ICPerMed
INTERNATIONAL CONSORTIUM

Action Plan

Actionable Research and Support Activities

Identified by the International Consortium for Personalised Medicine

Imprint

EU grant

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Executive Summary

ICPerMed (www.icpermed.eu/) is a newly established platform of over 30 European and international partners representing ministries, funding agencies and the European Commission (EC).

Since November 2016 the consortium is supported by a secretariat which is funded via a Coordination and Support Action (CSA) within the European Union's Horizon 2020 research and innovation programme. The central aim of ICPerMed is to align and encourage joint efforts in personalised medicine research and implementation. This will be achieved by different activities, such as meetings, workshops and congresses; surveys on personalised medicine programmes, successes and actions; strategic publications and joint initiatives.

In preparation for the official launch, five working groups were established, with topics covering all aspects along the value chain and beyond:

1. Developing awareness and empowerment
2. Integrating big data and ICT solutions
3. Translating basic to clinical research and beyond
4. Bringing innovation to market
5. Shaping sustainable healthcare

In these groups, ICPerMed members and nominated experts worked hand in hand to develop a collection of actions to advance personalised medicine in all relevant areas and at all levels. This work was complemented by an international conference on personalised medicine organised in conjunction with the European Commission in June 2016.

ICPerMed's Action Plan is the culmination of these efforts. It represents an extract of this collection and lists research activities (A1–A22) and research-supporting activities (B1–B8) that are deemed to be "ready for action". The Action Plan is intended to be the blueprint for establishing research activities within the entire range of personalised medicine either at national level, European or international level. This Action Plan will feed into national and European strategic discussion of research funders shaping their future programmes including both single actions and joint efforts.

One of the latter will be the European Research Area Network for personalised medicine (ERA-PerMed), which is in preparation and should begin work by end of 2017 with Joint Transnational Calls (JTCs) on personalised medicine as a core element.

All important information and development in the context of ICPerMed will be available on the ICPerMed website and in upcoming publications.

Introduction

Personalised medicine uses information specific to an individual to target therapeutic and prevention strategies more accurately, putting citizens and patients at the centre of healthcare and innovation. Recent developments in areas such as molecular profiling, medical imaging and diagnostics are making personalised medicine a reality in healthcare.

In addition, a revolution in information technology has made it possible for researchers to collect and analyse ever greater quantities of data so that the impact is evident on the entire healthcare continuum, from health research to patient care. Together with an improved understanding of the biological mechanisms and environmental interactions that govern disease progression and working with the policy and regulatory environment to encourage widespread use, these developments will change the way that healthcare is delivered in the future.

Background to the establishment of ICPerMed

The International Consortium for Personalised Medicine (ICPerMed) builds on a number of previous initiatives in personalised medicine at EU and national level. In 2010, the European Commission organised a series of preparatory workshops, with a particular focus on the role of 'omics'-related research in personalised medicine (e.g. genomics, proteomics, metabolomics, epigenomics, pharmacogenomics).[1] This was followed a year later by a conference on 'European Perspectives in Personalised Medicine',[2] and further by the Personalised Medicine Conference 2016.[3] In their Council conclusions on personalised medicine for patients published in December 2015,[4] EU Health Ministers set out their views, noting the benefits and challenges, and in particular noting that EU health systems and innovation should be patient-centred.

Alongside policy developments, the Seventh Framework Programme for Research and Technological Development (FP7) committed over €1 billion, from 2007 to 2013, to support research projects and activities in personalised medicine. Of particular note was the establishment in 2011 of EuroBioForum, a four-year project that aimed to create a platform for public funders and performers in the area of personalised medicine, fostering dialogue, cooperation and coordination. This led to an increased understanding of the relevance to personalised medicine of a range of diverse topics such as health economics, education and training, IT infrastructures, big data, communication and public awareness. This was complemented by the establishment of another consortium, CASyM (www.casym.eu), which set out to formulate a European-wide implementation strategy for Systems Medicine.

An important outcome of EuroBioForum was the establishment of 'PerMed'. Supported by the EU as a Coordination and Support Action from 2013 to 2015, PerMed brought together 27 international partners representing key decision-makers in healthcare and patient organisations, research and research policy, and industry to generate a Strategic Research and Innovation Agenda (SRIA) for personalised medicine. Published in 2015, *Shaping Europe's Vision for Personalised Medicine*[5] set out a comprehensive set of recommendations aimed at furthering the implementation of personalised medicine approaches. The SRIA was organised around five interrelated challenges, namely:

- Developing awareness and empowerment
- Integrating big data and ICT solutions
- Translating basic to clinical research and beyond
- Bringing innovation to market
- Shaping sustainable healthcare

1 See European Commission *Staff Working Document*, Use of '-omics' technologies in the development of personalised medicine October 2013, https://ec.europa.eu/research/health/pdf/2013-10_personalised_medicine_en.pdf

2 http://demo.intrasoft.be/research/health/pdf/personalised-medicine-conference-report_en.pdf

3 http://ec.europa.eu/research/conferences/2016/permed2016/pdf/permed-2016_report.pdf

4 http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52015XG1217(01)

5 *Shaping Europe's Vision for Personalised Medicine*, http://www.permed2020.eu

It also made nine prioritised recommendations with the potential for the greatest impact and outcome in facilitating the introduction of personalised medicine for the benefit of patients, citizens, and society.

A key point of the SRIA was that personalised medicine research required to adopt a different approach. In particular, research was needed across the entire healthcare value chain. This meant that alongside traditional funded consortia, additional funding would be necessary for clinical implementation and 'real world' assessment of personalised diagnostics and therapies. The SRIA noted that driving innovation in personalised medicine would require research projects to be carried out in close cooperation with regulatory bodies, healthcare providers, policy-makers, ethical, legal and social experts, and patient organisations. The SRIA also identified a need to move beyond classical research funding schemes to include communication and training modules, outreach activities and non-research cross-sectoral projects. It noted that to implement this ambitious agenda would require new transnational networking structures and it suggested that an international consortium of research funders may provide an appropriate model.

Personalised medicine approaches are already being implemented at EU, national and organisational levels. At EU level, the EU Horizon 2020 Framework Programme 2014–2020 continues to support the broader research agenda whereas the focus of the Innovative Medicines Initiative (IMI) research agenda is on the development of new medicines, with patient access to new medicines a key theme. At national level, many countries are integrating personalised medicine approaches into healthcare, for example the French National Cancer Institute (INCa) now has an organisational framework to integrate personalised medicine into routine cancer care. Population-based biobanks (e.g. in Estonia, Iceland, the UK) enable linkages to be made between biomarkers, medical history and lifestyle information. At organisational level, and with attention focused on patient-centred care, programmes have been designed and implemented to teach patient-centred communication skills to practising physicians. The importance of communication and citizen engagement is evident in the increased popularity of Science Slam events, while professional organisations offer an opportunity for stakeholders to learn from each other; for example, the development of appropriate methodologies for health technology assessment of personalised prevention is evident in the work of ISPOR (the International Society for Pharmacoeconomics and Outcomes Research) and the CNR S&T Foresight Group. However, in order to fully realise the potential of personalised medicine, knowledge, research activities and best practices need to be shared and where appropriate, aligned.

Overview of ICPerMed

The International Consortium for Personalised Medicine (ICPerMed)[6] was formally established in November 2016. Building on work done by PerMed and taking implementation of the SRIA as its starting point, ICPerMed aims to:

- Establish Europe as a global leader in personalised medicine research
- Support the personalised medicine science base through a coordinated approach to research
- Support research to investigate the benefits of personalised medicine to citizens and healthcare systems
- Pave the way for personalised medicine approaches for citizens

The Consortium brings together more than 30 funding bodies from EU Member States and beyond, which together will identify and implement priority actions in personalised medicine research. Members include public and private 'not-for-profit' health research funding and policy organisations (see Annex 2 for a full list of members). Although the focus of the initiative is on Europe, organisations from other parts of the world are also included. ICPerMed is organised around an Executive Committee, currently chaired by Mairead O'Driscoll from the Health Research Board (Ireland), with vice chairs Ain Aaviksoo from the Ministry of Social Affairs (Estonia) and Wolfgang Ballensiefen from DLR (Germany). The

6 www.icpermed.eu

Development of the ICPerMed Action Plan

Executive Committee, which includes representatives of member organisations, is supported by the ICPerMed Secretariat, coordinated by DLR, Germany, with partners from France (ANR), Italy (Ministry of Health) and Spain (ISCIII). The secretariat's work will be financed by the EC over the next four years.

There is no monetary commitment required to join ICPerMed, but members commit to working actively towards achieving the overall aims of the Consortium. In addition, members will be expected to report annually on their activities and to actively participate in the running of the initiative.

How the Action Plan was developed

Throughout 2016, members of ICPerMed worked to develop a roadmap with actionable research activities based on the PerMed SRIA, other strategic publications, interviews and discussions as well as the contributions at the Personalised Medicine Conference in June 2016. As a first step, five challenge groups were established under the leadership of a 'Challenge Facilitator', with members drawn from the Consortium itself and input from external experts. The roadmap identified a large number of research actions, as well as their expected impact and the means and timelines for their implementation. Although not a formal publication, this document will be updated regularly by ICPerMed so that it remains relevant and 'live'. In addition, other interested funding organisations can join such activities and the ICPerMed platform or suggest potential collaborations. This Action Plan will also feed into the proposed European Research Area Network on personalised medicine (ERA-PerMed), which will begin its work by end 2017.

The actions identified through this process were refined further by the Executive Committee of ICPerMed, with a focus on those deemed 'ready for action'. The resulting Action Plan sets out a discrete set of activities which will form the basis of the work programme for ICPerMed member organisations over the next two years. For clarity, these are divided into two parts; Part A lists research actions while Part B identifies policy and support actions. Furthermore, both chapters are organised in several subcategories. Wherever possible, the sequence of action items in each subcategory corresponds to the value chain (e.g. data generation – translational sciences – healthcare system). The sequence of action items does not reflect priority in terms of relevance. In the appendix of the document, the expected timeframe for each action item is listed along with the estimated level of action, e.g. regional, national, European or international.

The expectation of ICPerMed is that over the next two years, ICPerMed members and the European Commission (EC) will work together to implement these actions, reporting regularly on its own progress as well as on other actors active in this field, sharing knowledge and bringing real benefits to health systems and to citizens.

Research Activities – Part A

In order to develop and use the full potential of personalised medicine, truly interdisciplinary research and inter-sectoral collaboration is needed. In addition to the achievements already accomplished in several areas, the generation of best available evidence in basic and translational research, and also taking into consideration ethical aspects, is crucial, in order to provide sound and comprehensive information for citizens and patients, healthcare professionals and providers, payers and researchers of the potential of personalised medicine.

Another important aspect in this context is the availability of comprehensive, validated, accessible and interoperable datasets. These require not only genomic, biomedical and clinical information, but should where possible also incorporate lifestyle and other personal data. These developments and datasets have to consider data protection, safety, security and ownership issues, harmonisation strategy of existing and newly collected data as well as evidence-based innovations for diagnosis, personalised treatment, prediction and prevention. However, data collection is only useful if we can ensure that the collected data are of a sufficient quality. In order to integrate information from multiple sources, it must be ensured that it is well characterised and compatible.

Furthermore, as a consequence of new insights into the underlying molecular causes for disease, it is debatable whether the established disease classification is still valid. A new classification taking this new knowledge into account may have to be developed and would need constant refinement in the light of new scientific achievements.

Other important areas are the development of models and decision-making processes which focus on the individual citizen at all levels, including assessment of the safety and efficacy of interventions, and the development of long-term, patient-centred, strategic approaches on how to meet, with a public health perspective, the challenges associated with access to personalised medicine, while ensuring the sustainability of national health systems and fully respecting Member States' competencies. Thus on the basis of up-to-date ICT options and 'big data' handling, tools need to be developed that support personalised approaches and make the enormous amount of data accessible and manageable in clinical practice. These tools should aim to support all healthcare providers, but particularly general physicians, in utilising the best current personalised strategies for each patient in a real life setting. Moreover, patient involvement is required as early as possible in all research activities either at national or European level.

Thus, last but not least, personalised medicine approaches need to demonstrate not only their evidence but also their cost-effectiveness in order to support the sustainability of the different health systems.

In summary, the action items listed in Part A therefore are aimed at a wide range of research, with the ultimate aim of producing significant results to foster and evaluate existing as well as newly generated personalised medicine methods.

Data

A.1 Research projects to ensure the quality, completeness, validity and analysis of datasets

It is crucial to develop informatics, ICT and mathematics tools to integrate, analyse and extract value from databases (e.g. omics, health records, clinical data, imaging data, data from mobile devices and wearable sensors, behavioural, environmental) with specific attention on interoperability of the respective databases. This should include research to ensure the quality, completeness and validity of data.

A.2 Support research on data harmonisation in the context of personalised medicine needs

Research on data harmonisation is needed to ensure that existing and even more importantly future datasets with important information for personalised medicine approaches, can be utilised and where appropriate be aligned. This effort will need the development of specific ICT using either existing or newly established supporting infrastructures taking into consideration national rules on data protection. As a first step this would need the development and definition of minimal datasets for clinical as well as general population databases. Only then can all available and relevant datasets such as from medical/clinical, lifestyle

and other sources be utilised for the benefit of citizens and patients. This effort will be crucial in order to further develop and implement existing as well as innovative personalised medicine strategies.

A.3 Studies on data integration and interpretation of multifactorial diseases

Studies on data integration and interpretation of multifactorial diseases that focus on personalised medicine approaches should be supported. These should utilise various datasets – e.g. public data as well as data derived from clinical studies, medical records, etc. and include different forms of mathematical frameworks. Thus, these studies aim to provide successful examples of feasible systems medicine approaches that should result in potential diagnostics or therapeutic candidates for personalised medicine. Those candidates should reach the level for further preclinical validation (animal, cell culture, etc.) and thus the results can be the basis for future proof of concept studies.

A.4 Support research on enabling the extraction of structured data from unstructured sources

This action item is strongly connected to efforts in data collection and harmonisation; it would be of great benefit if already existing information, for example within text documents, could be edited in a way that would ensure that these sources could also be utilised. Therefore, research is needed to adapt documents in different languages or specific cultural areas, non-standardised clinical records and other sources, effectively and if possible automatically. Thus, already existing significant datasets, especially at regional and national level, could be made accessible, not only for research but also for their best possible implementation of innovative personalised medicine strategies.

A.5 Pilot projects to assess the impact of sharing data for researchers and other parties

Such pilot projects should use evidence-based methods to gather and analyse the short and long-term benefits, and the difficulties, of sharing datasets related to personalised medicine approaches. This analysis should be performed for all actors involved from the public and private sectors. Such results could help to convince all involved parties to share existing datasets, but could also avoid risk and disadvantages in setting up such open collaborations. For data sharing common rules need to be developed and established, taking into consideration the maintenance of data once a project has been completed, ensuring sample sizes which are statistically relevant, balancing open access with the need to protect innovation data privacy and intellectual property.

A.6 Research projects to optimise data security, privacy and ownership within personalised medicine approaches

Ensuring the security and privacy of all citizens' and patients' data is of fundamental importance to the further development and implementation of personalised medicine. This includes for example adequate and early informed consent explicitly restricting the use of datasets by health insurers, employers or providers of long-term life care. This also includes how to handle the ownership of individual and collective datasets with the support of all available information and communication technologies. The aim is to find manageable solutions and approaches for these issues; therefore research is needed which considers the above aspects in conjunction with the recent 'big data' setting.

A.7 Research projects to develop innovative decision support tools for healthcare providers

Progress towards personalised medicine relies fundamentally upon data and information on current diagnosis and treatment options. On the one hand, all healthcare providers should support ongoing research efforts with their knowledge and data. On the other hand, they also need suitable and easy handling support tools based on the latest ICT developments and research results. Only then can their decision-making be supported and if possible optimised, considering the latest personalised medicine improvements. Not only will citizens and patients benefit, but economic aspects can also be considered, for example, if non-responders should receive the respective drugs, or if multi-medication can be reduced or avoided.

A.8 Support research to develop telehealth and telemedicine applications to support the implementation of personalised medicine

Such research should develop and evaluate existing and innovative e-health and m-health options. Thus, there is a significant need for additional understanding of patient outcome measures. This raises legal, social, ethical challenges as well as a need for new and reasonable ways to handle 'big data'. Data sharing resources include Internet-based patient involvement, spontaneous reporting from many channels and analysis of electronic health records as patient repositories across national borders. Research in this area can outline what needs to be done to facilitate the adequate use of data across nations and cultures.

Technologies, Methods and Processes

A.9 Development and implementation of high-throughput preclinical models

Research is needed to develop and implement high-throughput preclinical models including e.g. animal models, cell culture models, etc. to validate hypotheses generated from population, clinical and molecular studies. The study findings should lead to functional test models and tools to understand the phenotypical and functional effects of genomic, epigenomic and metabolomic variation more rapidly and efficiently.

A.10 Implement translational programmes with shared access to, for example, genetically defined patient populations

Currently, diseases are generally classified based on symptoms. However, when diseases in the future are classified based on molecular finger prints/characteristics, the number of similar (and in some cases identical) patients gets smaller and the conventional way of conducting clinical testing becomes difficult. Therefore, there is a need to create and stimulate interface structures between academia-clinicians-industry to expedite research-based and patient-centred discoveries, improving tailored medicines and speeding up market entry. As the number of certain genotypes of biological phenotypes is expected to be very low, these collaborations need to be international by nature.

A.11 Integrate actions aimed at supporting and developing research for clinical validation of pharmacogenomics. Global impact evaluations of these actions on health systems

A wide range of technologies are suited to detect alterations in genetic material (e.g. approaches into gene therapy, rare disease, hereditary disorders and genetically divergent population). The main objective is to integrate actions directed to improving and validating analytical methods and genome sequencing that allow the discovery of allelic variants of genes involved in drug metabolism, pharmacokinetics or pharmacodynamics. This complex process should facilitate a more rational treatment choice and should stratify patients into non-responders and responders. This action will be developed in three phases: promoting clinical trials of new diagnostic systems; innovative technological platforms for clinical validation and standardisation, and dissemination in order to facilitate the implementation in ordinary clinical practice. These efforts should be made in cooperation with other consortia such as IRDiRC. The final aim should be the establishment of an appropriate method of global impact evaluation.

A.12 Classification of diseases at the molecular level

Actualised classification of diseases at the molecular level is necessary for a successful implementation of personalised medicine. It is necessary to characterise pathogenic mechanisms at the molecular level, and validate them at preclinical and clinical levels, allowing translation to the diseases level. In parallel, biomarkers for diagnosis, prognosis, molecular classification and therapeutic response should be identified and characterised in animal, preclinical and clinical studies. Identification of these pathogenic mechanisms and biomarkers will allow further study on modulation effects and lead to recognition of possible new drug targets.

A.13 Support research for clinical trials – a three-level process

Standardisation for clinical trial designs for PM is needed to demonstrate the feasibility and importance of PM approaches. Support of research for clinical trials will occur at three levels: (1) development of new clinical trial design methodo-

logy for PM, including refinement of existing and – where appropriate – development of new guidelines and reflection papers for researchers to facilitate the approval process with regulatory authorities and their communication with reimbursement authorities; (2) clinical and cohort pilot studies for PM adopting new clinical trial methodologies and including new stratification strategies based on redesigned disease classification, e.g. biomarker based (molecular/genetic/epigenetic/etc.) and (3) combination trials on diagnostics and therapeutics for the development of products together with companion diagnostics (theranostics).

A.14 Longitudinal cohort studies of disease outcomes

Support is needed for longitudinal cohort studies of disease outcomes, including therapy outcomes with integration of biological data, gut microbiota characterisation, natural history, nutrition and epidemiology (demographic, life style, clinical history, environment, etc.) information. Cohort studies with long-term follow-up will allow subgroup analyses of outcomes depending on different therapies for biomarker-positive and biomarker-negative patients. This will lead to a stratified risk-benefit analysis for therapy in biomarker positive and negative patients. Finally, such studies will provide common knowledge on clinical utility (efficacy, safety) of PM and will support regulatory decision-making processes. Furthermore, from a Health Technology Assessment (HTA) perspective the goal of proving clinical utility of PM, controlled cohort studies are recommended, ideally performed as randomised controlled longitudinal studies.

A.15 Research in adequate regulatory structures and pathways in personalised medicine

A key issue to promote innovative personalised medicine solutions is the move from scientific value to patients' benefit through optimised transparent regulatory processes. Increased understanding of barriers and optimised regulatory pathways can lead to faster patient access to new personalised medicine. Important aspects are inter alia the evaluation of the status quo of regulatory processes and the consideration of new aspects of regulatory needs driven by fact-based knowledge of PM.

A.16 Support research in and development of health economics models and pharmaeconomic models for personalised medicine

The most commonly used health economics models and pharmaeconomic models are based on non-personalised medicine approaches. Research is needed to investigate whether a patient-centred, personalised medicine approach requires refinement of or even new health economics models and pharmaeconomic models, including prevention. In this regard, a possible impact on the speed of translation should be analysed.

A.17 Support research in post-marketing surveillance methodologies aimed at assessing patient outcomes

In order to increase likelihood of successful personalised medicine development there is a significant need for post-marketing surveillance methodologies. This raises legal, social, ethical challenges as well as need for new ways to handle big data. Data sharing resources include Internet-based patient involvement, spontaneous reporting from many channels and analysis of electronic health records as patient repositories across national borders. Research in this area can outline what needs to be done to facilitate the use of data across nations and cultures.

A.18 Support health economics research and assessments of available as well as newly developed personalised medicine approaches

Health economics analyses of personalised medicine treatments are crucial, as they will generate important knowledge about the economic opportunities and threats of personalised healthcare in comparison with standard treatments. In addition, such research needs to be aligned with analysis of patient outcomes and quality of life aspects. Such research will provide important evidence to support effective and sustainable healthcare systems, now and in the future.

People

A.19 Research and develop the tools and modus operandi of a knowledge network for enhancing health and digital literacy

Health literacy is a key determinant of health; digital literacy is becoming increasingly important in healthcare. This action aims to develop a European Knowledge Network platform for enhancing health and digital literacy, which is an international knowledge management platform for health and healthcare using web-based and social media instruments. There is a need to develop comprehensive measurements of health literacy and to provide guidance on what interventions might be needed to respond to individuals and communities with limited health literacy.

A.20 Develop and share best practices of patient engagement approaches for the needs of a variety of European citizens

The aim of this action is to improve patients' experience and their need to have greater control over their care; to advance population health; to reduce costs by focusing on patient engagement (improve efficiency, reduce out-migration and reduce overall costs of patient care). We need to perform feasibility studies on the use of treatment adherence measurement methods in clinical practice and evaluate strategies to embed fidelity measurement in implementation support and monitoring systems. We have to enable citizens to become actively involved in all phases of research and development. The introduction of e-health applications can facilitate data generation about the safety and effectiveness of interventions.

A.21 Research and develop the instruments for the evaluation of the effectiveness and impact of public engagement initiatives in PM

Development of IT applications and adequate interfaces is needed to enable the use of smartphones, tablets, other mobile services, 'smart homes' and tele-health systems for the different user groups, such as citizens, patients and GPs (e.g. m-health). There is a need to research the effect and the feasibility of the use of m-health applications, to develop mobile health applications to maximise engagement of patients with their treatment pathways and track the safety and effectiveness of these interventions. To improve the quality of care and effectiveness we need to collect data on patients' reported satisfaction about a healthcare provider and develop patients' reported outcome measure instruments to analyse the quality of patient care, taking into consideration ethical and data protection aspects. We also need to identify the instruments and evaluate the effectiveness of public engagement initiatives in PM (research agenda, clinical trial design, post-marketing surveillance).

Cross-cutting

A.22 Support interdisciplinary research in challenges and drivers that influence bringing PM innovation to the market, from ethical, legal and societal perspectives

Perspectives of personalised medicine include ethical and social issues; for example allocation of resources, access to expensive personalised treatments, data privacy, data safety, consequences of gene diagnostics and handling "big data". It is important to further understand how these factors affect the likelihood of successful and timely implementation. Research is also needed to clarify how these factors can be modulated in different settings, thereby creating opportunities for better PM in the future e.g. by early interaction with cross-nation ethics.

Research-supporting Activities – Part B

Other activities are also needed to further elaborate and implement personalised medicine approaches. For example, existing and newly established infrastructures, resources and frameworks must be supported to foster the availability of core infrastructure, including the access to core technology and frameworks for education and training of professionals and the wider community. In addition, citizens have to be empowered to manage their own datasets and in return support not only their personalised treatment and diagnosis, but also future research activities. Other crucial steps to develop and implement personalised medicine are regulatory strategies and decisions while ensuring the sustainability of national health systems. This includes developing long-term, patient-centred, strategic approaches on how to meet, with a public health perspective, the challenges associated with access to personalised medicine. Furthermore, HTA bodies rely on sufficient data in order to assess the additional benefit for patients. However, one has to keep in mind that the responsibility for health systems as well as education systems rest with Member States. The activities listed in Part B are aimed at a whole range of activities needed to support personalised medicine research in the areas of policy, structures, patient involvement and empowerment as well as the education of healthcare providers.

Structures

B.1 Promote the development of high-quality sustainable databases for personalised medicine-relevant data

There is an urgent need to establish sustainable databases with all relevant datasets, such as general and individual genome and proteome files, health records, clinical information, imaging data, information from mobile devices and wearable sensors, life-style and environmental information. In parallel with the establishment and operation of such databases, research on quality, completeness and validity of data is crucial. Furthermore, the harmonisation of data and the interoperability of databases are essential.

B.2 Development and maintenance of biobanks and population/disease cohorts

It is crucial to maintain and further develop and integrate high-quality sustainable biobanks and population/disease cohorts. This should be done through the European infrastructure/cohorts networks, thus providing the basis to overcome the difficulty of undersized cases studies. The process must be accompanied by adequate efforts in standardisation, harmonisation, quality insurance and validation of associated data.

Methods and Processes

B.3 Establish a new collaborative funding organisation model with healthcare providers to facilitate investment in disease prevention research and therapy research

A system of competitive grants to individual researchers is not always the most appropriate way to finance PM research. It may be more beneficial to use a model that recruits and funds groups of top researchers and healthcare providers who agree to work as collaborators in solving problems on disease prevention and therapy. Firstly, the new model has to encourage stakeholders to collaborate, and other funders to join the effort to align with healthcare providers. Secondly, a funding model must be flexible and adaptable to in order to achieve the intended outcome with stakeholders. Finally, this model could build the capacity of multiple organisations to work together.

B.4 Develop common strategies in research to support comparative and effective research, and sustainable technology transfer capacities

These common strategies should be based on common goals and measures of collective effort, and on shared measurement systems to standardise the process of research evaluation. The action provides content expertise on evidence-based medicine practice and encourages funders and other stakeholders to align evaluation sharing measures. The final objective is to support the improvement of appropriate transfer technologies with low initial costs.

B.5 Support strategies to identify financial and risk-sharing instruments to develop personalised medicine approaches

As a first step, activities should be established to identify the risks of innovative personalised medicine approaches and products. These undertakings should be collaborations

between academia, industry and regulatory authorities. This could include the review and optimisation of the available financial plan and project outline. Therefore, industry, financial advisers and other interested parties should perform risk evaluations for the PM approaches and products from all relevant perspectives. Secondly, different scenarios could be build and analysed. Finally, these collaborations should elaborate on each step in the process and thereby identify and avoid potential risks and improve the regulatory and economic framework (e.g. with the help of flow charts, checklists and quality management).

B.6 Support research to analyse, compare and optimise national and regional health systems in the light of personalised medicine implementation

National and regional health systems differ in several aspects and in the way personalised medicine approaches have been implemented. Research projects should be conducted to analyse and compare selected heath systems, with a focus on personalised medicine aspects. Thus suggestions for the optimisation of health systems can be elaborated in order to support the reasonable implementation of existing best practice and lessons learned in the light of sustainable solutions. The investigation of social consequences, such as insurance and employment, should form part of this research.

People

B.7 Introduce curricula reforms to create new models of healthcare for patients and citizens and broaden the focus on basic and clinical sciences to include health systems sciences in the education of all healthcare professionals

In many European countries, there is a strong need to change patient care from a physician-centric to patient-centric model, and move traditional reactive healthcare management towards adopting a more proactive approach. In order to achieve this goal, curricula reforms will have to be introduced at both graduate and post-graduate levels. In addition to curricula reforms, lifelong learning and training programmes have to be introduced for all stakeholders - citizens, patients, and healthcare providers – in order to broaden the focus on basic and clinical sciences. Intellectual and communication infrastructure will have to be created to support interdisciplinary interaction and training for ICT and healthcare professionals taking into account the national and regional health systems.

B.8 Build sustainable resources for educating and training citizens, patients and patient advocates on involvement of patients and patient organisations across the entire research and development lifecycle of personalised medicine

Translation from research to development of innovative healthcare products needs the incorporation of the patient perspective and new sciences/genome-based knowledge. Health professionals' role is increasing in informing and engaging patients within a personalised medicine context. Including patients as active partners in health research will lead to improved health outcomes and an enhanced healthcare system. Patient-oriented research should focus on priorities that are important to patients and it should produce information that is truly adopted and used to improve healthcare practice, therapies and policies. Patients and citizens can contribute to identifying the right research question, as well as study design, recruitment, data collection, and analysis of findings.

Outlook

Personalised medicine is already transforming biomedical and clinical research, and all healthcare disciplines, both conceptually and methodologically. Based on the principle that care and prevention can be informed by an ever increasing quantity and variety of data, personalised medicine aims to achieve the optimum outcome for individuals, rather than populations or subgroups. Furthermore, by employing powerful and adaptive computational assistance, it will enable the prediction of future probabilities, and guide decisions by healthcare providers. This change in the way healthcare is delivered is becoming widely accepted and is a leading focus of activity in health-related science globally, with all industrialised countries investing substantially in personalised medicine across different domains. Nonetheless, investment in personalised medicine has to be reasonable, emphasising the most promising approaches and excluding unqualified methods or technologies.

Accordingly, the current ICPerMed Action Plan is intended to provide a tool to coordinate and augment the activities of individual ICPerMed members in this area. By improving coordination and scaling up our activities, the plan aims to maximise impact and to improve global competitiveness. The Action Plan reflects current consensus among the ICPerMed members and the European Commission (EC) on research and development needs and challenges, and the support actions needed for comprehensive and high-impact implementation of personalised medicine approaches. As such, it reflects a common view among ICPerMed members of those concerted activities that would deliver the most benefit. Reaching this shared understanding was a worthwhile process in itself, while implementing the actions set out in the Action Plan will undoubtedly reveal new insights, aspects and needs.

Alongside the activities of the ICPerMed members and the EC's own activities in the area of personalised medicine and care, the majority of the ICPerMed members are also involved in the preparation of a European Research Area Network for Personalised Medicine (ERA PerMed). We are confident that ICPerMed will be the platform for the development of further bilateral and mulitlateral initiatives in the area of personalised medicine.

Such an ambitious goal warrants sustained commitment from individual members of ICPerMed over a meaningful period of time, as well as a readiness to adapt to the demands of new knowledge, global developments and the expectations of European societies. Therefore, it is expected that a follow-up strategy will be needed to tackle further crucial aspects in research and to support future implementation strategies of personalised medicine. These should include patient involvement, adapted regulation procedures and Health Technology Assessments (HTAs), educational aspects, and reimbursement issues related to personalised medicine. In parallel, it will be important to use systematic surveys and databases to capture ongoing activities and successes in personalised medicine along the entire value chain; such an activity is planned by ICPerMed.

Over the coming years, workshops and congresses will be organised under the ICPerMed umbrella to support the continuity of the concerted activities and to strengthen the team spirit among members of ICPerMed. We aim to promote state-of-the-art understanding and new advances in the domain of personalised medicine by facilitating the exchange of experiences and ideas, and discussing new potential solutions from ICPerMed members and global stakeholders.

Moreover, by including new members as well as essential institutions, organisations and initiatives, ICPerMed aims to promote the exchange of ideas and experiences, to further evolve the concept of personalised medicine, to support innovations in prevention, diagnosis, therapy, information and communication technology, and to promote economic value and fair access for all citizens to the best possible healthcare.

Annex 1:
Summary table of actionable items indicating a reasonable time frame and scope

Action Item Number	Title	Time frame*	Scope**
A.1	Research projects to ensure the quality, completeness, validity and analysis of datasets	S	E
A.2	Support research on data harmonisation in the context of personalised medicine needs	M, L	E, I
A.3	Studies on data integration and interpretation of multifactorial diseases	S	R/N, E
A.4	Support research on enabling the extraction of structured data from unstructured sources	S, M	R/N, E, I
A.5	Pilot projects to assess the impact of sharing data for researchers and other parties	S, M	R/N, E, I
A.6	Research projects to optimise data security, privacy and ownership within personalised medicine approaches	S, M	R/N, E, I
A.7	Research projects to develop innovative decision support tools for healthcare providers	S, M	R/N, E, I
A.8	Support research to develop telehealth and telemedicine applications to support the implementation of personalised medicine	M, L	R/N, E
A.9	Development and implementation of high-throughput preclinical models	M	R/N, E
A.10	Implement translational programmes with shared access to, for example, genetically defined patient populations	S, M	E, I
A.11	Integrate actions aimed at supporting and developing research for clinical validation of pharmacogenomics. Global impact evaluations of these actions on health systems	M	R/N, E, I
A.12	Classification of diseases at the molecular level	L	R/N, E
A.13	Support research for clinical trials – a three-level process	S, M, L	R/N, E
A.14	Longitudinal cohort studies of disease outcomes	S, M, L	R/N, E, I
A.15	Research in adequate regulatory structures and pathways in personalised medicine	S, M	E
A.16	Support research in and development of health economics models and pharmaeconomic models for personalised medicine	M, L	E, I
A.17	Support research in post-marketing surveillance methodologies aimed at accessing patient outcomes	S, M	E, I
A.18	Support health economics research and assessments of available as well as newly developed personalised medicine approaches.	S, M	R/N, E
A.19	Research and develop the tools and modus operandi of a knowledge network for enhancing health and digital literacy	S, M	I

Action Item Number	Title	Time frame*	Scope**
A.20	Develop and share best practices of patient engagement approaches for the needs of a variety of European citizens	S, M	R/N, E, I
A.21	Research and develop the instruments for the evaluation of the effectiveness and impact of public engagement initiatives in PM	S, M	E, I
A.22	Support interdisciplinary research in challenges and drivers that influence bringing PM innovation to the market, from ethical, legal and societal perspectives	M, L	E, I
B.1	Promote the development of high-quality sustainable databases for personalised medicine-relevant data	S, L	R/N, E, I
B.2	Development and maintenance of biobanks and population/disease cohorts	S, M, L	R/N, E, I
B.3	Establish a new collaborative funding organisation model with healthcare providers to facilitate investment in disease prevention research and therapy research	M	R/N, E
B.4	Develop common strategies in research to support comparative and effective research, and sustainable technology transfer capacities	M	R/N, E, I
B.5	Support strategies to identify financial and risk-sharing instruments to develop personalised medicine approaches	M	R/N, E, I
B.6	Support research to analyse, compare and optimise national and regional health systems in the light of personalised medicine implementation	S, M	R/N, E, I
B.7	Introduce curricula reforms to create new models of healthcare for patients and citizens and broaden the focus on basic and clinical sciences to include health systems sciences in the education of all healthcare professionals	S, M, L	R/N, E, I
B.8	Build sustainable resources for educating and training citizens, patients and patient advocates on involvement of patients and patient organisations across the entire research and development lifecycle of personalised medicine	S, M, L	R/N, E

* S: short term = 2-4 years

M: medium term = 5-7 years

L: long term = 8-12 years

The timeframe indicated here refers to the time for taking steps to address these actions (e.g. the initiation of a funding programme or a coordination action), not the time to reach results.

**R/N: regional/national

E: european

I: international

Scope indicates whether the respective action is regarded as suitable for implementation at a regional/national, European and/or international level-

Annex 2:
List of ICPerMed members (as of March 2017)

Country	Organisation
Austria	Federal Ministry of Science, Research and Economy (BMWFW)
Austria	Federal Ministry of Health and Women's Affairs
Canada	Canadian Institutes of Health Research (CIHR)
Canada	Genome British Columbia**
Republic of Croatia	Ministry of Science and Education of the Republic Croatia
Cyprus	Research Promotion Foundation (RPF)*
Czech Republic	Ministry of Health of the Czech Republic
Denmark	Innovation Fund Denmark (IFD)
European Commission	European Commission; Personalised Medicine Unit in DG Research and Innovation*
Estonia	Ministry of Social Affairs
Finland	Academy of Finland - Suomen Akatemia
France	National Research Agency - Agence Nationale de la Recherche (ANR)
France	Ministry of Higher Education and Research
Germany	Federal Ministry of Health (BMG)
Germany	Federal Ministry of Education and Research (BMBF)
Hungary	Ministry of Human Capacities
Ireland	Health Research Board (HRB)
Israel	Ministry of Health (CSO-MOH)
Italy	National Research Council of Italy - Consiglio Nazionale delle Ricerche (CNR)
Italy	Ministry of Health - Ministero della Salute
Italy	Regional Foundation for Biomedical Research - Fondazione Regionale per la Ricerca Biomedica (Lombardy)**
Lithuania	Research Council of Lithuania
Luxembourg	Luxembourg Ministry of Health*
Luxembourg	Luxembourg National Research Fund - Fonds national de la Recherche
Netherlands	The Netherlands Organisation for Health Research and Development (ZonMw)

Country	Organisation
Norway	The South-Eastern Norway Regional Health Authority
Poland	Ministry of Science and Higher Education (MNISW)
Portugal	Foundation for Science and Technology - Fundação para a Ciência e Tecnologia (FCT)
Portugal	Instituto Nacional de Saude Doutor Ricardo Jorge (INSA)
Republic of Moldova	Academy of Science of Moldova
Spain	The National Institute of Health Carlos III
Spain	Ministry for Health - Basque Government**
Sweden	Swedish Research Council - Vetenskapsrådet
Sweden	Vinnova
Turkey	Turkish Research and Business Organisations a.i.s.b.l. (TURBO)*
United Kingdom	Medical Research Council (MRC)

* observer status

** regional member