Research and Implementation of Personalised Medicine

Strategic Research and Innovation Agenda
"Personalised Medicine – SRIA"

Online Open Consultation
Triplets of Action (ToA) and related questions

1) GENERAL INFORMATION:

Timing:
The open consultation will **close on 21 December 2022**.
This questionnaire will take around 30 min to complete.

Background information:

- https://www.icpermed.eu/en/EP-PerMed-SRIA-Consultation.php
- https://erapermed.isciii.es/ep-permed-towards-a-european-partnership-in-personalised-medicine/ep-permed-open-consultation-for-the-sria/

Link to the open consultation questionnaire:
http://enquetes.agencerecherche.fr/index.php/survey/index/sid/976696/lang/en

Definition of the Triplets of Action:

Challenge	Should describe the status quo, indicate/indication what is still lacking, why this is the case and what negative consequences this has.
Objectives	Should indicate what exactly should be done to address the challenge in terms of specific actions
Outcome	Should describe how the situation will have improved once the actions described in the objectives have been successfully implemented.

The Triplets of Action (ToA) are presented in this consultation in 4 categories:

- Personalised Medicine related research (ToA numbers 1.1 - 1.17)
- Innovation System and Personalised Medicine (ToA numbers 2.1 - 2.8)
- Personalised Medicine Implementation Setting (ToA numbers 3.1 - 3.16)
- Overarching Activities (ToA numbers 4.1 - 4.6)

2) THE 47 TRIPLETS OF ACTIONS PRESENTED IN THE OPEN CONSULTATION

1. Personalised Medicine related research (17 ToAs)

Triplet of Action 1.1 **"A collaborative approach between pre-clinical and clinical research"**

Challenge	Integration of basic research with clinical research and public health is complex and often difficult when lacking a collaborative approach. Researchers and clinicians have diverse ways of thinking and decision making. Only a limited number of clinicians participate in research, which is a bottleneck for developing and implementing PM approaches. In consequence, the translation of research (from bench to bedside) is not yet optimal, as too few promising results from basic research reach the clinical research stage.
Objectives	A two-way interaction is required from basic to clinical research and vice versa. Dedicated exchange formats and networks within institutions or regions could be established. Clinician scientist programmes that already exist in some countries and regions could be a taken up more widely. Dedicated research funding programmes could be set up that require collaboration between the preclinical and clinical field.
Outcome	An interdisciplinary collaborative ecosystem between basic and clinical researchers is in place. This will lead to both more comprehensive and faster uptake of PM approaches from pre-clinical to clinical research and implementation – with the ultimate aim that "Today's research is tomorrow's healthcare".

Triplet of Action 1.2 **"Early considerations of security, efficacy and evidence for advanced therapies"**

Challenge	There are several new methods and technologies for advanced therapies in the pipeline with potential for PM approaches, but they are too premature to be translated into clinical practice. These advanced therapies or ATMP (advanced therapy medicinal products) include gene therapy, somatic cell therapy and tissue-engineered medicines. They may contain one or more medical devices as an integral part of the medicine (combinded ATMP).
Objectives	New advanced therapy approaches for PM need to be enabled to show proof of safety, efficacy, and functional evidence to allow the fast development into clinical practice. These new approaches are mostly applications of stem cell therapies.
Outcome	Several new advanced therapy approaches are accelerated in direction of clinical studies.

Triplet of Action 1.3 **"New treatment modalities for PM"**

Challenge	New technologies and a more detailed understanding of disease mechanisms do not always lead to improved PM treatment options yet. New modalities of treatment could help overcome this gap between knowledge and clinical applicability.
Objectives	Development of new treatment modalities building on an understanding of the biological mechanisms is needed. To be able to personalise treatment based on multi-dimensional diagnostics we need to develop a range of treatment options such as Advanced medicinal Product and technologies including cell and gene therapies, and oligonucleotide-based drugs. The development of a therapeutic "tool box" will be supported. Furthermore, the development of the targeted delivery of these new modalities needs to be addressed.
Outcome	A new, broader range of treatment options/modalities allows more individuals to get the right treatment reaching the right target based on a precise diagnosis.

Triplet of Action 1.4 **"Interdisciplinary PM research projects co-developed with experts in social sciences"**

Challenge	The societal impacts that arise with PM research and implementation are not yet fully understood. PM might cause positive and negative impact on society as a whole or may be perceived differently by different societal groups. Since PM is a dynamic field, its various impacts on society are difficult to anticipate and might change over the time course.
Objectives	Interdisciplinary and co-developed research projects should be established, e.g. with experts in social sciences and public health. Implementation research should be part of scientific projects from the very beginning, fostering the implementation of PM in society. They should address societal and ethical issues of PM from early research and development and anticipate potential impacts if these PM approaches would be upscaled and implemented widely in health care systems. Research should address the development of countermeasures, recommendations, policy briefs etc. to avoid negative impact on society, such as loss of equity for access to PM.
Outcome	Publications, recommendations and policy briefs are available that address the impact of PM on society and are widely disseminated.

Triplet of Action 1.5 **"Active involvement of patients in PM research"**

Challenge	The active involvement of patients or patient representative in research projects is increasing, but there is still room for improvement. So far, not

	enough sustainable resources and tools for educating and training citizens, patients and patient advocates are in place, hindering their active participation across the entire research and development lifecycle of personalised medicine. An active participation of patient representatives can increase the relevance and applicability of research results.
Objectives	Foster involvement of patients and citizen representatives in personalised medicine developments from the early stages of research, e.g. through mandatory involvement of these stakeholders in research and development projects. Train patient representatives so that they can contribute to research projects at all stages, e.g. by co-designing research activities or information campaigns about research outcomes. Support investigators who commit to focus their research endeavours on patient-oriented research. A mentored patient-oriented research career development award on the European level might be established.
Outcome	PM research is accompanied adequately by citizen and patient representatives. The involvement of patients in PM research result in PM approaches that better follow the patients' needs, have a higher potential to be accepted by the end users and will be more easily applicable in healthcare.

Triplet of Action 1.6	**"More biomarker evidence for PM"**
Challenge	Not enough suitable biomarkers are available to guide treatments, clinical studies, and disease progression or remission. More in-depth knowledge and experience in interpreting biomarker data is needed.
Objectives	Further development of biomarker discovery and analytical methods should be supported. This should be done as public-private activities with involvement of end users. The framework for running clinical validation studies of biomarkers and diagnostics should be improved.
Outcome	. Biomarkers and diagnostics are available to diagnose and follow disease progression and treatment outcomes in a real-world clinical setting. Biomarkers are available to identify the right patient cohort for the right treatment and for the right clinical study.

Triplet of Action 1.7	**"New targets for Personalised therapies making use of an improved understanding of disease mechanism"**
Challenge	Personalised treatments are not yet widely available across disease areas due to lack of understanding of disease pathologies, lack of knowledge of treatment targets, and lack of effective treatments/drugs.

Objectives	Pre-clinical research efforts to understand the relevant disease pathologies and identify the most promising treatment targets and accompanying biomarkers are needed. In a second step, for each potential target a verification is needed that the target is indeed detectable or druggable.
Outcome	More targets for the development of targeted treatment/drugs are available.

Triplet of Action 1.8 **"Combination Treatments"**

Challenge	When developing treatment biomarkers, the focus is on detecting the effect of one drug. The reality is that we in principle almost always combine treatments. There is not enough knowledge about the effects of such combinations yet, so that patients often don't receive the most effective combination of treatments.
Objectives	Tools and biomarkers need to be developed to enable a systematic multimodal diagnostic and a system level understanding of PM treatments, taking into account multi-medication and comorbidities. Methodologies for a follow-up of each patient in a real-world context should be developed, and the data generated should be used for further improving the system level diagnostics and treatments.
Outcome	Precision health is implemented and individual treatments are much more effective, also in cases of combination treatments and multimorbidity.

Triplet of Action 1.9 **"Single-cell technologies in combination with AI and ML for PM"**

Challenge	An earlier and more accurate disease diagnosis, personalised therapy selection and population health monitoring is needed to reach the full potential of PM, for example based on early cellular pathological changes.
Objectives	Single-cell technologies could support the development of new diagnostics by applying single-cell spatial approaches to longitudinally acquired patient samples and/or patient-derived disease models obtained from well-defined cohorts, covering health, early stages of disease, disease progression and response to therapy. New AI-driven analytics are essential for the analysis of such large datasets. The predictive computational models may lead to the identification of new, more informative, molecular and cellular biomarkers that are directly linked to the mechanisms that drive disease onset and progression. This approach may also identify new drug targets for disease modifying therapies.
Outcome	The increased knowledge of the early molecular and cellular changes that drive the onset of diseases will lead to improved disease screening and detection, precise and personalised interventions and earlier detection of therapy resistance and relapse in patients – and even prevention. The identified new drug targets enable the health care industry to develop

disease-modifying therapies, incl. cellular and RNA-based therapies, to intercept disease.

Triplet of Action 1.10 **"Broader biomarker approaches to enable more informed health decisions"**

Challenge	There is still a high risk for biases in and accuracy of AI approaches, including the understanding and consideration of complex biological processes. Currently, mainly single-biomarker approaches are promoted by industry for their interventions. There is a need to develop inclusive models of 'signatures' or marker profiles, considering several relevant pathways, thus going beyond single markers.
Objectives	Identify methods to seek unbiased inference and inclusion of multilevel data by fostering the collaboration between data sciences and pre-clinical/clinical disciplines.
Outcome	Shift from a single-biomarker approach to multiple tests and comprehensive characterisation to inform several choices and options that health professions and patients can consider. This will lead to improvement in robustness and interpretation of personalised diagnosis outcomes.

Triplet of Action 1.11 **"Medical cohorts for collecting high-quality health and molecular data"**

Challenge	Access to high-quality health and molecular data is still limited. The aim that health data should be accessible, interoperable and re-usable is not yet reached. In addition, the necessary algorithms and machine learning tools are not yet in place.
Objectives	Medical cohorts are a valid tool for structuring and annotating health and molecular data. Additional systems and tools should be created for improving the accessibility of health data under the given regulatory framework. New significant algorithms and machine learning tools for PM approaches should be developed for the analysis of the data in various disease areas. Pilot projects or point of care calls could improve and showcase data utilisation and outcomes.
Outcome	More well-structured medical cohorts are established and provide qualitative data for research and care. A couple of well characterised and validated algorithms and machine learning tools are ready to be implemented into healthcare. Data generated within healthcare is utilised to a larger extend for generating valuable information on health outcomes, for improving healthcare and for a realistic cost estimation.

Triplet of Action 1.12 **"Inclusive clinical PM research inclusive that avoids bias"**

Challenge	Due to uncomplete datasets, PM approaches are not broadly applicable and lack to target the right interventions, i.e. underrepresentation of certain groups of patients or populations. The critical mass and necessary baseline of information is not yet available.
Objectives	Boost the participation/representation of different groups in clinical research and clinical trials in multiple dimensions (age, gender, socio-economic status, races, etc.); more diverse, equitable and inclusive biomedical research that could truly guide and support PM.
Outcome	PM applications are broadly ((internationally) applicable and in different settings (age, gender, socio-economic status, genetic backgrounds, etc.).

Triplet of Action 1.13 **"Online recruitment strategies to support PM clinical research"**

Challenge	Current data protection regulations prevent easy access to patients, which makes setting up clinical trials and recruiting patients difficult. Stratification amplifies this as it leads to a development of "rare diseases" with only few patients per stratification group.
Objectives	Online recruitment strategies (e.g. patient registries) should be set up, sharing patient cohorts and adhering to data protection regulations. Support to improve infrastructure/network for patient recruitment across Europe and globally.
Outcome	Easier and faster, but still ethical access to patients for clinical trials.

Triplet of Action 1.14 **"Metabolic profiling"**

Challenge	Extending the analyses of the individual metabolic profile by NGS (next generation sequencing) to (healthy) citizens, mainly focusing on mitochondrial and germline mutations on metabolic pathways has a high and as yet unrealised potential for supporting PM approaches.
Objectives	Whole genome or whole exons analysis could be extended to genes related to metabolism performed for each citizen/patient, Thus, an individual map of metabolic vulnerability could be created. Integration of the data with lifestyle, type of alimentation, smoke and alcohol abuse, etc. might enable to addressing personalised diets and suggestions of lifestyle for the prevention of cardiac, metabolic and cancer. The tools for this kind of analysis and interpretation of genomic data need to be established.
Outcome	Metabolic vulnerability can be predicted and allows recommendations for personalised diets and lifestyle that are beneficial for the individual in preventing disease, especially in the field of non-communicable diseases.

Triplet of Action 1.15 **"PM clinical research in a wide variety of disease indications"**

Challenge	Clinical trials for PM approaches are costly and complex to be set up. In addition, it is difficult to identify the right patient cohorts, mainly due to the small size of these cohorts and due to the lack of precise diagnostic data. Some disease areas, e.g. cancer, are already quite advanced in this field. Others lack behind, even though there are very promising approaches for PM applications.
Objectives	Funding of clinical research, if possible including early clinical trials, in PM covering a wide variety of diseases, in particular the large field of noncommunicable diseases.
Outcome	Results and reports of PM clinical studies for different disease areas are available for further implementation into health care.

Triplet of Action 1.16 **"Early consideration of health economic aspects"**

Challenge	Health economic aspects of PM approaches are often considered late in the development or market access phase, leading to unnecessary delays in implementation.
Objectives	PM research projects are co-developed and performed with health economic expertise.
Outcome	PM research results are more valuable for the private sector and the implementation into health care is accelerated and improved.

Triplet of Action 1.17 **"Early consideration of regulatory frameworks and authorities"**

Challenge	Pre-clinical research in PM is not always well-informed about the requirements of the regulatory framework needed for later translation and implementation. This can slow down or even prevent the implementation of PM approaches into commercial products and clinical practice.
Objectives	More networking and early guidance about the requirements of the regulatory framework (e.g. IVDR, MDR) should be offered already in pre-clinical research. On a similar line, an early dialogue with EMA (European Medicine Agency) /NCAs (National Competent Authorities) should be supported where relevant.
Outcome	A research community that is informed about the regulatory framework, follows measures for a smooth innovation and implementation process of PM and considers all methodological standards.

2. Innovation System and Personalised Medicine (8 ToAs)

Triplet of Action 2.1 **"Expanded knowledge on value for PM"**

Challenge	We need to expand our knowledge on value beyond the clinical and health economic domains. Reimbursement strategies (diagnostics and therapeutics) are needed which have a value perspective and not an exclusive cost one (value over time and not the costs of the diagnosis and therapy itself). So far, we have a good understanding in regard to HTA value, on the health economy side. But there are other repertoires of value, e.g. how does a treatment affect a person's social functioning, or their capabilities. At the moment there is no systemic way to address this.
Objectives	The matrix of value needs to be broadened, beyond the clinical and health economic value. Evidence development studies should be performed, considering clinical and economic data of PM approach benefits and challenges that might occur in different healthcare systems. In addition, Interdisciplinary research projects are needed that address societal issues and develop methods for ethically dealing with personal data. Further research is needed in order to broaden the matrix of value systemically. The value question goes beyond ethics; it is relevant for regulation as well.
Outcome	Health economic evaluation and assessment of PM will be more "personalised", taking into account ethical and regulatory aspects. This would result in fairer and broader health economic evaluation and implementation approach. Reimbursement regulations are in place when PM diagnostic tools or therapies are ready for clinical practice.

Triplet of Action 2.2 **"Adapted payment models for PM"**

Challenge	Existing payment models cannot capture dependency of diagnostic and treatment nor the data acquisition.
Objectives	Adapted payment models for PM have to be developed by the responsible stakeholders. For example, the Drug Rediscovery Protocol (DRUP)-like trials with pragmatic risk sharing models are a promising first step for that**.**
Outcome	Adequate payment models exist, leading to faster and easier implementation of PM approaches into healthcare systems

Triplet of Action 2.3 **"Improved market access for companion diagnostics"**

Challenge	The development and full-value chain integration of comprehensive innovative diagnostics is an essential prerequisite to achieve

	personalisation of therapeutic interventions. PM can only realise its potential if companion diagnostics (CDx) are not only developed, but also marketed and applied in clinical routine. Currently, lots of therapeutic potential is lost due to insufficient use of existing testing options. Regulatory fragmentation poses an important bottleneck in this context.
Objectives	Market access regulation as well as reimbursement policies should set incentives to support the approval and application of companion diagnostics, allowing faster market approval and uptake. Risk sharing strategies between industry and healthcare payers & providers will enable a more rapid access to companion diagnostics for patients.
Outcome	Patients can be better stratified to existing therapeutic options, leading to improved treatment results.

Triplet of Action 2.4 **"Value based reimbursement models for PM"**

Challenge	Often new treatments approaches are available, but they are not implemented. Sometimes this is due to arguments that evidence of cost-benefit is lacking. There is a need for a new paradigm on how to collect data for pricing. Convincing and PM adapted cost-benefit analysis are missing. Reimbursement strategies (diagnostics and therapeutics) are needed which have a value perspective and not an exclusive cost one (value over time and not only the costs of the diagnosis and therapy itself).
Objectives	Research in novel health economics models that could demonstrate value to payers is needed. These should be better suited to PM approaches/treatments. Also, access to real-world evidence (RWE) is crucial, that allows the follow up of clinical effects in combination with testing and development of new models for health economic assessment.
Outcome	Payers embrace both the concept and the value proposition and adapt accordingly. That could increase the "pull" mechanisms in order for PM innovation to be implemented in health systems. Effective and sustainable treatments are available for more patients and strategies for reimbursement are in place.

Triplet of Action 2.5 **"Early cooperation between public research and the private sector"**

Challenge	An early cooperation with the private sector is needed to get PM into the market / health systems.
Objectives	Facilitate the communication of successful PM research projects with industry and SMEs. This could be achieved by establishing an appropriate platform to enable such meetings. This approach could be supported or even developed by existing platforms, e.g. EIT Health. The platform should

	also provide a forum to understand user needs, with users, HC professionals, patients, citizens. Innovations that serve no users will not be successful even when brought to the market.
Outcome	PM research achievements are communicated to the private sector in a timely manner; public-private partnerships are formed which will increase the chances to get PM innovations into the market and accessible to the patients and citizens. User needs are adequately considered when developing innovations.

Triplet of Action 2.6 **"Medical devices and *in-vitro* diagnostics to support PM innovations"**

Challenge	The potential of medical devices and in-vitro diagnostics to support PM approaches are not yet fully utilised.
Objectives	Research into the development of medical devices and *in-vitro* diagnostics that address medical and market needs should be supported. Pre-clinical or clinical researchers should be encouraged to cooperate with medical device experts for setting up pre-clinical studies and identifying or establishing suitable patient cohorts. This could be done by partnering with suitable medical organisations Guidelines could be developed for medical devices and in vitro diagnostics to reach the market. This may include preclinical testing.
Outcome	Assure safety, security and feasibility and accelerate the time-to-market of medical devices in order to utilize their potential to contribute to PM approaches.

Triplet of Action 2.7 **"Adapted Intellectual Property (IP) for PM approaches and products"**

Challenge	The development of PM approaches and products poses significant challenges that already begin with appropriate Intellectual Property (IP) strategy/agreement. In many technologies underpinning PM, IP protection is limited and complex in use (e.g. in the case of algorithms and artificial intelligence or databases) thus failing to convey proper protection where needed. In some parts, this uncertainty derives from too vague definitions, and also a lack of international consistency. Thus, IP rights for PM products may differ significantly in important markets.
Objectives	A clear IP protection is fundamental to channel R&D investments and support entrepreneurship. Establish a clear IP regulation and support ad-hoc training programmes, especially in relation to data and data processing systems.

Outcome	More safety for industries who invest in PM, especially in Small and Medium Enterprises (SMEs) and start-ups.

Triplet of Action 2.8	**"Incentives for enterprises supporting research and development"**
Challenge	Enterprises do not have the proper incentives in place to allow PM developments, including incentives tackling the costs (e.g. for treating a disease intervention compared to long-life treatment drugs).
Objectives	Adapt policies to encourage innovation. Develop risk and cost sharing models that allow enterprises to make the paradigm shift from treating symptoms to curing a disease. Add an open dialogue with the pharma industry/MedTech about the challenges with pricing and reimbursement models building on sharing risks. Support to pilot and demonstration projects.
Outcome	Incentivised environment for industry (pharmaceutical and diagnostics) which allows to focus on PM-based approaches and at the same time ensures long-term sustainability for industry. The resulting lower risk for commercial research and development accelerates innovation.

3. Personalised Medicine Implementation Setting (16 ToAs)

Triplet of Action 3.1 **"Efficiency and value of PM approaches consider the full healthcare chain"**

Challenge	To develop individualised care programmes and visualise the effects of PM approaches, we need to understand the complete care consumption incl. home care and the individual's own experience in terms of **Patient Reported Outcome Measures (PROM)** and **Patient Reported Experience Measures (PREM)**. Healthcare needs to be coordinated around the individual instead of around the care centres. Today, healthcare is focusing mainly on productivity instead of efficiency.
Objectives	Establish activities that strengthen the possibilities of evaluating complete care chains over time. Support the knowledge exchange and collaboration between clinics and regions across Europe, e.g. to use information driven decision making not only on an individual level but also on a system level. Develop patient centric value-based reimbursement models that incentivise integrated care measuring how well the patient is feeling, reported by the patient, using a method that moves from "What's the matter with you" to "What matters to you". Support the development of AI models that predicts a primary care clinic result from the population mix in the area. To reach a focus on efficiency, healthcare needs to be data driven.
Outcome	The effects of PM can be adapted on the individual patients need, monitored and evaluated using value-based reimbursement models.

Triplet of Action 3.2 **"*Test Beds* in hospitals"**

Challenge	Successful PM approaches are not implemented into the health system/s and the healthcare setting
Objectives	Install 'Test beds', e.g. in (university) hospitals, that create the environment for conducting rigorous, transparent and replicable testing of PM approaches, computational tools and new technologies. Funding of 'Test beds' could be supported through demonstration pilot funding. They can also serve as knowledge and dissemination hubs for other clinics around Europe to visit and exchange knowledge
Outcome	PM approaches are tested under a suitable, real-life setting. This will speed up validation and implementation of these approaches. In replicating hospital conditions, 'Test beds' serve both, companies and healthcare professionals, to test the suitability of their innovative healthcare ideas or devices. The time for product development is shorter and access to wider markets is accelerated.

Triplet of Action 3.3 **"Training and Education of healthcare professionals"**

Challenge	Medical communities, at the start of their career and constantly during their professional practise, need to be trained in PM approaches.
Objectives	Establish healthcare professionals (HCP) PM buy-in by integrating PM as part of their curriculum and continuous training of HCP during the course of their professional career.
Outcome	The right competencies and knowledge are available to implement PM approaches for improved health and care.

Triplet of Action 3.4 **"Accessibility and knowledge of genomic tools for healthcare professionals"**

Challenge	Lack of knowledge and of accessibility for healthcare professionals to use genomic tools for their daily work with the patient, not only for the diagnostic and treatment but also for prevention.
Objectives	Activities and tools are needed to support all healthcare workers and healthcare providers in their daily routine to consider and interpret genomic information.
Outcome	Increased knowledge, abilities and mindset of all healthcare workers and providers towards genomic tools in PM approaches, which will support the implementation and gain of PM in the healthcare systems.

Triplet of Action 3.5 **"Data collection by healthcare professionals for PM"**

Challenge	High quality data collection from healthcare professionals required for advancing drug development and standard of care on top of patient's care is not realistic.
Objectives	Working with patients' groups and healthcare professionals, establish data collection centres of excellence at regional/national level with key hospitals that can access and install coordinated data collection and data management technical and IT support, e.g. by working with Innovation hubs.
Outcome	Accelerate or revise Drug Development and Standard of care by having access to high quality data in a timely manner.

Triplet of Action 3.6 **"Availability and accessibility of real-world data and real-world evidence"**

Challenge	Optimisation of and innovation in PM is highly dependent on the availability of and access to high-quality real-world data (RWD) and real-world evidence (RWE). This in turn requires the availability and accessibility of high-quality interoperable data regarding patient characteristics, therapeutic interventions and integrated (both clinical and patient

	reported) outcomes data. Both availability and access are currently not optimal and represent a bottleneck in PM research.
Objectives	Frameworks, tools and incentives should be developed, that support the healthcare systems in producing and using integrated data sets. These should be made available for secondary data use according to FAIR (findability, accessibility, interoperability, and reusability) principles.
Outcome	Improved treatment outcomes and sustainability of health care systems through better and faster development and monitoring of PM approaches.

Triplet of Action 3.7 **"Data Sharing for PM on central platforms"**

Challenge	Data protection regulation and general ethical concerns can be a major obstacle for using sensitive patient data – despite best efforts to meet FAIR principles.
Objectives	Conceptualise adequate (meta) data usage strategies that enable anonymisation and pseudonymisation for important applications such as personalised use of antibiotics.
Outcome	Providing an IT platform for automated and anonymised health (meta) data handling.

Triplet of Action 3.8 **"Feedback loops from clinical application and patients experiences to research & development/innovation"**

Challenge	Feedback loops from the patients and healthcare system back to the research community and the innovation system/players are not yet in place. "Information silos" need to be opened out and should be avoided. The tools and knowledge generated are not synchronised with the needs of healthcare and patients.
Objectives	Develop and establish tools/platforms to allow feedback loops from the patient/healthcare system providers and payers back to the research community.
Outcome	Better and faster refinement of already implemented, secure and tailored PM approaches in diagnosis and treatment.

Triplet of Action 3.9 **"Establishment of Learning Healthcare Systems (LHS)"**

Challenge	A true Learning Healthcare System (LHS) is not yet implemented. The idea of an LHS describes a health system in which science, informatics, incentives, and culture are aligned for continuous improvement and innovation, with best practices seamlessly embedded in the delivery

	process, [with] patients and families active participation in all elements, and new knowledge captured as an integral by-product of the delivery experience.
Objectives	Clinical data needs to be collected to generate knowledge and to apply it to improving practice. For example, from the Electronic Health Records, clinical registries or other routinely collected sources. Establish an LHS where clinical data (including genomic data) can be accessible for research and AI applications to produce innovation that can subsequently inform clinical care.
Outcome	Research would be informed on real world health issues and could more directly impact clinical care

Triplet of Action 3.10 **"Improved awareness for patients and citizens for PM"**

Challenge	There is currently a lack of awareness of patients and citizens for PM and its concept and abilities. The general population needs to be informed about PM approaches, including diagnostic, therapeutic and prevention strategies.
Objectives	Increase the PM knowledge of patients and citizens. Work with key patients' organisations and non-governmental organisations (NGO), representing different populations (gender, age, ethnic, etc.). Develop web-based tools to support the knowledge and awareness for PM approaches as well as a platform for the public exchange about PM in general and innovative approaches in specific.
Outcome	The impact of "Internet Fake Information" is significantly reduced. A "pull" effect for PM approaches in diagnosis, treatment and prevention by patients and citizens is created, and the request of the population to access existing and develop new PM approaches is increased. Perception and ethical challenges linked to PM are overcome and therewith acceptance is increased. The impact of PM is accelerated, leading to better standards of care.

Triplet of Action 3.11 **"Establishment of decision support systems facilitating PM implementation"**

Challenge	There is still a lack of appropriate decision support systems (e.g. diagnosis, treatment choice, follow-up decisions and prevention) (infrastructure) that are suitable for the implementation into practice.
Objectives	It is crucial to developed and integrate decision support systems, which are easy to understand and simple to use, e.g. to help the healthcare practitioners to consider and analyse multiple and diverse data sets.

Outcome	Successful integration and acceptance of PM related decision support systems in clinical practice in hospital and ambulant setting. Allow healthcare professionals to consider multiple data sets without the need to be specialist in all disciplines (epidemiology, modelling, image analysis, biomarker analysis, etc.). This will lead to improved care and treatment outcomes, decreasing adverse effects and time to correct diagnosis or adapt the treatment.

Triplet of Action 3.12 **"Use of pharmacogenomics and pharmaco-metabolomics in standard healthcare"**

Challenge	Pharmacogenomics and -metabolomics as well as more basic electronic medication plans are currently not yet standard across Europe although their efficacy was already demonstrated.
Objectives	Make pharmacogenomics and -pharmaco-omics as well as comprehensive electronic medication and treatment plans standard of care across Europe.
Outcome	Reduction in medication induced adverse-effects, better treatment outcomes due to optimised dosing and prevent wrong or not necessary medication and treatment and reduced interaction during multi-morbidities and related multi-medication.

Triplet of Action 3.13 **"Establishment of chronic disease management along with PM"**

Challenge	Chronic disease management has greatly improved in the past, but disease management programmes currently still mostly do not operate along PM concepts and approaches.
Objectives	Use PM approaches, e.g. by including multidata consideration, to better understand each patient's situation and personalise the chronic disease management for the benefit of the patient in a structured and standardised approach.
Outcome	Better and more efficient treatment, less adverse effects and most likely reduced costs by PM optimised models, especially in light of frequently occurring multi-morbidity.

Triplet of Action 3.14 **"Patient-centred care pathways"**

Challenge	The individual's specific health needs and desired health outcomes are currently not or only to small extend considered in healthcare decisions and quality measurements. This hampers the acceptance of PM approaches and interventions.

Objectives	Shift the focus from considering solely basic and clinical sciences but include also health systems sciences, including patient-centred care. Adapt national/regional curriculum frameworks for healthcare professionals in order to enhance communication skills with patients and citizens. Support curricula reforms for healthcare providers to create a new model for care together with patients and citizens. As a basis and in parallel: support train-the trainers' programs on national and European level.
Outcome	Patient-centred care has positive impact on patient satisfaction, treatment adherence and self-engagement. Outcomes and quality of life will be improved, and care disparity and care costs reduced. PM approaches and developed intervention will support patient-centred care and increase both quality of care and patient outcomes.

Triplet of Action 3.15 **"Create evidence and communicate PM success stories"**

Challenge	Many new methods and treatments never reach the patient. The very same time, healthcare needs to be adapted in order to be ready to uptake new developments.
Objectives	Create a collaborative-partnership environment so that the healthcare system better utilises new or refined tools and knowledge developed. Showcase the good examples. Fund efforts to connect researchers/clinicians across Europe and globally for knowledge and exchanges of personnel.
Outcome	More new treatments and knowledge is integrated into clinical practise and reach patients.

Triplet of Action 3.16 **"Clinical trial design adapted to smaller patient groups"**

Challenge	There is a lack of evidence from small patient groups to allow the approval and decide on reimbursement levels.
Objectives	Where large double-blind studies cannot be performed and efficacy is lacking, develop tools that include real world data to build evidence. Support continued evidence generation post introduction of new treatments/therapies.
Outcome	Clinical trial design available that is adapted to smaller patient groups, allowing studies that build evidence on outcome measures and thereby feed into reimbursements models fit for purpose.

4. Overarching Activities (6 ToAs)

Triplet of Action 4.1 **"More widely implemented, ethical and secure genetic screening programmes"**

Challenge	Both patients and society could benefit from comprehensive knowledge of each individual's genetic information. This could even be implemented as a genetic screen for new-borns. However, today access to genomic profiling varies greatly across (EU) citizens, mainly because of economic and social barriers. In addition, ethical and security issues are still a challenge for implementing large-scale screening programmes.
Objectives	Demonstrate the benefits of such programs by establishing and supporting pilots to analyse and screen the genetic information on a regional or national level where possible. Learn from countries which have this already in place. Ethical and security aspects have to be considered before such an activity is launched. Establishing a genomic "passport" or "avatar" containing a whole genome or whole exons analysis for each citizen/patient could be considered.
Outcome	Genetic screening programmes and the respective date are available to be utilised when needed to inform and accelerate prevention, diagnostic and treatment, e.g. as actionable genomic variants for specific diseases.

Triplet of Action 4.2 **"PM innovations in a regional environment"**

Challenge	Development of medical products (incl. *in-vitro* diagnostics) and therapeutics that address medical and market needs.
Objectives	Making use of local innovation systems to ensure early contact for possible cooperation with enterprises and suitable handover points for R&D processes; involvement of clinical/medical experts; establish and maintain forum of experts from technology research and engineering, industrial development and medical practice.
Outcome	Facilitate the comparison of parallel structures in order to detect and avoid it faulty developments from proof of concept to market-ready products

Triplet of Action 4.3 **"Connected large-scale health databases"**

Challenge	Access to large-scale health databases is still limited. So is the number of these databases, as well as the amount, interoperability and quality of health data available. Multidimensional, time-series data for people of diverse ethnicities will be required to avoid bias – and so will powerful computing infrastructure to analyse these data.

Objectives	Support is needed for linking large-scale health databases containing high-quality, multidimensional, time-series data for people of diverse ethnicities including powerful computing infrastructure to analyse these data.
Outcome	Large-scale health databases are accessible, connected and utilised with an adequate balance between privacy and public benefit. They are a valuable resource of high-quality health data for research and health care and contribute to speeding up the development and implementation of PM approaches.

Triplet of Action 4.4 **"PM adapted and focused biobanks and real-world data registries"**

Challenge	Biobanks and Real-world data (RWD) registries are powerful data generation tools which employ highly trained staff, standardised and quality-controlled procedures, an elaborate data management system and an adequate infrastructure. Despite the benefits, investment in these infrastructures are still lagging behind. In addition, missing access policy for researchers and innovators makes the valuable source of information greatly unexploited.
Objectives	Invest in regional and interregional centralised, connected and interoperable biobanks and health data repositories. Establish access policy for research and innovators which meet ethical and security standards. The legal framework needs to be adapted to allow for sample collection and data collection for a broader systemic analysis. Today, it requires, on the research side a broad ethical approval and informed consent. Need for optimised protocols for biological sample collection to allow systemic multimodal diagnostic approaches not only for one single purpose.
Outcome	Well curated, easily accessible, high quality data infrastructures and biobanks are generated for example as basis for application of Artificial Intelligence (AI) or Machine Learning (ML) methodologies.

Triplet of Action 4.5 "**Network of national and regional innovation hubs"**

Challenge	Currently, there is no equal access to breakthrough technologies and advanced personalised medicine approaches, education and training across Europe and no equal citizen engagement. Furthermore, implementing innovative approaches requires a coordinated approach that integrates multidisciplinary and intersectoral expertise. Due to the lack of methodology, there are often delays in the development of innovative PM approaches.
Objectives	This could be achieved through a connected network of regional and national centres, fostering activities to deliver novel research results,

	insights and solutions that promote the translation of personalised medicine research into clinical practice, upscale to market access and accelerate the uptake into healthcare systems. The network could share resources, gather the critical mass for global competitiveness and be open for collaboration with the entire scientific community.
Outcome	Creating a network of excellence in Europe will provide access to and uptake of new technologies. Innovative personalised medicine approaches for diagnosis, treatment and prevention will be developed faster, and their uptake in regional/national healthcare policies will be improved.

Triplet of Action 4.6	**"Genome-wide association studies within and beyond Europe"**
Challenge	PM approaches are often developed with a restricted dataset (for that the right to use the data was permitted) and are therefore often not applicable globally and in different genetic settings. It is still challenging to share genome data cross borders and globally for one common goal.
Objectives	Attaining a critical and more diverse mass of data by collaborating with researchers from non-EU countries to develop and train algorithms and models utilised in PM approaches. Identify and link with relevant international PM communities and develop a global PM agenda, integrating and promoting common standards. Ensure that developed approaches are applicable as broadly as possible and not limited to a specific European context and support EU foreign policy contributing to UN development goals. International knowledge exchange programmes where clinicians meet and exchange experiences.
Outcome	Very large and diverse genome-wide association studies uncover many novel genetic factors associated with important diseases. Trans EU coordination efforts improves the international standing of EP PerMed members and partners and implementation of PM at an international level.

3) QUESTIONNAIRE: OPEN CONSULTATION FOR THE STRATEGIC RESEARCH AND INNOVATION AGENDA (SRIA) IN SUPPORT FOR THE EUROPEAN PARTNERSHIP FOR PERSONALISED MEDICINE, EP PERMED

This section outlines the questions concerning the validation and refinement of the Triplets of Action listed above and presented in the open online consultation.

For each category of Triplets of Action (corresponding overall to Questions 1, 2, 3 and 4):

- Personalised Medicine related research (ToA numbers 1.1 - 1.17)
- Innovation System and Personalised Medicine (ToA numbers 2.1 - 2.8)
- Personalised Medicine Implementation Setting (ToA numbers 3.1 - 3.16)
- Overarching Activities (ToA numbers 4.1 - 4.6)

the participant is asked to answer three sub-questions:

1) Validation of the "Triplets of Action" presented of the respective category (see section 1 of this document).

To which extent do you agree with each of them by a scale from 1 - 10. (10 corresponds to "agree completely" and 1 "disagreement")

	1	2	3	4	5	6	7	8	9	10
Triplet of Action 1.1 "A collaborative approach between pre-clinical and clinical research"	○	○	○	○	○	○	○	○	○	○
Triplet of Action 1.2 "Early considerations of security, efficacy and evidence for advanced therapies"	○	○	○	○	○	○	○	○	○	○
Triplet of Action 1.3 "New treatment modalities for PM"	○	○	○	○	○	○	○	○	○	○
Triplet of Action 1.4 "Interdisciplinary PM research projects co-developed with experts in social sciences"	○	○	○	○	○	○	○	○	○	○
Triplet of Action 1.5 "Active involvement of										

2) Indicate the urgency of the "Triplets of Action" in this category according to your judgement with a scale from 1 - 10.

(10 corresponds to "high urgency" and 1 "less urgent")

	1	2	3	4	5	6	7	8	9	10
Triplet of Action 1.1 "A collaborative approach between pre-clinical and clinical research"	○	○	○	○	○	○	○	○	○	○
Triplet of Action 1.2 "Early considerations of security, efficacy and evidence for advanced therapies"	○	○	○	○	○	○	○	○	○	○
Triplet of Action 1.3 "New treatment modalities for PM"	○	○	○	○	○	○	○	○	○	○
Triplet of Action 1.4 "Interdisciplinary PM research projects co-developed with experts in social sciences"	○	○	○	○	○	○	○	○	○	○
Triplet of Action 1.5 "Active involvement of										

3) Choose five (5) "Triplets of Action" of this category that you think are the most important to accelerate the development and implementation of personalised medicine approaches in general.

Please only choose five (5) Triplets of Action. You can leave a comment to explain your choice.

- ☐ Triplet of Action 1.1 "A collaborative approach between pre-clinical and clinical research"
- ☐ Triplet of Action 1.2 "Early considerations of security, efficacy and evidence for advanced therapies"
- ☐ Triplet of Action 1.3 "New treatment modalities for PM"
- ☐ Triplet of Action 1.4 "Interdisciplinary PM research projects co-developed with experts in social sciences"

Furthermore, the following four (4) questions are asked for the entire set of 47 presented Triplets of Action:

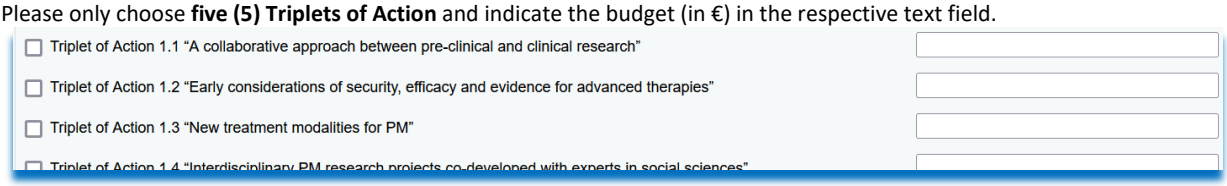
5.1) Considering all above presented 47 "Triplets of Action" of the four categories, please choose in total five (5) “Triplets of Action” with the highest importance to foster the development and implementation of a personalised medicine approach.

- Personalised Medicine related research (ToA numbers 1.1 - 1.17)
- Innovation System and Personalised Medicine (ToA numbers 2.1 - 2.8)
- Personalised Medicine Implementation Setting (ToA numbers 3.1 - 3.16)
- Overarching Activities (ToA numbers 4.1 - 4.6)

Please only choose in total **five (5) Triplets of Action**. “drag and drop” table: Double-click on an item in the list „Your Choice” or move the item to the list “Your Ranking”. Start with your highest-ranked item, moving through to your lowest ranked item. To remove an item from the right side: double click on that item again or move it through “drag and drop” on the other side. To change the order of items in “Your Ranking” use drag and drop.

5.2) Between the five "Triplets of Action" that you prioritised in question 5.1, how would you distribute a 15 M€ budget to support them?

Please only choose **five (5) Triplets of Action** and indicate the budget (in €) in the respective text field.



6) Would you like to suggest an additional “Triplet of Action”?

If yes, please follow the structure of the Triplets of Action:

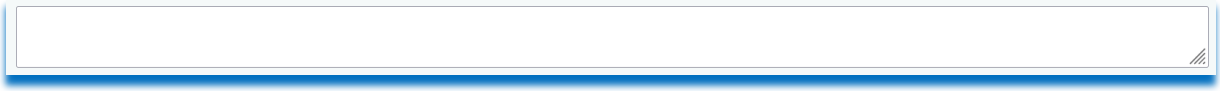
- *Challenge:* Description of the status quo, indication/indicates what is still lacking, why this is the case and what negative consequences this has.
- *Objectives:* Indicates what exactly should be done to address the challenge in terms of specific actions.
- *Outcome:* Description of how the situation will have improved once the actions described in the objectives have been successfully implemented.

Please insert your suggestion below and, if possible, indicate the category:

- Personalised Medicine related research,
- Innovation System and Personalised Medicine,
- Personalised Medicine Implementation Setting,
- Overarching Activities.

Please note: Max. 2.000 characters including spaces.

Text field



7) Please comment below on the wording of presented “Triplets of Action” according to your judgement and expertise.

Please indicate the category and the number of the Triplet of Action for that you would like to proposed adaptions of the wording. **Comments and suggestions are welcome for up to 3 of the 47 Triplets of Action presented in this consultation.**

Please note: Per Triplet of Action max. 2.000 characters including spaces.

Text field