RESEARCH PROJECTS ON PERSONALISED MEDICINE – PERSONALISED MEDICINE: MULTIDISCIPLINARY RESEARCH TOWARDS IMPLEMENTATION"

ERA PerMed

NATIONAL GUIDELINES FOR APPLICANTS FOR THE IMPLEMENTATION OF ERA-NET ACTION ON PERSONALISED MEDICINE (PM)

JOINT CALL 2019

The Ministry of Science and Education of the Republic of Croatia (here after, MSE) is the national funding and coordination body responsible for the implementation of the ERA PerMed programme in the Republic of Croatia.

As such, the MSE hereby prescribes the National guidelines for applicants for the implementation of ERA PerMed in the Republic of Croatia (2017 – 2022) which provides information regarding national participation criteria, including scientific criteria, funding, consortium and other requirements.

FUNDING BODY DETAILS

National funding body	Acronym	Address	Telephone	Fax
Ministry of Science and Education of Republic of Croatia	MSE	Donje Svetice 38 10 000 Zagreb Republic of Croatia	+385 1 4569 000	+385 1 4594 301

NATIONAL CONTACT POINT DETAILS

NCP name and surname	E-mail	Telephone Number
Staša Skenžić	Stasa.Skenzic@mzo.hr	+38514594359

TOTAL BUDGET

Republic of Croatia has financially committed to contribute to *ERA PerMed programme* with a contribution of EUR 301.250,00. Hence, the Croatian applicants will have a budget for the Joint Call 2019 in the amount of EUR 120.000,00.

In particular, in 2019 Ministry of Science and Education is open to project proposals within both of the research areas (see "Scientific criteria"). The highest ranked project proposals evaluated on merit based criteria will be approved for funding, subject to available budget.

NATIONAL CRITERIA

Participation criteria: Terms and conditions of eligible entities

MSE funding is limited to a Croatian project partners only. Croatian project partner could be consortium (consisting of at least three national legal entities) or single legal entity.

Eligibility criteria for Croatian project partners are as follows:

- research organizations registered in the Register of Research Organizations at the Ministry of Science and Education of Republic of Croatia[1]:
    - public research institutes
    - public higher education institutions
    - other legal entities performing research activity

- other legal entities performing research activities
    - non-governmental and non-profit organizations (NGO's) or institutions whose main object is research activity or research and development activity registered by the Ministry of public administration
    - small and medium enterprises (SME's) registered by the Ministry of economy, entrepreneurship and craft.

- Only transnational projects shall be funded.

- Each consortium submitting a proposal must involve, at least, three partners eligible for funding coming from three different countries whose funders participate in the call. All three legal entities must be independent from each other.

- The project coordinator must be eligible to be funded by his/her regional/national participating funding organisation.

- The maximum number of partners per project at the pre-proposal stage is six. At the full-proposal stage, the consortium can be increased up to seven partners in total only by inclusion of a partner coming from an underrepresented country. A list of underrepresented countries will be provided to the coordinators invited for full-proposal submission.

- Within one consortium, not more than two partners from the same country participating in the call will be accepted, including those partners with own funding. For some funding agencies the maximum number of eligible partners that can be funded in one project is limited to one partner (see also "Guidelines for applicants" regarding individual funding rules).

- Partners, not eligible for funding by one of the organisations participating in this JTC (e.g. from non-funding countries or not fundable according to the regional/national regulations of the participating funding organisations), may participate in projects if they are able to secure their own funding. Maximum one partner with own funding is allowed in consortia with at least 3 partners who are eligible for funding.

The eligibility criteria of the applicant will be verified based on the Excerpt from the Register of Scientific Organizations, which will be provided by the Ministry of Science and Education.

[1] According to Article 22 of the Scientific Research and Higher Education Act (Official Gazette 123/03, 198/03, 105/04, 174/04, 02/07, 46/07, 45/09, 63/11, 94/13, 139/13, 101/14, 60/15, 131/17

We strongly encourage that the consortia submitting applications to this call include partners coming from different categories (A, B and C) to follow the crosscutting/multidisciplinarity character of the call, allowing the integration of partners from different levels of the value chain. The number of participants, the category of partner organisation and their research contribution should be appropriate for the aims of the transnational research project and be reasonably balanced in terms of international participation. Each transnational collaborative project should represent the critical mass to achieve ambitious scientific goals and should clearly demonstrate an added value from the cooperation.

Research groups, SMEs and industry partners (non-SMEs) not eligible for funding by one of the organisations participating in this Joint Transnational Call (e.g. from non-funding countries or not fundable according to regional/national regulations of the participating funding organisations) may participate in transnational projects if they are able to secure their own funding. Such partners must state, in advance, their source of funding for the project. They are considered as full partners and have to be integrated in the pre- and full-proposal templates as such. **Please be aware that maximum one partner with own funding** is allowed in consortia with at least 3 partners that are eligible for funding (i.e. proposals with 4-6 partners in total, including the partner with own funding, in the pre-proposal stage, and up to 7 for full-proposals). A letter of commitment must be included as an annex to the proposal in the full-proposal step summarising the commitment of this partner to the project and demonstrating the source of funding. The budget of a non-funded partner shall not exceed 30% of total transnational project budget requested.

To collect the necessary patient data and/or samples for the proposed study, a consortium may need to collaborate with other centres. If the unique role of those centres is only to provide patient' data and/or samples for the study, they will not be considered as partners of the consortium but can be included otherwise, e.g. via cooperation agreements or subcontracting.

Number of partners in the proposal*	**Pre-proposal**				**Full-proposal** (only by inclusion of one underrepresented country)
	3	**4**	**5**	**6**	**7**
Maximum number of partners with own funding	0	1	1	1	1
Maximum number of partners per country	1	2	2	2	2

*** minimum 3 partners eligible for funding from three different countries participating to the call**

Each consortium must nominate only one **project coordinator** among the project's principal investigators. The integration of a co-coordinator is not allowed. The coordinator must be eligible to be funded by his/her regional/national participating funding organisation. The project coordinator will represent the consortium externally and towards the JCS and **Call Steering Committee**[2] **(CSC)**, and will be responsible for its internal scientific management such as project monitoring, reporting, intellectual property rights (IPR) management and the contact with the JCS.

Only one principal investigator will represent each project partner. Within a joint proposal, each project partner's principal investigator will be the contact person for the JCS and the relevant regional/national funding organisation.

[2] Call Steering Committee: composed of a single representative from each country/region funding organisation.

Whilst proposals will be submitted jointly by research groups from several regions/countries, research groups will be funded by the individual funding organisation of the respective region/country from which applicants have applied. The applicants are therefore subject to the eligibility criteria of the relevant funding organisations of the respective region/country (see also Annex II and "Guidelines for applicants"). It is highly recommended to carefully read the funding rules and eligibility criteria of the relevant funding organisations. Applicants are strongly advised to contact their relevant funding organisation (see also Annex I) prior to submission; please note that for some regions/countries this step might be mandatory.

Please note that if a **partner** is found to be non-eligible by one of the funding organisations after the formal check, the entire proposal may be rejected without further review. For a definition of eligible partners see "Guidelines for applicants", the regional/national regulations, and contact your regional/national funding organisation (see also Annex I).

Nevertheless, the applicant will be informed that a redress procedure is available. The redress procedure pertains to the eligibility – checking process only; it is not an automatic re-evaluation, and the judgement of appropriately qualified experts is not called into question.

Applicants must indicate in the pre-proposal form if the study submitted is subject to other evaluation processes, such as other joint transnational calls (e.g. NEURON, E-RARE, EJP-RD, ERA-CVD, JPND, HDHL, EuroNanoMed, ERACo-SysMed, Transcan and others) and national calls due to question of regional/national eligibility. Applicants shall avoid applying for same research activities in different calls. Double funding is not allowed.

Double submission of the same proposal on neurodegenerative diseases focusing on medical imaging in the light of PM within the co-funded JPND JTC2019 and the ERA PerMed JTC2019 is not eligible. Double submission of the same proposal within the co-funded EJP Rare Diseases JTC2019 and the ERA PerMed JTC2019 is not eligible.

Patient involvement

ERA PerMed strongly encourages the active involvement of members of the public in the proposed research projects. This includes patients, citizens/potential patients, carers, people who use health and social care services as well as patient organisations. The goal is to enable awareness, share knowledge and improve the dialogue between the researchers, healthcare providers, policymakers, industry and the public.

Therefore, consortia submitting proposals to this call are asked to describe the level of public involvement in the research throughout the various stages of research design, conduct, analysis and dissemination. The extent of public/patient involvement may vary according to the context of the study proposed and regional/national regulations of participating funding organizations.

REPORTING

Each project coordinator, on behalf of all participating partners, shall submit to the JCS an annual and final scientific progress report (first year, second year and final report) of the transnational project (in English). A report template will be provided by JCS stating the scientific progress, the goals that have been met, and corrective measures set in case that the annual project plan has not been fulfilled. It may also be necessary for project partners' principal investigators to submit reports individually to their

national funding agency/body in accordance with the respective national/regional regulations. In addition, project coordinators may be asked to present the project results during ERA PerMed meetings (invitation to attend at least one midterm seminar and one final symposium). Accordingly, travel expenses to attend these mandatory meetings should be included in the proposal budget plans.

Additionally, Croatian project partner receiving the funding under this call will be monitored by MSE. Croatian project partners have the obligation to submit annual and final financial and narrative reports on the project progress, describing in clearly manner whether or not they achieved the set of key performing indicators. MSE will proscribe the form for the annual and final reports. Furthermore, Croatian project partners also have the obligation to submit the final financial and narrative reports.

The eligibility criteria for the applicant will be verified based on the Excerpt from the Register of Scientific Organizations, which will be provided by the Ministry of Science and Education. Legal entities receiving basic funding from the MSE can only be granted for funds covering extra expenditure, i.e. as an addition to their basic financing.

Maximum limit requested per partner / per country / per proposal

Only costs directly related to the proposed research activities are eligible for financing under this call. Activities supported by other sources are not eligible for financing. Applicant must ensure that there is no double financing during the whole project implementation.

Total available budget for Joint Call 2019 for **Croatian project** partners is 120.000,00 Euro.

Project duration

The maximum duration of the projects must be three years in accordance with ERA PerMed funding organisation regulations. The performed studies should be finalised at the latest within the 3rd year of funding period. Eligible costs and funding provisions may vary according to the respective funding organisation's regulations. Project partners must refer and adhere to their own specific regional/national regulations and scientific remits as detailed in the relevant regional/national announcements (see Annex II).

SCIENTIFIC CRITERIA

Thematic areas and topics to be funded

The JTC2019 of ERA PerMed comprises three Research Areas:

Research area 1 "Translating Basic to Clinical Research and Beyond"	**Research area 2** "Integrating Big Data and ICT Solutions"	**Research area 3** "Research towards Responsible Implementation in Health Care"
Module 1A: Pre-clinical Research	Module 2A: Data and ICT – Enabling Technology	Module 3A: Optimising Health Care System
Module 1B: Clinical Research	Module 2B: Data and ICT - Towards Application in Health Care	Module 3B: Ethical, Legal and Social Aspects

Each project proposal **MUST** address **at least one module of Research Area 3** and **at least one module of Research Area 1 or 2**:

Research Areas/Modules combined in proposal	**Research Area 1 Module 1A and/or 1B**	**Research Area 2 Module 2A and/or 2B**	**Research Area 3 Module 3A and/or 3B (mandatory)**
Eligible	X		**X**
Eligible		X	**X**
Eligible	X	X	**X**
Not eligible	X	X	

The coherent integration and combination of the different Research Areas and Modules in the proposals is part of the evaluation process.

Research Area 1: *"Translating Basic to Clinical Research and Beyond".*

Research proposals should aim to improve the exchange between basic and clinical research. This is needed to allow the transition from bench to bedside (e.g. by translational science, transferring preclinical technologies/predictive models to clinical application) but also vice versa by using e.g. existing databases, repositories and cohorts, and by sharing experiences obtained in classical and innovative clinical studies/trials. This aims for a better identification and validation of known biomarkers (including omics data and others, e.g. obtained by imaging-based, biosignal monitoring approaches, etc.).

Proposals are expected to thoroughly describe appropriate validation strategies according to the translational gap to be bridged. The inclusion of a strategy to ensure the reproducibility of results is encouraged.

Research projects on diseases other than cancer are also encouraged.

Module 1A: Pre-clinical Research

Scope

- Development and implementation of high-throughput pre-clinical models for the (A) validation of data and hypothesis from human population, clinical and molecular studies and/or (B) prediction of clinical outcome. This may include animal models, cell culture models, organoids etc.
- Classification of diseases at the molecular level, which can be instrumental for a successful implementation of PM, including pre-clinical studies for validation of biomarkers that can be used in diagnosis, prognosis and prediction of response to treatment.
- Validation (in preclinical models, in terms of reproducibility, safety and efficiency) and characterisation of the role of biomarkers in predictive medicine for future prevention, assessment and management of diseases.

Module 1B: Clinical Research

Scope

- Improvement, validation and combination of different tools as e.g. imaging as well as omic tools for diagnostics and different integrated analytical methods, allowing the discovery of molecular characteristics involved in disease etio-pathogenesis, development and progression and in patient's treatment including pharmacokinetics or pharmacodynamics.
- Development and evaluation of concepts for innovative clinical trial methodologies, suitable for PM approaches, taking into account that more flexible and innovative trial design is needed.
- Development of new concepts and stratification strategies in exploratory clinical studies (for further indications, see also the blue box on page 11).
- Clinical and omics data integration, use of machine learning technology to provide a personalised treatment for patients.

Research Area 2: *"Integrating Big Data and ICT[3] Solutions".*

Systematic integration of different bioinformatic resources (databases, algorithms, etc.), Big Data and ICT solutions should be an essential part of the research proposals submitted to this call wherever appropriate. The re-use of data is encouraged. Developed PM approaches should support the easy flow, robust analysis and interpretation of information such as clinical data (including imaging data and physiological monitoring data), omics data, data on biological samples, as well as patient outcomes among different institutions while ensuring data security and data protection.

Applicants are asked to describe new or existing tools, methodologies, technologies and digital support used in the project. This includes ICT solutions (e.g. eHealth and mHealth solutions and telehealth) for timely and safe transfer of health information and facilitating the use of data, including electronic medical records (structures and unstructured sources), by respecting on one hand data security, protection and privacy, and on the other hand ensuring interoperability, completeness, sufficient documentation and comparability of data.

The re-use or combination of already existing tools is also welcome. It is encouraged to outline how developed/used ICT solutions will be maintained after the end of the project.

Module 2A: Data and ICT – Enabling Technology

Scope

- Research on data harmonisation strategies and development of specific ICT solutions for research questions addressed in the consortium.
- Strategies for developing common quality standards, semantics and minimal indicators, and metrics for data and metadata.
- Development of biomedical and/or computational (ICT) tools respecting interoperability of the databases as well as data privacy regulations.

3 Information and Communications Technology (or Technologies)

- Development of bioinformatic models/methods to integrate, analyse and extract value from databases, allowing e.g. the (automated or manually curated) integration and processing of data from unstructured sources and the combination of multiple data sources by maintaining statistical power.
- Development of new devices/tools for data collection (e.g. mHealth, wearable devices for continuous online physiological monitoring, haptic devices, etc.).

Module 2B: Data and ICT – Towards Application in Health Care

Scope

- Research on data integration and interpretation of complex/multifactorial diseases but also other diseases, aimed to advance PM. Demonstration of the potential clinical benefit using various datasets (e.g. from large, multimodal and multicentric public data repositories and clinical records from different sources), various data types (e.g. behavioural and molecular data) and different forms of mathematical, statistical and modelling frameworks for the exploration and validation of data quality and its information content as basis for future proof of concept studies.
- Development of innovative and easy to handle clinical decision support tools tailored to healthcare professionals to provide suitable and consequent interpretation of complex multifactorial and multimodal data (including e.g. clinically validated data and information on current diagnosis and treatment options).
- Development of telehealth and telemedicine applications to support the implementation of PM, e.g. by using and combining innovatively already validated and novel e- and mHealth options, such as e.g. innovative physiological sensor and patient monitoring technologies combined with mHealth solutions for real-time personalised feedback.

Research Area 3: *" Research towards Responsible Implementation in Health Care"*

Even though promising approaches in PM exist, the implementation in the healthcare systems on a large scale is still to come. Research is necessary on how healthcare systems of different countries could be adapted and outcomes of these studies be taken into account during implementation processes. This comprises research on future optimisation of health care systems including research on regulatory frameworks in health economics (e.g. until market access, if applicable). Health economics aspects can assess the cost-effectiveness of PM approaches or even develop recommendations and/or new models and tools to enable this kind of assessment.

In addition, there is a broad range of ethical, legal and social aspects (ELSA) to consider, e.g. research on regulations in diagnostics and drugs, fundamental societal challenges, as well as research in citizen/patient involvement.

Both of these cross-cutting topics (research on the optimisation of healthcare system and ELSA) should be addressed as early as possible during the development of PM strategies.

Proposals submitted to this call should integrate research on at least one of these topics (Module 3A or 3B). The research conducted in research area 3 should have a direct relation to the research question(s) addressed in research area 1 and/or 2.

Module 3A: Optimising Health Care System

Scope

- Research on the analysis, comparison and optimisation of national and regional healthcare systems in the context of PM. Suggestions for the optimisation of healthcare 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 the social conditions, such as availability of insurance and employment, should form part of this research.
- Research on development, application and adaptation of new models and approaches for healthcare and their application/adaptation to healthcare systems in different regions/countries. This should lead e.g. to support models and tools (such as pharmaco-economy, clinical risk assessment and management, and others), enable better diagnosis and care for the benefit of citizens and patients, based on available data and information on current diagnosis.
- Research on health economic aspects of PM, e.g. on cost-effectiveness of PM approaches for treatments, taking into account patient outcome and quality of life. Research investigating whether a patient-centred, PM approach requires refinement of or even new health economic and pharma-economic models; not only for treatment of diseases, but also for prevention.
- Research on the overall economic impact of an optimised health care system based on improved treatment of diseases and prevention within the frame of PM. This includes the identification of the different economic actors (market players) and their economic strategies.
- Research on provision of equitable access to PM approaches for all patients – regardless of economic, educational or geographic status (including research on the effect of PM on social inequalities).

Module 3B: Ethical, Legal and Social Aspects

Scope

- Research on optimised data security, protection, confidentiality, privacy and ownership within PM approaches; responsible ways to enable the use of personal and patient data for research purposes.
- Research in adequate regulatory structures and pathways in PM; e.g. in the context of development of new clinical trial design methodology for PM. Research on 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.
- Research on how to overcome the challenges posed by different regional or national regulatory frameworks, for example in multi-centred clinical trials with study centres in several countries, including e.g. the impact of different cultural codes (affecting the collection of informed consent), the level of education and/or the social/economic status.
- Research on fundamental societal challenges evoked by PM, e.g. questions of solidarity, fairness or rationality of allocation of resources and research foci.
- Development of new forms and interplay of stakeholder exchange (including all different key players from academic researchers of different disciplines, health care providers, industry/pharma and regulatory authorities but also citizen and patients).
- Research on responsibility and liability as well as challenges for our view on the nature of humans and humankind, human dignity; heritability and generational responsibility or the interface and tension between the state of health, and illness.

- Research on ethical, legal and social aspects in the context of decision support systems, especially with the use of artificial intelligence: availability and suitability of training data (in machine learning), requirements on transparency of decisions, questions of responsibility and liability, potential changes in the role and self-image of physicians.
- Research on appropriate ways and methods for participatory health research/patient involvement in research projects for PM.

Research on the different user's perspectives (expectations vs. capacity and voluntariness to provide requested input) of the different key players (e.g. researchers, health care providers, etc.) and professional dynamics connected to PM approaches. This research might also include reflections on organizational innovation (changes in the organisation of the health service).

Croatian Principal Investigator

Principal investigator for Croatian project partner must hold a Ph.D. degree and should have at least 5 years of research experience after having obtained Ph.D. Research leader must be employed under employment contract at Croatian institution participating in transnational consortium. Croatian project partner will commit that minimum 30% of research leader's workload will be dedicated to the ERA PerMed project. Croatian project partner research leader will repost on project progress to national coordinating and funding body – MSE.

If coordinator of transnational consortium, Croatian project partner will appoint one research leader (principal investigator) who will monitor the implementation of transnational project activities, and report on it to ERA PerMed secretariat.

The funds will be allocated to the Croatian project partner when evaluated positively by ERA PerMed Secretariat and validated by MSE.

Only one principal investigator represents each project partner. Within a joint proposal, each project partner's principal investigator will be the contact person for the JCS and the relevant national/regional funding organisation.Each consortium must nominate only one project coordinator among the project's principal investigators. The coordinator must be an eligible project partner for the national/regional funding organisation participating in the call. The project coordinator will represent the consortium externally and towards the JCS and Call Steering Committee (CSC), and will be responsible for its internal scientific management such as project monitoring, reporting, intellectual property rights (IPR) management and the contact with the JCS.

FUNDING CRITERIA FOR CROATIA'S PROJECT PARTNER IN ERA-NET ACTION ON PERSONALISED MEDICINE (PM)

Eligible costs categories

For Croatian applicants, eligible costs are as follows[4]:

[4] For more information on the eligible and ineligible costs please consult: http://www.obzor2020.hr/userfiles/Smjernice_O2020_projekti_final.pdf.

PERSONNEL COSTS	DIRECT COSTS	SUBCONTRACTING	INDIRECT COSTS
- living allowance only for the new employees on the project - mobility allowance (accommodation and transport costs, per/diem allowances, meeting/seminar/conference organizational directly connected with the research)	-research costs - dissemination and visibility costs	-only in justified cases and subjected to the evaluation	- up to 25% of total approved project budget for the Croatian project partner - management cost overheads

All budget items must be justified and provided for eligibility. All costs must be made during the period of the project duration. Applicants are advised to contact the national contact point for the pre-eligibility check.

VAT eligibility

For Croatian applicants, the general H2020 rule applies regarding VAT eligibility within the ERA-Net Action on Personalised Medicine (PM) programme. VAT is an acceptable cost for all applicants that are non-profit legal entities if there is no right to tax deduction. VAT is in that case the ultimate expense for the applicant and as such is recorded in the accounting books. Regarding profit organizations (that are liable for paying and collecting VAT, and VAT for them is not the ultimate expense, the VAT expense is not eligible cost for the project cost within the ERA-Net Action on Personalised Medicine (PM).

Subcontracting rules

Subcontracting for the sake of performing and implementing certain tasks/activities that are part of the main project activities is allowed and considered eligible. For more information regarding subcontracting rules please consult http://www.obzor2020.hr/userfiles/Smjernice_O2020_projekti_final.pdf.

LINKS AND REFERENCES TO FIND SPECIFIC (NATIONAL) REQUIREMENTS

http://www.obzor2020.hr/userfiles/Smjernice_O2020_projekti_final.pdf
Applicants are advised to contact the national contact point for the pre-eligibility check.

The full version of ERA PerMed national guidelines for applicants for the implementation of ERA-Net Action on Personalised Medicine (PM) in the Republic of Croatia (2017 – 2022) will be published on the MSE website.