Report on the Open Consultation for the Strategic Research and Innovation Agenda (SRIA) in Support for the European Partnership for Personalised Medicine, EP PerMed

Summary

In preparation of the European Partnership for Personalised Medicine (EP PerMed) an open consultation was launched with the objective to receive additional input for the Strategic Research and Innovation Agenda (SRIA) in support of EP PerMed. The open consultation was developed around the so called "Triplets of Action", short "ToAs", defining challenges, objectives and the expected outcome of actions to foster Personalised Medicine (PM) research and implementation of innovative PM approaches. These ToAs will be the core element of the SRIA and will be presented along the main areas crucial for an effective development of PM: Interdisciplinary research efforts, a versatile PM-focussed innovation system and successful implementation settings of PM approaches into health systems. Additionally, the SRIA will contain ToAs for overarching activities to support PM development and implementation. The open consultation resulted in an overall validation of the identified ToAs. Beyond that, seven additional ToAs were suggested by the participants of the open consultation and in total 13 ToAs received suggestions for adaptions in wording or content. Thus, several additional ToAs for the SRIA were inspired by this open consultation.

The results of the open consultation were presented on the ICPerMed Workshop "Preparing the Future for Personalised Medicine: EP PerMed" on 17 and 18 January 2023 in Pamplona. The final SRIA document will be available on the ICPerMed webpage by the end of April 2023.

Background

The concept of Personalised Medicine (PM) has been established over the last 10 years. In the first period, genetic information of patients and its analysis supported research for tailored diagnosis and treatment of diseases. Here mainly treatment of cancer and rare diseases progressed. Lately, PM further advanced and the information utilised is much broader now as well as the disease areas for which PM approaches were developed. In addition, also personalised prevention strategies are now in the focus of research and health systems. Today, not only research funders and researchers, but also the public, healthcare providers and payers as well as industry and policy recognise the potential value of PM in all areas. To further support these developments, the European Commission (EC) and the Member States (MS), incl. several regional entities, joined forces and supported the development of a Strategic Research and Innovation Agenda for PM (SRIA). This process was highly triggered by the plan of the EC to set up a European Partnership for Personalised Medicine (EP PerMed) by the year 2023. Thus, a drafting group was established to prepare a SRIA. From the beginning, these activities were strongly supported by the International Consortium for Personalised Medicine (ICPerMed) and related EC-funded coordination and support actions as well as ERA PerMed (ERA-Net co-fund for Personalised Medicine 2017-2023) and other PM related initiatives.

The SRIA for PM primarily aims at presenting gaps, needs and challenges which should be addressed to maximise the benefits of PM approaches and ensure an equal access to these approaches. This SRIA will support all stakeholders and experts to further develop programs, activities and research towards PM and care as well as prevention. In line with this mission, its main intention is the support of the planned new partnership EP PerMed. The SRIA will ensure that the long-term vision of EP PerMed is translated into tailored roadmaps with activities, objectives and measurable outcomes. The structure and content of the document was elaborated on the basis of the drafting group members' expertise, published strategic documents and information, and along specific activities and events organised to support the SRIA development. One of these activities were semi-structured interviews with over 60 experts and stakeholders related to PM identified by the SRIA drafting group members and the EC. The interviews were translated into the so-called Triplets of Action (ToAs) related to PM, where applicable.

The ToAs describe needs and gaps and guide the prioritisation of challenges and subsequent actions along the following structure:

Challenge: Description of the status quo, indication of 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.

A total of 47 Triplets of Action have been identified that were the basis for the open consultation, which was a pre-final step in the preparation of the SRIA with the following aims:

- Communication of the SRIA in general and the identified "Triplets of Action" in specific,
- Obtaining general input, especially related to the "Triplets of Action",
- Obtaining input regarding the urgency and timing of the "Triplets of Action",
- Obtaining suggestions refinement of presented and for additional "Triplets of Action".

By taking part in the open consultation, participants had the opportunity to share their view on future activities and research for accelerating the development and implementation of PM approaches. Input from the whole spectrum of stakeholders and experts involved in the PM areas was encouraged, such as scientists, healthcare professionals, patients, citizens, policy advisors or individuals working in the pharmaceutical or biotech industry.

Study design and analysis

The open consultation for the SRIA in support for EP PerMed was developed by the SRIA drafting group. The questionnaire was based on the previously collected 47 ToAs. These were assigned to four different categories in line with the foreseen structure of fields of action in the SRIA:

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

The ToAs are listed according to their numbers in **Annex 1**. Besides general questions on the participants' background, the first survey questions were designed to validate the ToAs of each category. The respondents were asked to assess their level of agreement on a scale of 1-10 (10 corresponded to "agree completely" and 1 to "disagreement") on single-ToA level. It was possible to skip ToAs in the evaluation. In the same manner the participants were asked to determine the urgency of the ToAs within each category. In addition, the participants were asked to prioritise the ToAs within the above-mentioned categories according to their importance to accelerate the development and implementation of PM approaches. They should name the five most important ToAs per category. Technically it was possible to nominate more or less than five ToAs per category (78 persons chose exactly five ToAs, seven persons chose less than five ToAs and four persons chose six or seven ToAs). Disregarding the categories, the participants were asked to assign, a fictive budget of 15 Mio. Euros to five ToAs of choice with the highest importance to foster the development and implementation of a PM approach. This task aimed at determining an order of important ToAs. It was technically possible to nominate more or less than five ToAs and to allocate more or less than 15 Mio. Euro but the majority of respondents (75 out of 89) adhered exactly to the task. The analysis shown in **table 1** and **figures 5-6** was performed including the answers of all 89 persons who answered this specific question. Besides these assessments, the participants also had the opportunity to suggest one new ToA as well as adaptions for wording of the existing ToAs according to their judgement and expertise.

The open consultation was technically implemented using LimeSurvey. The questionnaire complied with the General Data Protection Regulation. The launch of the open consultation on 21 November was kindly announced by ICPerMed and ERA PerMed. ICPerMed used various communication channels like social media, a special edition of the ICPerMed newsletter and emails to the ICPerMed bodies (Executive Committee, Advisory Board, Stakeholder Forum) to reach out to a broad range of stakeholders. The ICPerMed members were asked to spread the information via their regional and national channels as well. Additionally, the coordinators of the ICPerMed-related Coordination and Support Actions were asked to activate their stakeholders and also the EC supported the dissemination activities. ERA PerMed reached out to the ERA PerMed network steering committee, i.e. all steady ERA PerMed partner organisations, as well as additional funders that joined the calls and project coordinators that received funding through ERA PerMed calls. The open consultation was open between 21 November and 31 December, 2022.

Respondents were included in the analysis if they provided their consent to save and analyse their data. Results were calculated as proportions of particular answers in relation to the total number of responses given to a specific question. The total number of responses per question could differ in the analyses. The number of responses per question is indicated in the figure caption. The analysis focused on the collective results without assessing possible stakeholder-specific or country-specific aspects. Microsoft Excel and

Tableau were used to create the figures. The questionnaire as well as the raw data files are available in Excel format upon request.

Results

The open consultation raised a high interest in the PM community. More than 700 persons visited the survey-webpage. As the open consultation had a very specific focus dealing with highly complex ToA the questionnaire was finally completed by 129 participants. The participants came from 21 countries (see **figure 1**), besides the European countries there was also feedback received from South Africa, Iran and Turkey. Italy and Germany brought in the highest number of participants with 40 and 20 completed questionnaires, respectively.

Figure 1 Country distribution of respondents (total numbers)

The participants assigned themselves to diverse stakeholder groups (multiple assignments were possible). Among the participants, academic scientists and healthcare professionals represented the biggest stakeholder groups (64% and 25% of respondents).

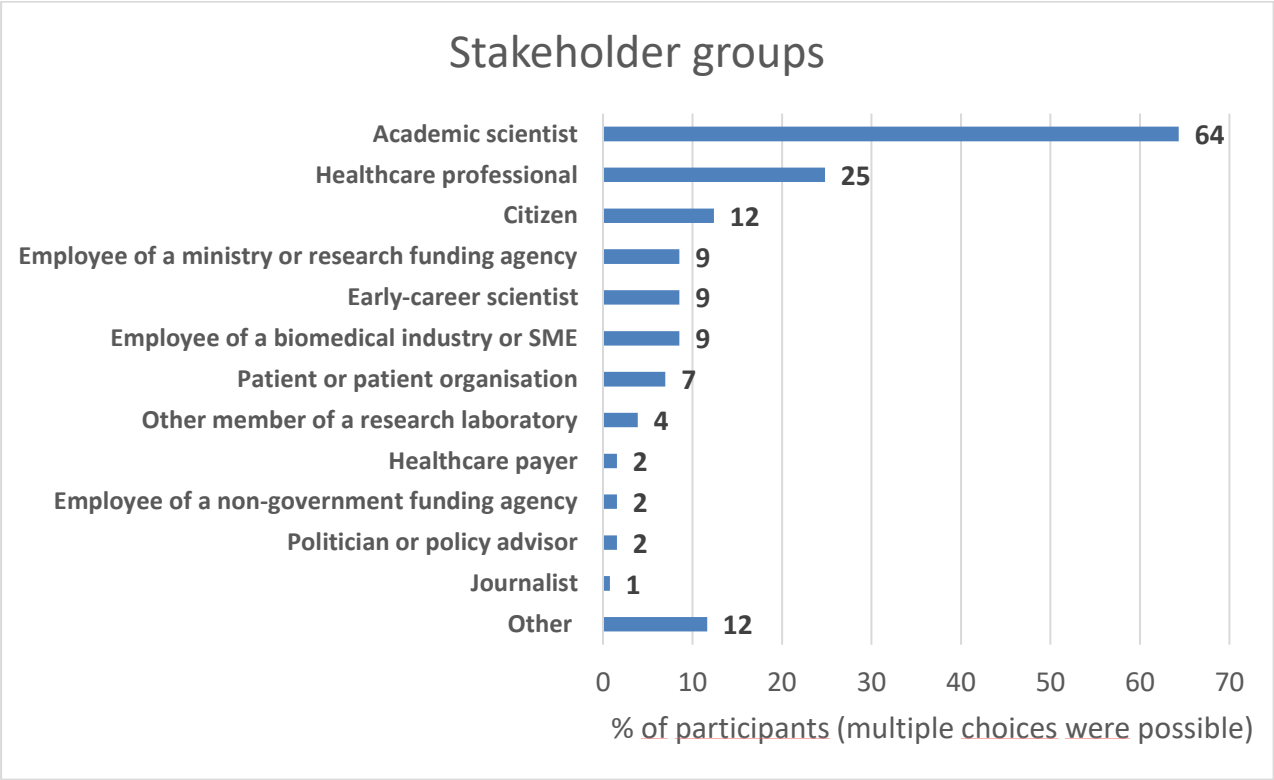

Figure 2 Allocation of respondents to pre-defined stakeholder groups (% of participants). Multiple assignments were possible.

Feedback to the defined categories

In a first step, the participants were asked to decide to which of the four main areas crucial for an effective development of PM related research (short: "Research"), Innovation System and PM (short: "Innovation System"), PM Implementation Setting (short: "Implementation Setting"), "Overarching Activities" they would like to provide feedback. The highest response rate was received in the category "Research" with 85% of participants but the three other areas also received a response rate of almost 50% (see **figure 3**).

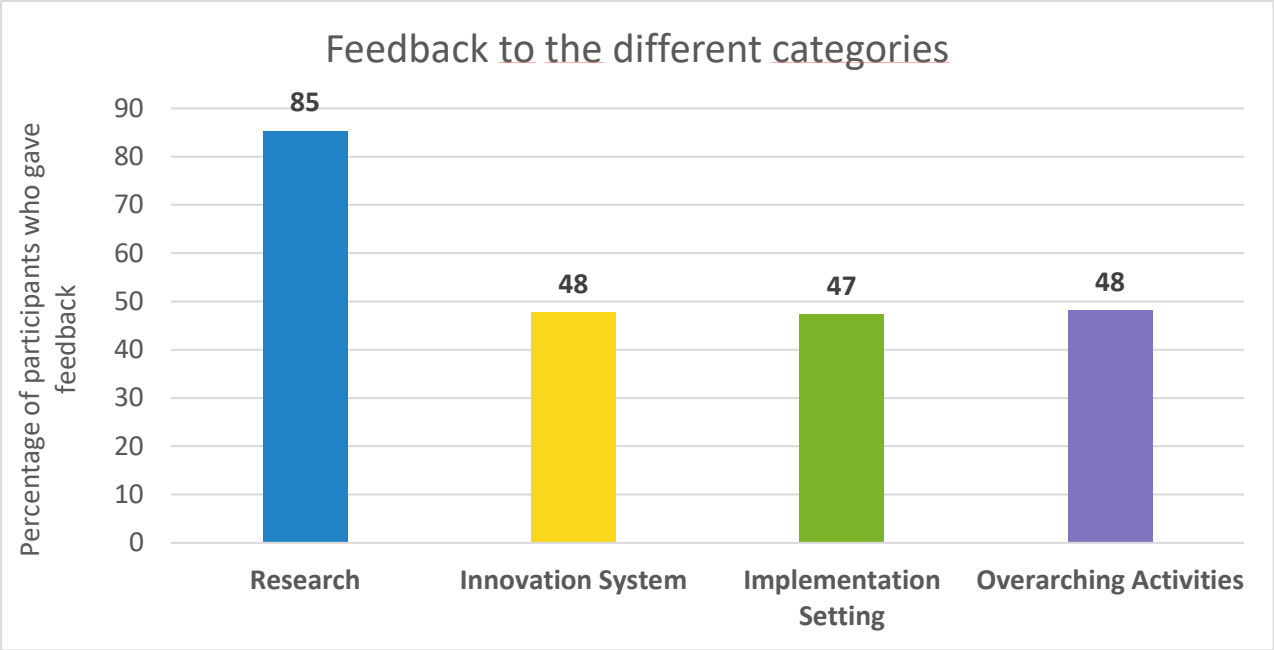

Figure 3 Response rate to the four areas "Research", "Innovation System", "Implementation Setting" and "Overarching Activities"

In the next step, the participants were asked to evaluate the degree of agreement to each ToA of the chosen area(s). **Figure 4** shows a summary of evaluations per category. The participants validated the ToAs with an overall agreement in each of the four areas between 7.1 and 7.9 on a scale of 1 to 10 (10 corresponded to "agree completely" and 1 to "disagreement"). The urgency of the ToAs was rated between 6.9 and 7.6 without a clear trend on category level (see **figure 4**). The diagrams in **Annex 2** depict the assessment of each ToA per category in terms of agreement level and urgency level.

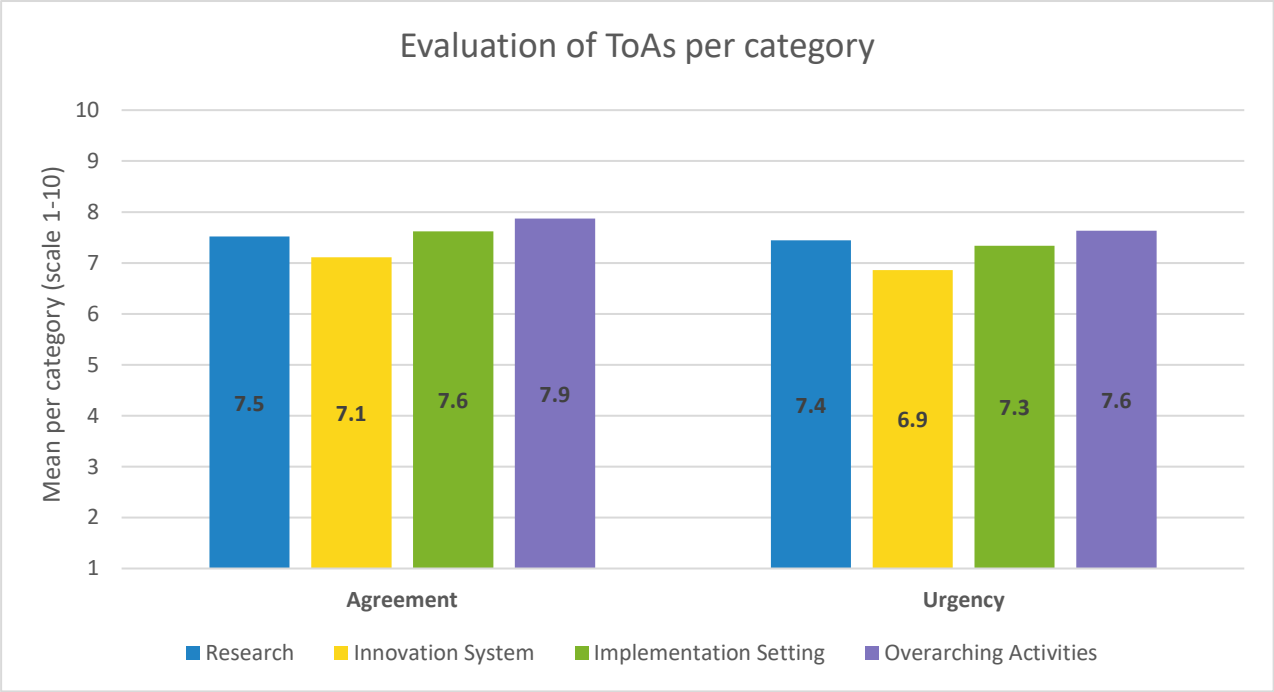

Figure 4 Summary of the degree of agreement to and urgency of the ToAs per category on a scale of 1 to 10 (10 corresponded to "agree completely" and 1 to "disagreement"). ToAs in the category "Research" were evaluated by 101-108 persons, the ToAs of the other categories were evaluated by 57-62 persons. STDEV between 1.87 and 3.08.

Prioritisation of ToAs – Category-specific ranking

When asking directly for indicating the five most important ToAs per category clear favourites were identified in the categories "Research", "Innovation System" and "Implementation Setting" with more than 10% advance to the second-ranked ToAs, while the result was very close in the Category "Overarching Activities". In the category "Research", **"A collaborative approach between pre-clinical and clinical research" (ToA 1.1)** was chosen by 72% of participants who answered that question. In the category "Innovation System", the top-ranked ToA was **"Early cooperation between public research and the private sector" (ToA 2.5)** with 75% of nominations by the participants. In the category "Implementation Setting", the highest priority was given to **"Training and Education of healthcare professionals" (ToA 3.3)** with 50% of nominations. When looking at the "Overarching Activities" the participants ranked **"Network of national and regional innovation hubs" (ToA 4.5)** and **"PM adapted and focused biobanks and real-world data registries" (ToA 4.3)** as equal important. These ToAs were nominated by 84% and 82% of participants who answered that question, respectively. The ranking of all ToAs per category can be found in **Annex 3**.

Prioritisation of ToAs: Overall Ranking

Besides the ranking of ToAs within a category, the questionnaire also aimed at understanding which of the 47 ToAs have the highest priority for the participants independent of the category the ToAs were assigned to. The participants were therefore asked to choose the 5 most important ToAs out of the 47 ToAs and amongst these they were asked to distribute 15 Mio. Euros. The top ten ToAs with the highest number of nominations is depicted in **table 1**. Besides seven ToAs from the "Research Category", two

ToAs of the "Overarching category" (**"Network of national and regional innovation hubs" (ToA 4.5)** and **"Connected large-scale health databases" (ToA 4.3)**) and one ToA of the category "Innovation System" (**"Early cooperation between public research and the private sector" (ToA 2.5)**) are ranked under the top ten. Please note that the participants would also invest in many of the ToAs of the category "Implementation setting": four of them (**ToA 3.2, ToA 3.3, ToA 3.1, ToA 3.14**) are ranked under the top twenty.

Table 1 Top ten of ToAs to which budget would be allocated by the participants (n=89). Depicted is % of persons who allocated budget to the respective ToA. Blue: category "Research", yellow: category "Innovation System", violet: category "Overarching Activities". Technically it was also possible to not choose exactly 15 Mio. Euros.

Number	Title	%
ToA 1.1	A collaborative approach between pre-clinical and clinical research	56
ToA 1.7	New targets for Personalised therapies making use of an improved understanding of disease mechanisms	40
ToA 1.6	More biomarker evidence for PM	30
ToA 1.9	Single-cell technologies in combination with AI and ML for PM	26
ToA 4.5	Network of national and regional innovation hubs	22
ToA 1.11	Medical cohorts for collecting high-quality health and molecular data	19
ToA 1.3	New treatment modalities for PM	19
ToA 2.5	Early cooperation between public research and the private sector	19
ToA 4.3	Connected large-scale health databases	17
ToA 1.10	Broader biomarker approaches to enable more informed health decisions	16

Allocation of a fictive budget: mean allocated budget

When analysing the highest mean fictive budget allocated to specific ToAs, two favourites were identified among the top ten nominated ToAs, namely: **"Network of national and regional innovation hubs" (ToA 4.5)** and **"Single-cell technologies in combination with AI and ML for PM" (ToA 1.9)** with 4.8 Mio. Euros and 4.7 Mio. Euros, respectively (see **figure 5**). These were followed by a group of five ToAs of the "Research" category (**ToA 1.6, ToA 1.10, ToA 1.11, ToA 1.7, ToA 1.3**), that received between 3 and 4 Mio. Euros. The third group of ToAs is led by **ToA 1.1**, which received the highest number of nominations but also shows the highest standard deviation in terms of budget that would be invested by the nominators. On rank nine and ten, the other two ToAs of the category "Overarching Activities" (**ToA 4.3**, 2.3 Mio. Euros) and Innovation System (**ToA 2.5**, 1.6 Mio. Euros) were nominated. Only ToAs with 14 or more nominations are shown to minimise the bias of single prioritisations.

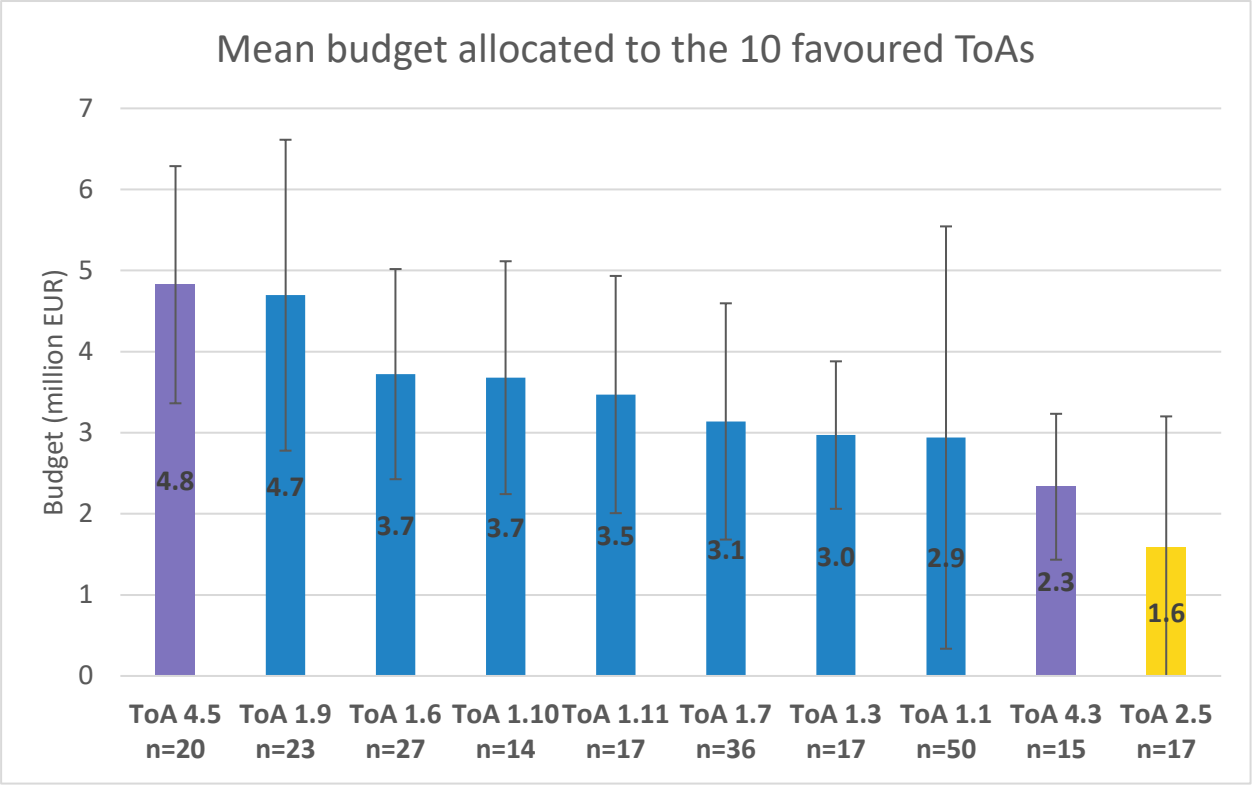

Figure 5 Mean budget allocated to the ten most-often nominated ToAs. The participants were asked to distribute a fictive budget of 15 Mio. Euros between five ToAs which they would evaluate as most important. Number of respondents: 89, number of nominations per ToA indicated in the graph. Technically it was also possible to not allocate exactly 15 Mio. Euros to exactly five ToAs.

Allocation of a fictive budget: total allocated budget

When analysing the sum of fictive budget that was allocated to the 47 ToAs, the ToAs of the "Research" category dominated the ranking list (see **figure 6**). The respondents would invest 144 Mio. Euros into work on **"A collaborative approach between pre-clinical and clinical research" (ToA 1.1)**. On ranks 2-5 follow ToAs that gathered around 100 Mio. Euros including one ToA from the category "Overarching Activities" (**ToA 1.7, ToA 1.9, ToA 1.6, ToA 4.5**). The third group of ToAs completing the top ten received a total budget between roughly 40 and 60 Mio. Euros (**ToA 1.11, ToA 1.3, ToA 1.10, ToA 1.15, ToA 1.14**). Please note that the biggest stakeholder group of respondents were "Academic Scientists" (64%).

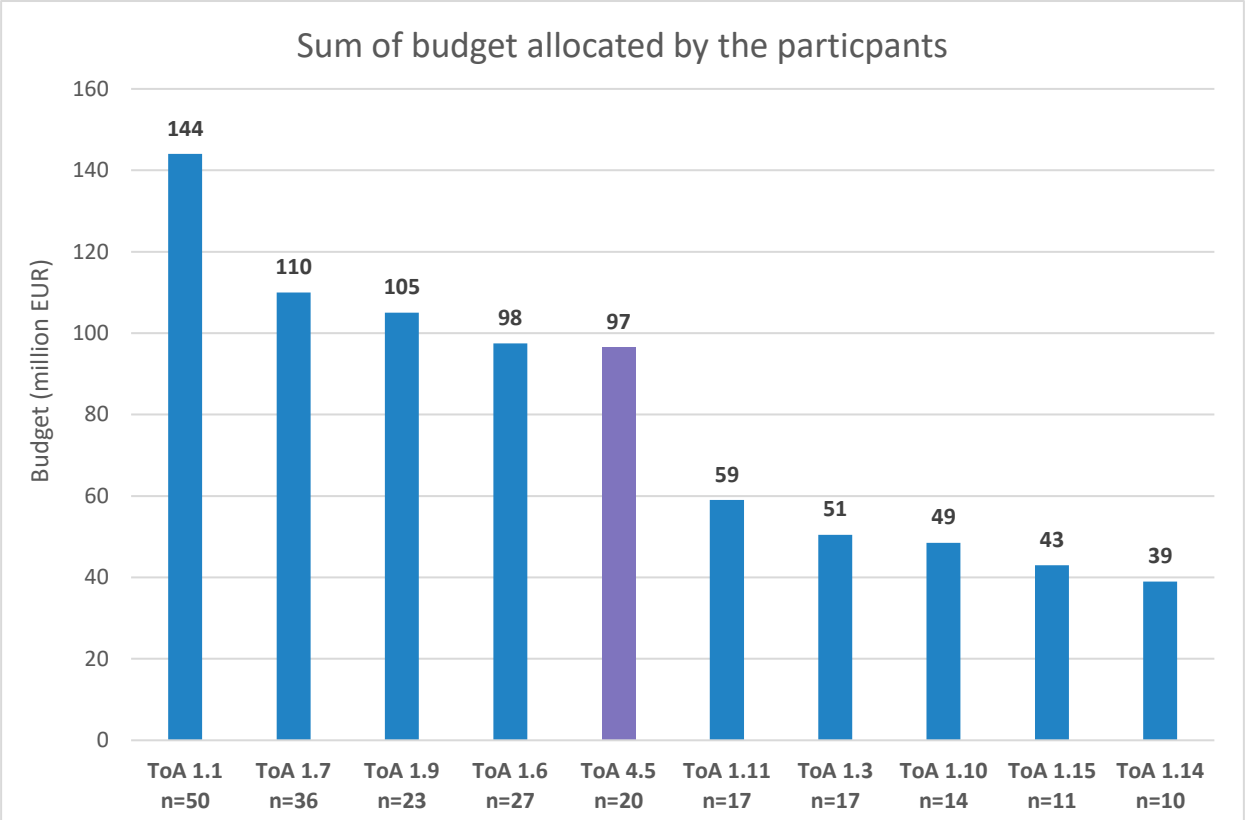

Figure 6 Sum of fictive budget that would be allocated to the respective ToA by the participants. Number of respondents: 89, number of allocations per ToA indicated in the graph. Technically it was also possible to not allocate exactly 15 Mio. Euros to exactly five ToAs.

Newly proposed ToAs and suggestions for adaptations

Besides evaluating the already existing ToAs, the questionnaire also opened the possibility to suggest an additional ToA. In total, seven concrete ToAs were elaborated using the ToA structure "Challenge", "Objectives", "Outcome":

Research:

- "Predictive patient-derived disease models for PM"
- "Early detection of non-communicable diseases"
- "High-throughput high-content profiling workflows for early stage evaluation of safety / toxicity (and off-target reactivity) of drug candidates"

Innovation System:

- "Technology Platforms for accelerating and de-risking of Advanced Therapy Medicinal Product (ATMP) innovations"

Implementation setting:

- "Improvement of patients' adherence"
- "Need to promote equity in PM clinical studies"
- "Improve equity in health and wellbeing across individuals and groups"

The detailed description of the proposed ToAs can be found in **Annex 4**. Besides those concrete suggestions of additional ToAs, 10 further ideas/topics for potential new ToAs were brought up. In addition, the respondents had suggestions for adaptations of the wording for 13 of the already existing 47 ToAs, that were part of the open consultation. The input was transferred to the SRIA drafting group for further discussion.

Conclusions

The open consultation was a pre-final step in the development of the SRIA in support for EP PerMed. The results confirm an overall validity and urgency of the presented ToAs. The ranking of ToAs within a category and also category-independent is an important real-world check and a landmark for planning and prioritising future activities for the implementation of PM approaches. Over that some valuable suggestions for new ToAs and adaptations and strengthening in wording of the existing ToAs were received. Thus, several ToAs for the SRIA were inspired by this open consultation. The results of the open consultation were presented at the ICPerMed Workshop "Preparing the Future for Personalised Medicine: EP PerMed" on 17 and 18 January, 2023 in Pamplona. The final SRIA document will be available on the ICPerMed webpage by the end of April. The results of the open consultation will further be considered in the preparation of the EP PerMed proposal and the development of activities and calls within the EP PerMed lifetime (Q4/2023-2030) and will also feed into a later update of the SRIA.

Acknowledgements

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Conflict of Interest

The authors declared no competing interests for this work.

Author contributions

The development of the questionnaire was done by the SRIA drafting group, coordinated by Monika Frenzel (ANR) and Wolfgang Ballensiefen (DLR). The technical implementation of the open consultation was done by Monika Frenzel (ANR). The ICPerMed Secretariat, represented by DLR, Alexandra Becker, and ANR, Monika Frenzel, performed the analysis of the survey results and wrote the manuscript.

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Annex 1: List of ToAs

PM related research

ToA 1.1 “A collaborative approach between pre-clinical and clinical research”
ToA 1.2 “Early considerations of security, efficacy and evidence for advanced therapies”
ToA 1.3 “New treatment modalities for PM”
ToA 1.4 “Interdisciplinary PM research projects co-developed with experts in social sciences”
ToA 1.5 “Active involvement of patients in PM research”
ToA 1.6 “More biomarker evidence for PM”
ToA 1.7 “New targets for Personalised therapies making use of an improved understanding of disease mechanisms”
ToA 1.8 “Combination Treatments”
ToA 1.9 “Single-cell technologies in combination with AI and ML for PM”
ToA 1.10 “Broader biomarker approaches to enable more informed health decisions”
ToA 1.11 “Medical cohorts for collecting high-quality health and molecular data”
ToA 1.12 “Inclusive clinical PM research inclusive that avoids bias”
ToA 1.13 “Online recruitment strategies to support PM clinical research”
ToA 1.14 “Metabolic profiling”
ToA 1.15 “PM clinical research in a wide variety of disease indications”
ToA 1.16 “Early consideration of health economic aspects”
ToA 1.17 “Early consideration of regulatory frameworks and authorities”

Innovation System and PM

ToA 2.1 “Expanded knowledge on value for PM”
ToA 2.2 “Adapted payment models for PM”
ToA 2.3 “Improved market access for companion diagnostics”
ToA 2.4 “Value based reimbursement models for PM”
ToA 2.5 “Early cooperation between public research and the private sector”
ToA 2.6 “Medical devices and in-vitro diagnostics to support PM innovations”
ToA 2.7 “Adapted Intellectual Property (IP) for PM approaches and products”
ToA 2.8 “Incentives for enterprises supporting research and development”

PM Implementation Setting

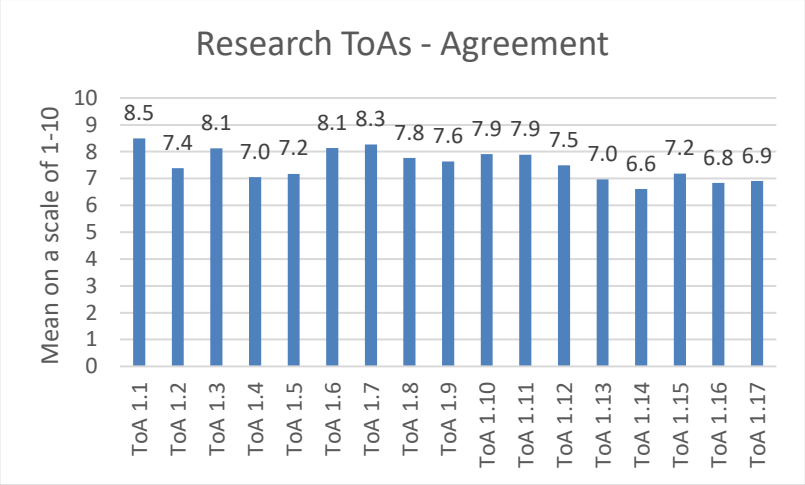
ToA 3.1 “Efficiency and value of PM approaches consider the full healthcare chain”
ToA 3.2 “Test Beds in hospitals”
ToA 3.3 “Training and Education of healthcare professionals”
ToA 3.4 “Accessibility and knowledge of genomic tools for healthcare professionals”
ToA 3.5 “Data collection by healthcare professionals for PM”
ToA 3.6 “Availability and accessibility of real-world data and real-world evidence”
ToA 3.7 “Data Sharing for PM on central platforms”
ToA 3.8 “Feedback loops from clinical application and patients experiences to research & development/innovation”
ToA 3.9 “Establishment of Learning Healthcare Systems (LHS)”
ToA 3.10 “Improved awareness for patients and citizens for PM”
ToA 3.11 “Establishment of decision support systems facilitating PM implementation”
ToA 3.12 “Use of pharmacogenomics and pharmaco-metabolomics in standard healthcare”
ToA 3.13 “Establishment of chronic disease management along with PM”
ToA 3.14 “Patient-centred care pathways”
ToA 3.15 “Create evidence and communicate PM success stories”
ToA 3.16 “Clinical trial design adapted to smaller patient groups”

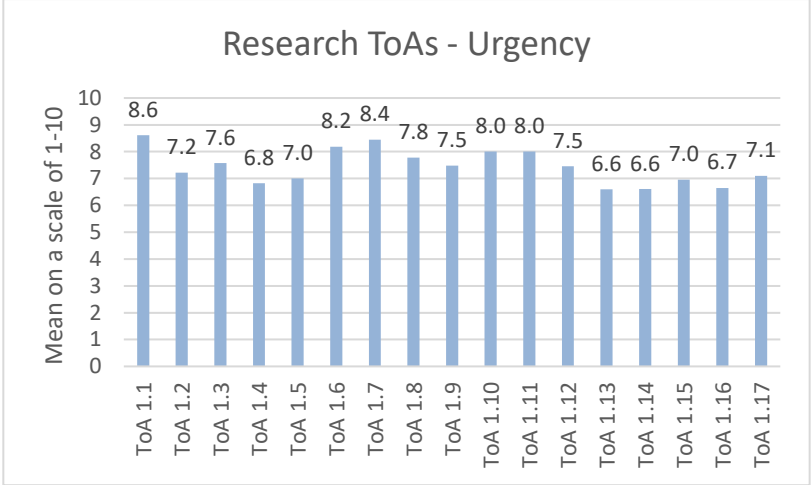
Overarching Activities

ToA 4.1 “More widely implemented, ethical and secure genetic screening programmes”
ToA 4.2 “PM innovations in a regional environment”
ToA 4.3 “Connected large-scale health databases”
ToA 4.4 “PM adapted and focused biobanks and real-world data registries”
ToA 4.5 “Network of national and regional innovation hubs”
ToA 4.6 “Genome-wide association studies within and beyond Europe”

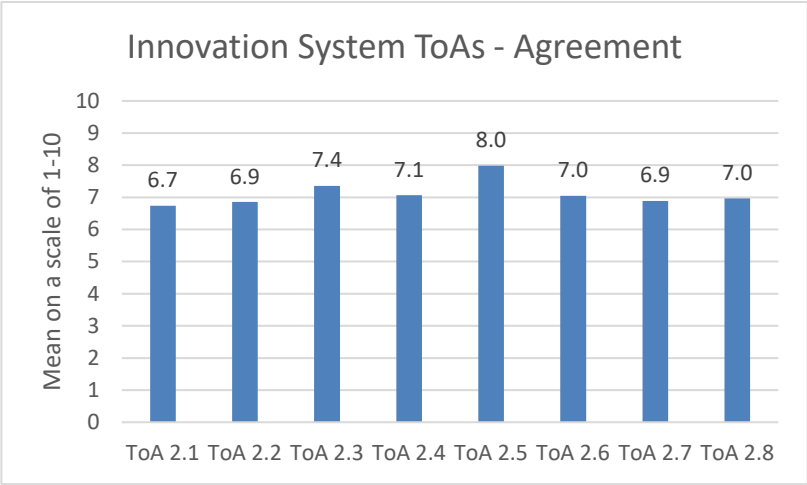
Annex 2: Assessment of each ToA in terms of agreement level and urgency level

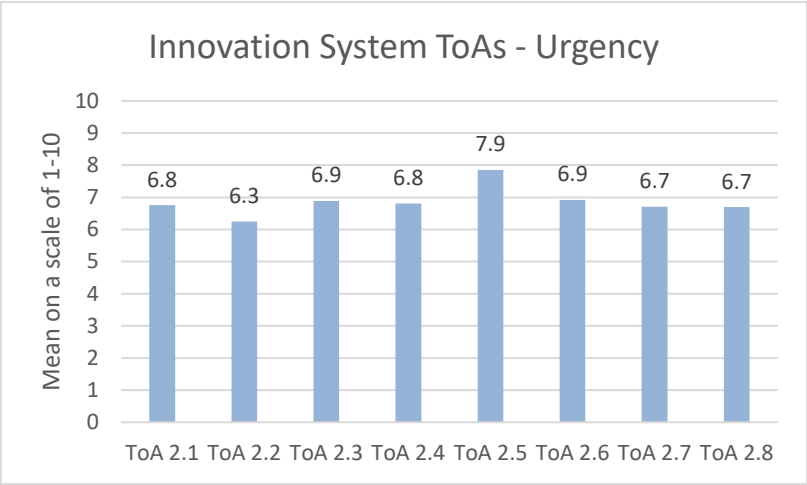
Category - PM related research (ToA numbers 1.1 - 1.17)



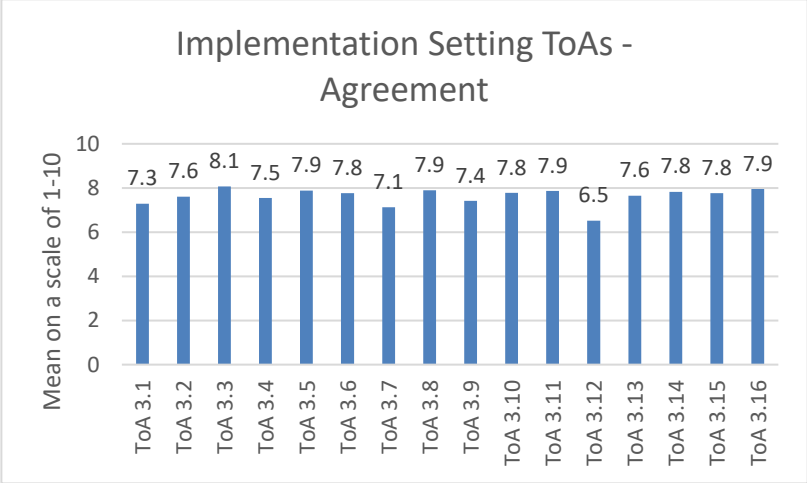


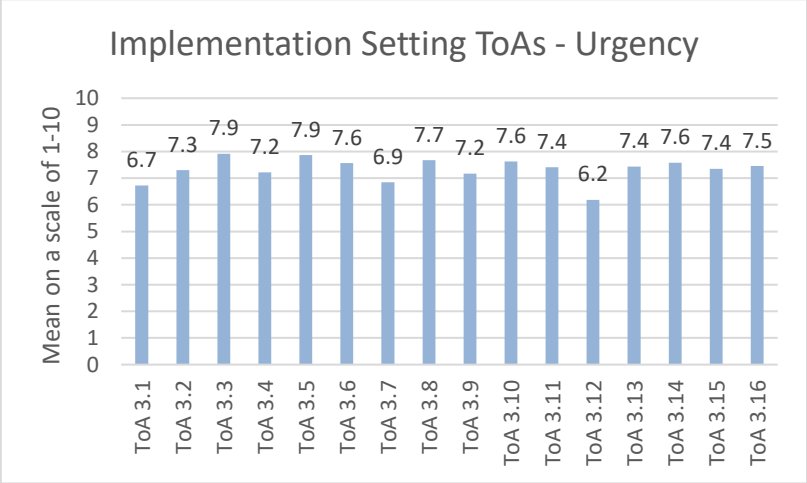
Innovation System and PM (ToA numbers 2.1 - 2.8)



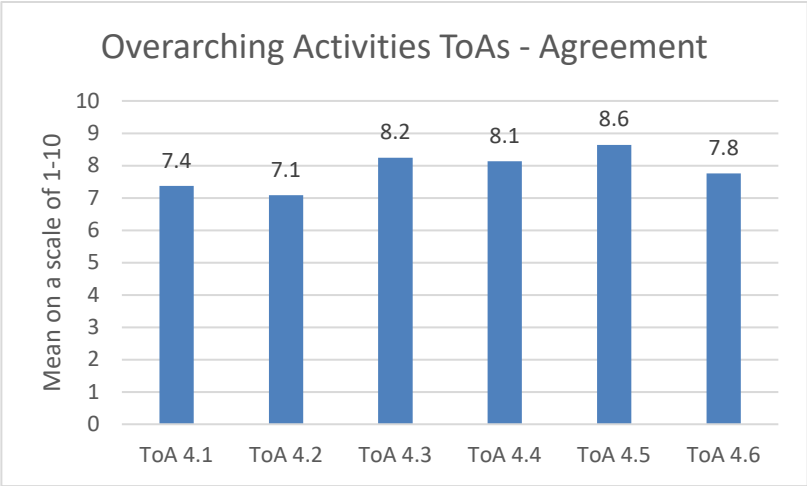


PM Implementation Setting (ToA numbers 3.1 - 3.16)





Overarching Activities (ToA numbers 4.1 - 4.6)


Overarching Activities ToAs - Agreement
Mean on a scale of 1-10
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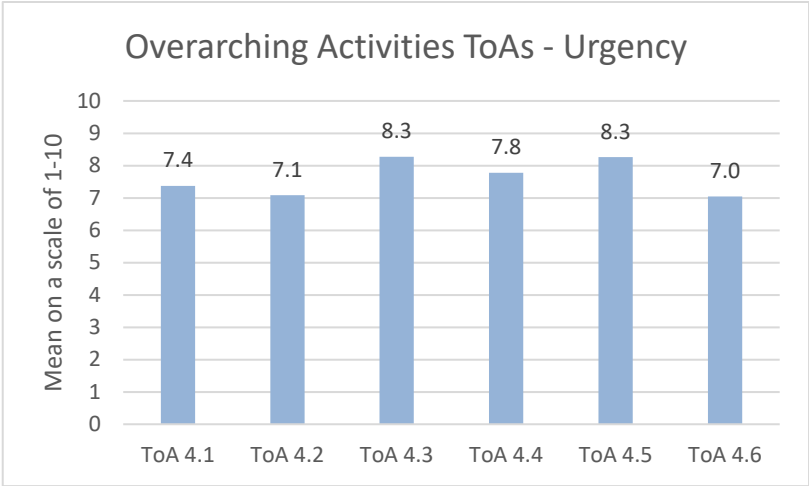
ToA 4.5
ToA 4.6


Overarching Activities ToAs - Urgency
Mean on a scale of 1-10
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ToA 4.1
ToA 4.2
ToA 4.3
ToA 4.4
ToA 4.5
ToA 4.6

Annex 3: Ranking of ToAs within each category

Category 1 PM related research (n=110 respondents)

(n=110; 91 persons nominated exactly 5 ToAs, 14 persons nominated less than 5 ToAs, 5 persons indicated more than 5 ToAs)

	% of nominations
ToA 1.1 "A collaborative approach between pre-clinical and clinical research"	72
ToA 1.7 "New targets for Personalised therapies making use of an improved understanding of disease mechanisms"	55
ToA 1.6 "More biomarker evidence for PM"	50
ToA 1.11 "Medical cohorts for collecting high-quality health and molecular data"	42
ToA 1.3 "New treatment modalities for PM"	31
ToA 1.8 "Combination Treatments"	30
ToA 1.9 "Single-cell technologies in combination with AI and ML for PM"	30
ToA 1.10 "Broader biomarker approaches to enable more informed health decisions"	29
ToA1.2 "Early considerations of security, efficacy and evidence for advanced therapies"	24
ToA 1.5 "Active involvement of patients in PM research"	24
ToA 1.4 "Interdisciplinary PM research projects co-developed with experts in social sciences"	19
ToA 1.14 "Metabolic profiling"	18
ToA 1.16 "Early consideration of health economic aspects"	16
ToA 1.17 "Early consideration of regulatory frameworks and authorities"	15
ToA 1.15 "PM clinical research in a wide variety of disease indications"	12
ToA 1.12 "Inclusive clinical PM research inclusive that avoids bias"	9
ToA 1.13 "Online recruitment strategies to support PM clinical research"	5

Category 2 Innovation System and PM

(n=61; 37 persons nominated exactly 5 ToAs, 23 persons nominated less than 5 ToAs, 1 person nominated 8 ToAs)

	% of nominations
ToA 2.5 "Early cooperation between public research and the private sector"	75
ToA 2.1 "Expanded knowledge on value for PM"	61
ToA 2.8 "Incentives for enterprises supporting research and development"	59
ToA 2.3 "Improved market access for companion diagnostics"	54
ToA 2.6 "Medical devices and in-vitro diagnostics to support PM innovations"	48
ToA 2.2 "Adapted payment models for PM"	43
ToA 2.4 "Value based reimbursement models for PM"	43
ToA 2.7 "Adapted Intellectual Property (IP) for PM approaches and products"	41

Category 3 PM Implementation Setting

(n= 61; 46 persons nominated exactly 5 ToAs, 14 persons nominated less than 5 ToAs, 1 person nominated 6 ToAs).

	% of nominations
ToA 3.3 "Training and Education of healthcare professionals"	51
ToA 3.2 "Test Beds in hospitals"	41
ToA 3.7 "Data Sharing for PM on central platforms"	41

ToA 3.6 “Availability and accessibility of real-world data and real-world evidence”	39
ToA 3.1 “Efficiency and value of PM approaches consider the full healthcare chain”	34
ToA 3.11 “Establishment of decision support systems facilitating PM implementation”	31
ToA 3.4 “Accessibility and knowledge of genomic tools for healthcare professionals”	30
ToA 3.8 “Feedback loops from clinical application and patients experiences to research & development/innovation”	30
ToA 3.14 “Patient-centred care pathways”	30
ToA 3.16 “Clinical trial design adapted to smaller patient groups”	28
ToA 3.5 “Data collection by healthcare professionals for PM”	26
ToA 3.10 “Improved awareness for patients and citizens for PM”	20
ToA 3.12 “Use of pharmacogenomics and pharmaco-metabolomics in standard healthcare”	18
ToA 3.15 “Create evidence and communicate PM success stories”	13
ToA 3.9 “Establishment of Learning Healthcare Systems (LHS)”	11
ToA 3.13 “Establishment of chronic disease management along with PM”	11

Category 4 Overarching Activities

(n=62; 42 persons nominated exactly 5 ToAs, 20 persons indicated less than 5 ToAs)

	% of nominations
ToA 4.5 “Network of national and regional innovation hubs”	84
ToA 4.3 “Connected large-scale health databases”	82
ToA 4.4 “PM adapted and focused biobanks and real-world data registries”	66
ToA 4.1 “More widely implemented, ethical and secure genetic screening programmes”	65
ToA 4.6 “Genome-wide association studies within and beyond Europe”	58
ToA 4.2 “PM innovations in a regional environment”	55

Annex 4: List of newly proposed ToAs

Category	Proposed ToA	Number of nominations
PM related research	**Title: Predictive patient-derived disease models for PM** **Challenge:** Human diseases are often difficult to precisely model in cells or model organisms. This makes it difficult to understand the underlying cause of disease or identify the most effective treatment for an individual patient. More accurate patient-derived disease models are needed to recapitulate disease at the level of individual patients and to be used in clinical decision making. **Objective:** Develop patient-derived disease models to understand early molecular and cellular changes causing disease and predict most effective personalised therapeutic strategies. New molecular, biosynthetic and engineering approaches to recapitulate more precisely human tissue in the dish (e.g. inclusion of nervous, vascular, immune and microbial inputs) and make systems such as organoids more physio-pathologically relevant. Support European efforts to standardise, automate, scale and benchmark stem cell reprogramming and organoid differentiation, propagation and banking and the creation of 'cohorts' of disease models to study diseases courses at high resolution and predict therapy responses. Standardisation of molecular and cellular phenotyping of disease models (single-cell, spatial and AI technologies, functional profiling), alongside perturbation of molecular targets (via genome/epigenome engineering) for mechanistic validation, are key to dissect human diseases across functional layers, developmental stages and inter-individual differences. **Outcome:** More precise predictive patient-derived disease models enable more effective PM by tailoring treatments based on a patient's molecular and cellular diseased tissues. They provide more fundamental insights and inter-individual variability in tissue development, homeostasis and pathogenesis by identifying and validating new translational approaches and AI predictions on disease diagnosis and treatment in a human setting. Patient-derived disease models have a key role in clinical decision making by indicating an individual patient's response to precisely targeted, RNA-, cell- and immuno-therapy, also identifying potential drug toxicity prior to treatment. 'Cohorts' of disease models improve the drug discovery process by enabling patient stratification based on disease mechanisms.	**10**
PM related research	**Title: Early detection of non-communicable diseases** **Challenge:** Early detection of non-communicable diseases. Often the disease is only recognised when irreversible damage occured already (many cancers, but also age related diseases like dementia, arthritis etc.). **Objectives:** Identifying early biomarkers and simple methods for their detection - preferably during routine visits at the physician (including centralised lab analyses) with predictive character to avoid disease onset. **Outcome:** Several diseases previously recognised too late for efficient treatment (e.g. pancreatic cancer, onset of dementia) are identified by lab analysis during or after routine visits at the physician. Rapid measures can be taken to avoid or delay disease progression.	**1**

PM related research	**Title: High-throughput high-content profiling workflows for early stage evaluation of safety / toxicity (and off-target reactivity) of drug candidates** **Challenge:** One of the main reasons for failure of drug candidates in clinical trials is their toxicity (off-target activity) which has not been captured at earlier stages of drug development. In addition, these toxicity effects and profiles may differ between patients. Insufficiently reliable evaluation of potential toxicity of drug candidates is due to the lack of appropriate assays and workflows that would capture not only an acute toxicity but also more subtle effects (and also diverse effects) of drugs on biological systems early on. **Objective:** Development of a robust panel of more reliable high throughput and high-content phenotypic and multiparametric assays (based on e.g. fluorescent imaging) to capture subtle, sublethal and yet undesired effects of drug candidates on healthy models and quick identification of their molecular targets and off-targets. Example of such assays include so called cell painting, but a wide variety of such assays could be developed to provide a thorough and yet swiftly accessible panels of tests for early stage toxicity off-target evaluation. Another approach would be focussing on robust, high throughput and reliable target and off-target identification (e.g. through chemoproteomics or similar). **Outcome:** Better evaluation of potential toxicity of drug candidates early on (even before preclinical trials) will allow for more reliable selection of safer drug candidates minimising the risk of off-target activity and subsequent failure of clinical trials due to toxicity, saving resources (money and time) otherwise wasted on carrying on with not sufficiently characterised drug candidates.	**1**
Innovative System and Personalised Medicine	**Title: Technology Platforms for accelerating and de-risking of Advanced Therapy Medicinal Product (ATMP) innovations** **Challenge:** Time to market, risk of failure, affordability and accessibility of personalised advanced therapies (ATMPs) are still limiting factors for the success of the novel curative medicine field. **Objectives:** Research to develop technology modules to rapidly generate and implement ATMPs that meet medical and market needs should be supported. Regulatory approved modules will be bundled into technology platforms, such as for manufacturing (gene transfer, gene editing, cell origin and enrichment, expansion), product analysis (potency testing, in-depth specification), preclinical testing in human in vitro test systems, therapy monitoring through biomarkers (safety, efficacy, mode of action, pharmacokinetics/dynamics), product delivery to the patient, and innovative reimbursement models. According to the principle of cooperation instead of competition, innovative technology platforms of European academic/industry translational hubs are to be networked in order to accelerate and de-risk the development and implementation of new advanced therapy products. **Outcome:** Fast track to affordable and widely accessible personalised advanced therapies (ATMPs) so that Europe will be a player rather than a payer in this innovative area of curative personalised medicine.	**2**

PM Implementation Setting	**Title: Improvement of patients' adherence** **Challenge:** No treatment works, even if personalised, if the patient is not adherent to the clinician's prescriptions. Currently, a lot of resources are wasted worldwide because of non-adherence problems. **Objectives:** To unveil patients' and caregivers' psychological and emotional needs, and beliefs in order to improve the adherence to medical and behavioural personalised treatments. **Outcomes:** To create a multidisciplinary care path (clinicians, psychologists, patients associations) in order to effectively turn patients in active subjects for tailoring their medical and behavioural treatments. Psychologists may facilitate the encounter between patients and clinicians through psychological support services for patients and for healthcare professionals. Moreover, psychologists may monitor and improve the patient's adherence through educational sessions (for patients and professionals) focused on risk and protective factors for adherence.	**1**
PM Implementation Setting	**Title: Need to promote equity in PM clinical studies** **Challenge:** The risk of difficulties to keep up the equity due to PM implementation due to a lack of knowledge about the importance of promoting equity in Pm clinical studies. **Objectives:** Acknowledging the importance of shared benefits from the results generated of clinical research, by working to reinforce the country's capacities to implement new treatment, diagnostic and prevention adapted to the national context. **Outcome:** Core competencies of research personnel will facilitate the conduction of clinical studies in connection with feasible health interventions.	**1**
PM Implementation Setting	**Title: Improve equity in health and wellbeing across individuals and groups** **Challenge:** Todays inequities in health and wellbeing across individuals and groups are driven by differential risk and differential exposures to determinants of health - social, economic, environmental and commercial. **Objectives:** Central to increased precision in interventions is predicting risk, in individuals as well as groups of individuals sharing different characteristics. This requires data across levels (biomarker, individual, environmental) across the promotion, prevention, treatment action levels. Addressing both level and distribution of health is crucial, not only to provide, protect and promote health services, but also to deliver physical, mental and social health, quality of life and sustainability for all populations across the life course. **Outcome:** While good and equitable health and wellbeing are desired outcomes in themselves, there is also a cost and capacity argument, where increased longevity, and adverse trends in health determinants like overweight and physical activity pose major and increasing challenges to health and social services within the next decades.	**1**