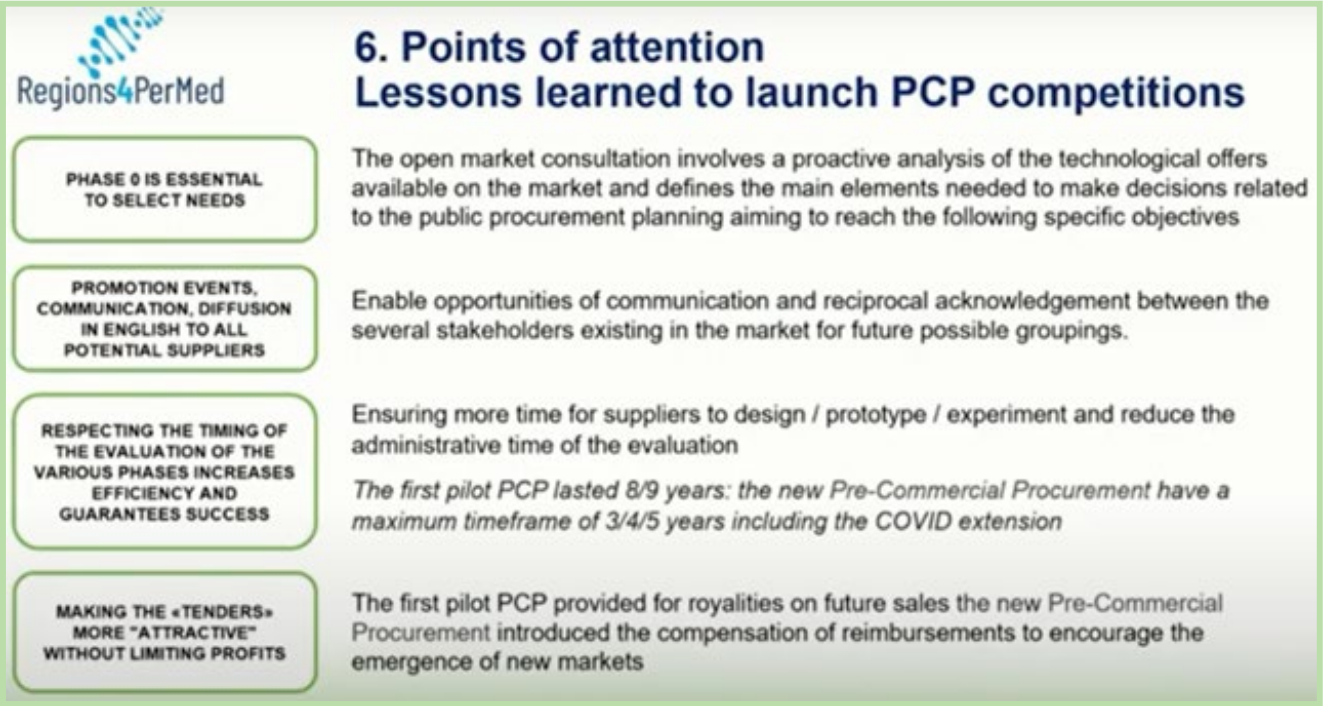


Figure 16. *Lessons learned by Lombardy region*

The two suppliers that won the first pilot PCP in Lombardy presented their experience: Oppent S.p.A and Info Solution S.p.A.

Oppent S.p.A showed in a prerecorded video the benefits obtained in PCP, remarking that the company gained more acceptance from its current and prospect costumers due to Oppent's capability to innovate. After application of PCP, Oppent S.p.A. signed contracts to supply hospital internal logistics (EvoBed) with different international companies.

Marco Penco from Info Solution S.p.A, the company that was awarded in the first pilot PCP launched by Lombardy region, presented the company and explained how the company benefited from the procurement procedure offered by the PCP. Info Solution S.p.A supplied the Hospital of a bed mover based on an electric safe vehicle to move beds effortlessly. From an industry perspective, the main positive outcomes were site inspection and detailed information about the needs, which led to the development of a product, tailored to match the specific health institution's need.

Marco Penco explained the difficulties that were faced during the PCP project, highlighting the length of the process as Matteo Pozzetti stated previously and also the need to test the product in real environment before the product delivery can take place (not present during the development in the PCP process).

Key Recommendations:

- *Public Procurement of Innovation (PPI) has successfully deployed to develop systems such as Personalised Oriented Prescription System (PoPS, a tool designed for evaluation and prediction of adverse drug reaction for the patient). Regional institutions should support by innovative tools such as Pre-Commercial Procurement (PCP), PPI or innovative partnership, the research, development, purchase and use of this type of e-systems to develop new screening and prevention programs towards personalised medicine;*
- *Supported by innovative instruments (PCP or PPI), regions need to promote pharmacogenetics in order to be accessible and used for the whole population;*
- *Identification of needs in the market is crucial in PCP and PPI, therefore efficient and user-tailored solutions and prototypes are obtained through these instruments. Regional authorities should foster the deployment of these innovative tools to enable the access of novel healthcare techniques, technologies or products;*
- *Promoting communication between stakeholders and extending the time for designing, meanwhile, reducing the time for evaluation are important in PCP initiatives;*
- *Tenders in PCP can be more attractive without limiting their profits when a product tailored for a specific need is purchased.*

3.1.3 The following panel on POLICY INTERVENTION AREA 3 Smart and future hospitals.

Rationale: *Significant healthcare improvements can be achieved through the application of the previously described R+I models and financial instruments. This includes hospitals equipped with installations to test innovative services, known as smart and future hospitals. The approach based on cutting-edge technological and technical facilities will support medical personnel and stakeholder's new treatments and patient-tailored diagnosis paving the way to the creation of a robust healthcare system based on personalised health approaches. Regions are important stakeholders to develop and implement the exploitation of these facilities within the hospitals of their regional healthcare systems. Therefore, regional discussions focus on the identification of common needs and goals will take place during the KA4 Workshop, including topics such as public-private partnerships and investments to contribute building up these hospitals' focus on user needs.*

Valentina Polylas – **Director at EUREGHA** has shared the action of European Regional Local Health Authorities (EUREGHA) as well as European Union activities, in particular the topics on healthy ageing, silver economy and digital innovation.

EUREGHA is the association of European Regional and Local Health Authorities aiming to support the development of people-centered sustainable and resilient health and social care systems based on value and measurable outcomes. One of the main pillars of EUREGHA's strategy is value-based healthcare (i.e. by using PCP and PPI instruments) as a solution for the sustainability of health and social care systems. Valentina Polylas remarked the importance of digital health, including data collection and exchange, that is underpinning the transformation of health and social care. Digital health and integration of health and social care are also applied in the aging activities of EUREGHA. As a public institution, EUREGHA also tackles health inequalities and public health measures in the context of health promotion and prevention and works in cross-border healthcare cooperation and the implementation of the European Directive on patient mobility. EUREGHA also promotes knowledge exchange among the members.

EUREGHA action is embedded in the Green Paper of the EU

Commission on aging, especially in the activities related to the active and healthy ageing part, the long-term care and tackling isolation and loneliness. In the context of silver economy, the development of market services and products for health and active aging can improve the efficiency of the health and social care systems.

There are different tools and projects for scaling up innovation for the ageing society in EUREGHA, including participating in the future partnership for health and care transformation of HORIZON Europe. Valentina Polylas stressed the strong implication of European Health Data Space, which EUREGHA is supporting as part of the working group, in the EU single market. She also described the EU care initiative launched by the EU Commission president Ursula von der Leyen that addresses the needs of citizens and caregivers and she brought the attention to the EUREGHA activities on digital skills for the healthcare workforce.

Valentina presented the Innovation Networks for Scaling Active and Health Ageing (IN-4-AHA) a project including all previously described activities as well as citizen empowerment. IN-4-AHA aims to build person-tailored integrated care systems on the legacy of the European Innovation Partnership on Active and Healthy Ageing (EIP on AHA) in 2020. EUREGHA was working to exchange the knowledge gathered within IN-4-AHA, to embed new stakeholders of the community of AHA and ensure cross-border scale up of new innovative solutions. To this extent, a new toolkit will be developed to provide guidance on how to test and validate innovative solutions by stakeholders and ensure impact evaluation and long-term investments.

Finally, she highlighted the relevance of the industry-policy maker partnership to bring digital transition for preserving a quality of life for elderly people in their ecosystems by adopting citizen-centered solutions and scale up innovation across Europe. She has also expressed the need of the support by EU institutions by building infrastructures and providing funds (in human capital and digital skills for citizens) as well as the reinforcement in the stakeholder collaboration of networks (need of improvement of public-private administration dialogue shown in PCP).

How technologies for Living Environments support Personalised Medicine was presented by **Cristina De Capitani**, **Cluster Manager at Lombardy Cluster Technologies for Living Environments**. Mrs. De Capitani introduced the approach of the Lombardy Cluster in PM, focusing on the patient lifestyle, including nutrition and rehabilitation that affect the management of chronicity.

She presented the Cluster of Technologies for Living Environment (Cluster TAV) as a network of research hospitals and centers, universities, companies and associations such as the chamber of commerce. The development of innovative technologies is centered on citizens in order to improve their quality of life and care.

Cristina De Capitani focused on the management of chronicity followed by some examples to tackle it in the healthcare system. The first product, NIA is a modular software medical device for telemonitoring and prediction for neurodenerative diseases, developed by a clinical center from Lombardy Cluster. She also presented a startup, Math Biology, which develops biosensor and artificial intelligence technologies for deep metabolism assessment (DMA), which is a decision support system based on non-invasive diagnosis for medical personnel. DMA biosensor was made possible by a network of technical researchers, medical professionals who defined the needs, and companies that develop the product, supported by the Lombardy region. She showed the example of personalised upper limb rehabilitation, a product that combines physical rehabilitation with a digital interface for clinicians. She also presented the personalised physical and cognitive training and virtual supermarket for patients that suffered heart attacks and strokes.

She mentioned SPATIALS3 project whose objective is to create an integrated hub of research, development and innovation in the context of nutrition by developing functional foods with nutritional needs of consumers based on four different pathologies. Finally, she stressed the importance of using technologies to support PM as well as for performing clinical trials.

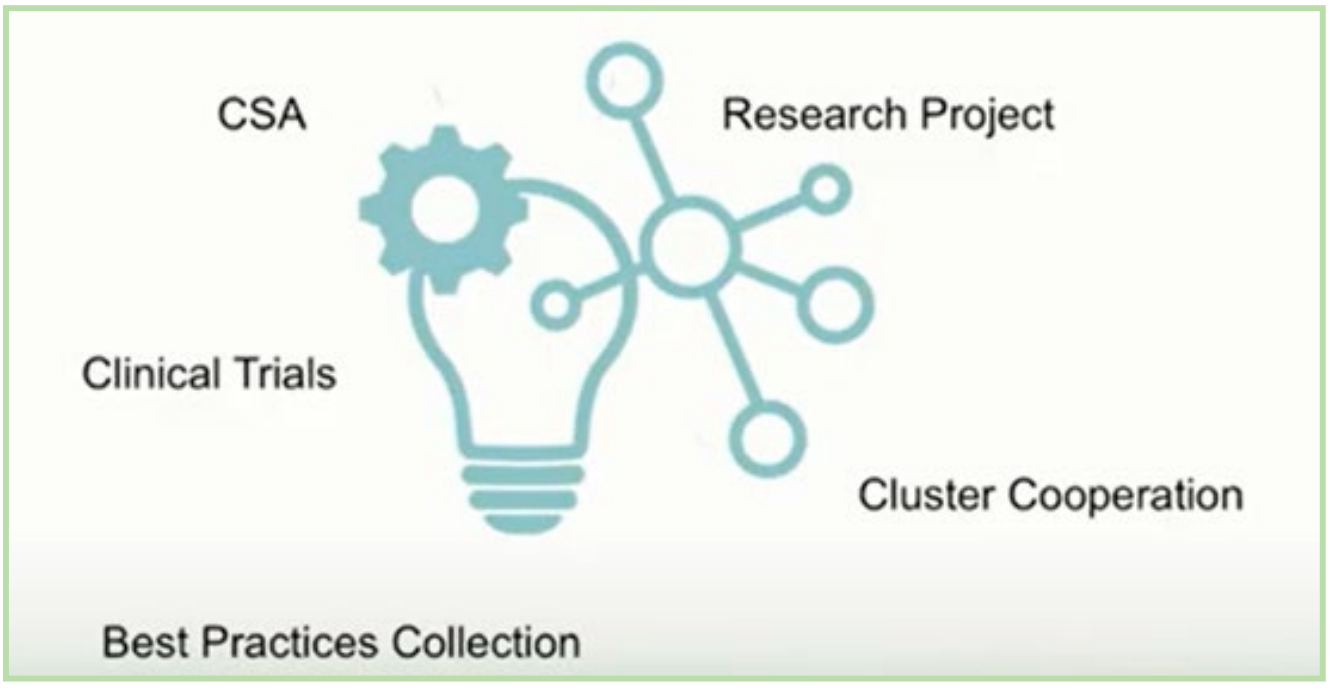


Figure 17. *Workflow in Lombardy Cluster TVA*

Dr. Jay Bradley – Research Fellow in Digital Health & Care Innovation Centre (DHI) - Scotland has presented DHI and the participatory design and simulation of new healthcare services in Scotland. DHI is part of the Scottish Funding Council's Innovation Center Program for translational collaboration of academic institutions and industry in the field of health and care.

Participatory design and simulation of new healthcare services are part of DHI Exchange, encompassing knowledge, ideas, data, and impact. In terms of participatory design, services should be designed by citizens that are going to be subjected to any healthcare service or technique and personnel that are involved in the development (innovation center or medical professionals). He described the design approach, which is based on interactive dialogue among affected patients (to find their needs) and researchers, technical personnel and clinicians for understanding and debating paper-based or electronic records in patient services and visual sense making to outline the "preferable future".

DHI has carried out 52 projects during the last 7 years, worked with 3.000 citizens, 1.000 professionals, 16 health boards, 15 charities and 10 social care organizations. Across these projects, DHI identified common requirements related to citizens, professionals and organizations. DHI integrated system enables exchanging of structure data between citizens and healthcare organizations (i.e., My diabetes My way) and provides platforms for storing best practices and guidelines. Through simulation, DHI intends to design, build and, finally, integrate a horizontal infrastructure with real patient data in NHS.

Figure 18. Building up a horizontal infrastructure

Dr. Bradley showed some outcomes obtained by different projects that are digital and asynchronous allowing citizens to remotely send images and messages to clinicians, such as a new dermatology service and remote patient management of lung and respiratory diseases. During the COVID-19 pandemic, DHI ran the participatory design for a national notification service for test results, built this as a simulated service and Scottish NHS decided to procure this system. At the same time, they also ran other services, like contact tracing services (64% channel shift of contact tracing through this digital channel). In the future, DHI will be working on a Living Lab to run these services with real citizens, by participatory design with the collaboration of citizens and professionals for identifying unmet needs and simulation to ensure that services are developed correctly and are/can be integrated in the NHS.

Key Recommendations:

- *Regions should invest more on the creation of sustainable and resilient health and care systems by adopting value-based approaches, embrace the digital transformation and ease integration of healthcare;*
- *Transferring knowledge gathered in previous initiatives on Active and Healthy Ageing supports the promotion of innovation. Regional systems should be consistent with all gained knowledge to improve the lifespan of citizens;*
- *The support of EU Commission is needed in crafting digital skills of healthcare workforce and reinforcement in the stakeholder collaboration of the overall ecosystems;*
- *Personalised Medicine should also focus on the patient lifestyle, encompassing nutrition and rehabilitation. Local, regional, national and international public organizations should consider all these features to develop effective healthcare strategies;*
- *The creation of a strong network for developing technologies and performing clinical trials based on the patient ecosystem. Through this environment, regions can test and validate new user-centered services in an efficient and sustainable way;*
- *Participatory design should be carried out by research and innovation centers and clinicians with the collaboration with affected patients for a "preferable future". Therefore, all stakeholders are involved in the health planning and management process leading to socio-economic regional progress.*

3.2 Capacity-building session

The last session of the Workshop, together with the speakers and all Regions4PerMed partners gathered the main conclusions discussed during the event and outlined the strategy of Regions4PerMed project to integrate and work on the implementation of Personalised Medicine in healthcare systems.

- Gianni D'Errico (Fondazione Toscana Life Sciences) stressed the importance of how regions can support innovation in healthcare in Personalised Medicine. The best practices and recommendations discussed during the KA4 Conference and Workshop will be made available to all regions from Regions4PerMed network through this report working closely with all speakers that were involved in both events. It is also intended to publish scientific and technical publications. The multifaced innovation forms that regions are enabling in their territories should be reflected and shared with ICPerMed and part in a forthcoming partnership or inititiaves in Personalised Medicine.

- Dorota Stefanicka (Wroclaw Medical University)remarked the relevance to foster the knowledge management among public institutions. As a clinical research coordinator, she was very interested in CAR-T production presented by Mariona Baliú-Piqué, particularly the academic activities.

Therefore, a supportive collaboration between Galicia and Wroclaw Medical University (WMU) to tackle administrative problems related to academic CAR-T production has already been envisaged.

- Paola Bello (Fondazione Regionale per la Ricerca Biomedica) brought the attention to the audience that the challenge is to learn from the others and to import the different experiences to the regional or the national context considering the differences among regions and countries.

- As the other partners expressed, **Eva-Maria Stegemann** (Saxon State Ministry for Science, Culture and Tourism) emphasized the inter-regional learning in a continuous and steady format as a key element to contribute stepwise to the integration of policies taking into account different regional conditions (i.e., different level of digitalization in healthcare across Europe). She highlighted the importance of sharing models and innovation tools in publicly available documentation in an open inter-regional exchange platform.

- José María Romero Fidalgo (Axencia de Conecemento en Saude) stressed the commitment of the Galician Health Service (SERGAS) in Personalised Medicine, for example, in CAR-T production or PPI- projects such as Código100, the Galician

Network of Living Labs and the Public Foundation of Genomic Medicine lead by Dr. Carracedo and created 20 years ago.

The second part of the capacity building was held internally on 17th of November via Zoom connection. In this session, **José María Romero Fidalgo** shared with the rest of the partners, a prerecorded video and followed by a presentation, the aim, mission and the outcomes shown in the Living Lab in Ourense University Hospital Complex of Ourense (CHUO). The Living Lab of Ourense is the pilot project of the Galician Network of Health Living Labs (LABSAÚDE).

The facilities (two new floors of CHUO) of the Living Lab of Ourense were constructed, thanks to a subproject of Hospital2050, as an experimental hospitalization. The facilities were built by Hospital2050 were double or single experimental room, experimental nursing station, posturography room and multi-sensorial stimulation room; and also, on the roof of the Hospital the bio-healthy park and therapeutic garden and a co-creation space in the basement. Patients are aware that they are part of a pilot innovative project without feeling in a lab environment. He presented the public call launched in the Living Lab of Ourense, the nature of participating entities and the innovative solutions as well as the Technology Readiness Levels (TRL) for these solutions that are 7 or higher. He also showed that the aim of the network is to spread to the rest of the Galician hospitals and the innovation lines of LABSAÚDE. Finally, he has explained that 9 projects were received in this public call and 6 agreements were signed with companies in November 2021.

Figure 19. Internal meeting of Regions4PerMed Workshop

An internal discussion and debate were performed after the presentation of José María Romero related to all information gathered during the Workshop that are best practices located in the whole value chain of innovation. The experience of each region part of the Regions4PerMed Consortium present at the online meeting was also shared and emphasized, particularly on Research and Innovation infrastructure deployment, innovation and innovation procurement.

3.3 Co-creation meeting

Following the debate of the capacity-building, the Regions4PerMed partners in an internal meeting, started an informal dialogue of the outcomes, inputs and further steps that should be jointly accomplished.

As a summary of the meeting, this document and other Regions4PerMed documentation should be publicly available and the diverse innovation tools and approaches which, regions are enabling in their territories should be shared among all stakeholders involved in Personalised Medicine and in innovation and it should be noted that innovation must be a part in forthcoming initiatives, projects and partnerships on PM.

Key message to European Regional Policy Makers

The conference and the workshop have established the key strategic role of the regional authorities that play in the implementation of Personalised Medicine. Diverse strategies to make Research and Innovation infrastructures profitable have been displayed. These models should be encouraged to outline new approaches to be integrated in regional or national systems according to the different policy structures across Europe. The relevance of the interregional cooperation among diverse European jurisdictions to create a network for exchanging interoperable and accessible human data, i.e., genomic data, should be prioritized, in compliance with privacy regulation and ethical aspects. Regional cooperation also enables the construction of research and clinical centers to respond to the demand of new products or technologies in different healthcare systems. Similarly, authorities should consider the economic impact of institutes based on applied research (like development of solutions, technologies, or creation of enterprises), thus, regions can be benefit of the developments and knowledge exchanged between applied research institutes and industry.

Besides, the exchange of experiences on the application and accomplishment of innovative procurement tools have demonstrated that they are instruments that allow the creation of user-tailored services and solutions by a dynamic dialogue (before launching tender calls) between healthcare buyers and procurers. However, the duration of the procedures and administrative workload are examples of barriers that should be addressed. Therefore, the commitment and awareness of policy makers on enhancing innovation must focus also on overcoming these issues in public procurement.

In both events, it was shown that although public procurement tools have been widely used to foster innovation in different regions, there is still a lot of room to boost their deployment in other regions. A deeper inter-regional learning should be incentivized for the development of accessible tools to all PM community to include innovation strategies (such as public procurement of innovation (PPI) or innovation partnership in PM.

Lastly, regions should support the construction of real-life settings for testing new methodologies, techniques, prototypes, and services to endeavor to create a comfortable real medical environment for patients and health personnel. The creation of these infrastructures can be possible by combination of the deployment of public procurement tools and the expertise of research and innovation institutes.


Regions4PerMed