Horizon Europe

Cluster 1 Santé

Appels à projet 2025

Le programme de travail Santé 2025 n'ayant pas encore été officiellement publié (publication attendue au printemps 2025), de légers ajustements restent possibles, et certains appels pourraient être modifiés ou supprimés

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1. Neurologie

HORIZON-HLTH-2025-03-ENVHLTH-01-two-stage: The impact of pollution on the development and progression of brain diseases and disorders

Budget total : 40M€

Budget par projet : entre 6 et 7M€ en lump sum

Type d'action : Research and innovation action

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination "Living and working in a health-promoting environment". To that end, proposals under this topic should aim to deliver results that are directed, tailored and contributing to most of the following expected outcomes:

- Global and EU policies preventing and reducing the health impacts of pollution are supported with up-to-date scientific evidence, tools and methodologies;
- Citizens are more protected by having a better insight into exposure to pollution and its impacts on brain health and adopting health enhancing behaviours;
- Public authorities, health stakeholders, the scientific community and the society at large have access to FAIR data on the link between pollution and brain health, particular windows of susceptibility to exposure and the impacts of pollution on the general population and vulnerable groups;
- Public authorities develop adequate evidence-based measures and guidelines to prevent and reduce the negative impacts of pollution in the development of brain disease.

Scope: Life-long exposure to pollutants in the living and occupational environment is an important risk factor for non-communicable diseases, leading to a variety of serious physical and mental health impacts and causing preventable disease burden with associated elevated economic costs. Pollution disproportionately impacts certain vulnerable groups (e.g. children and older adults) or groups who are more sensitive or more exposed (workers, populations living in polluted areas) to this type of environmental stressor. At present, over 10% of annual premature deaths in the 27 EU Member States are related to environmental pollution.

Age is the main risk factor for neurodegenerative diseases, but environmental exposure and lifestyle are important candidates for understanding their aetiology. Accumulating evidence suggests that the "exposome", described as the totality of human environmental exposures from pre-conception onwards, represents a major modifiable risk factor for most neurodegenerative diseases and dementia. Additionally, emerging evidence suggests that pollution, may contribute to the development of neurodegenerative disease, with increasing incidence in an ageing population.

The environment is known to be a significant determinant of child health, with increasing evidence that some industrial chemicals are toxic to the development of the human brain. The health impact of many potential neurotoxic chemicals remains unstudied in human populations, including in children. The developing brain is particularly vulnerable to toxic chemical exposures and this sensitivity is likely greatest in utero and throughout early childhood.

Chronic and repeated exposure to pollutants, in working environments but also for consumers, has also been associated with increased risk of cognitive impairment and neurodegeneration.

Research activities under this topic should explore evidence on the causal link between exposure to different pollutants (focusing on specific pollutants or a combination thereof) and the development or progression of neurological, neurodegenerative or neurodevelopmental diseases or disorders. Proposals can consider occupational, living and/or social environments and include one or more vulnerable, sensitive or exposed population groups. More specifically research actions under this topic should include several of the following activities while focusing either on neurological, neurodegenerative or neurodevelopmental diseases or disorders:

- Gain better insights on the pathogenesis and the molecular, genetic and epigenetic pathways and biological mechanisms involved in the onset and progression of disease, considering emerging pollutants, specific windows of susceptibility and adopting, when relevant, a life-course approach. Synergistic neurotoxic effects and realistic doses and duration of exposure should also be considered;
- Generate evidence on the impacts of pollution in comorbidities associated to neurodegenerative, neurological or neurodevelopmental diseases and disorders;
- Develop and/or validate better in-vivo, in-silico and in-vitro models, instruments and/or methods and take advantage (as applicable) of structural, functional and molecular imaging methods (e.g. MRI nuclear imaging), multi-omics and bioinformatics to study disease causation and evolution, considering, among others, also epigenetic factors and providing better biomarkers for early detection and disease progression;
- Apply the exposome framework to advance the understanding of the role of environment on neurodegenerative diseases research; elucidating the neuroexposome and emphasizing the brain's distinctive responses to environmental exposures;
- Contribute to the development of health indicators to inform mitigation and prevention measures, incorporating, when relevant, an intersectional approach that considers diverse individual characteristics such as gender, age, and disability and socioeconomic and lifestyle factors;
- Strengthen the understanding of the causative link between exposure and incidence of disease by taking advantage of well-designed longitudinal studies (considering exposure duration and differences in exposure composition, geographical location and sources), rigorously controlled epidemiologic studies and/or clinical, real-world and/or cohort data (building on existing national and international cohorts when available);
- Generate evidence on the potential association between the accumulated long-term exposure of workers and consumers to pollutants (including low-level exposure) and neurological and neurodegenerative diseases. The development of neurodevelopmental disorders in children following parental exposure could also be evaluated.

Gender and sex-related differences should be addressed, where appropriate.

Applicants are encouraged to consider the use of experimental methods not using live animals,where relevant and allowing to obtain data of comparable validity.

Proposals should adhere to the FAIR data principles and adopt wherever relevant, data standards and data sharing/access good practices.

The effect of nutrition on mental health should not be the main focus since this area will be covered by topic HORIZON-CL6-2025-02-FARM2FORK-13: “Towards modern, integrated, and effective fisheries monitoring, control and surveillance (MCS) systems”.

Applicants should be acquainted with the activities being developed under the Environment, climate and health research portfolio, the EFSA activities under EnvironmentalNeurotoxicants and Developmental neurotoxicity and the Partnership for the Assessment of Risks from Chemicals - PARC.

This topic requires the effective contribution of social sciences and humanities (SSH) disciplines and the involvement of SSH experts, institutions as well as the inclusion of relevant SSH expertise, in order to produce meaningful and significant effects enhancing the societal impact of the related research activities.

Proposals should take advantage of and connect to European research infrastructures and services in the area of environmental exposure assessment.

Proposals should ensure that chemical monitoring including human biomonitoring data are shared in the Information Platform for Chemical Monitoring (IPCHEM) through involvement with the European Commission's Joint Research Centre (JRC), and/or in the future Common Data Platform for Chemicals, through involvement with the European Chemicals Agency (ECHA) or other relevant agency (such as the European Environment Agency - EEA) responsible for the specific domain. In that respect, the JRC will collaborate with any successful proposal and this collaboration, when relevant, should be established after the proposal’s approval.

In order to maximise synergies and increase the impact of the projects, all proposals selected for funding from this topic will form a cluster and be required to participate in common networking and joint activities. Without the prerequisite to detail concrete joint activities, proposals should allocate a sufficient budget for the attendance of regular joint meetings and to cover the costs of any other potential common networking and joint activities. Guidance on the potential activities to be developed can be obtained by consulting the clusters of projects ongoing under the Environment, climate and health research portfolio.

Applicants invited to the second stage should provide details of their clinical studies in the dedicated annex using the template provided in the submission system. As proposals under this topic are expected to include clinical studies, the use of the template is strongly encouraged.

HORIZON-HLTH-2025-03-DISEASE-02-two-stage: Advancing innovative interventions for mental, behavioural and neurodevelopmental disorders

Budget total : 50M€

Budget par projet : entre 6 et 8M€ en lump sum

Type d’action : Research and innovation action

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination “Tackling diseases and reducing disease burden”. To that end, proposals under this topic should aim to deliver results that are directed, tailored towards and contributing to all the following expected outcomes:

- The scientific and clinical communities make effective use of state-of-the-art knowledge, data, technologies, tools, methods, best practices, and trainings to underpin and complement the development of innovative interventions aimed at achieving a lasting benefit.
- The scientific and clinical communities benefit from the exchange of data, knowledge and best practices, thereby strengthening their collaboration in the EU, the Associated Countries and beyond.
- The scientific and clinical communities make wide use of relevant databases and/or integrate them with existing infrastructures for storage and sharing of collected data according to FAIR principles, thereby encouraging further use of the data.
- Policymakers, funders, scientific and clinical communities, patient organisations, regulators, and other relevant bodies are informed of the research advances made and the requirements for a widespread implementation of the innovative therapeutic interventions and complementary approaches.
- Patients and caregivers are constructively engaged with the research, ensuring that their needs are catered for, with the aim of tangibly benefitting from the interventions.

Scope: Mental, behavioural and neurodevelopmental disorders, that include for example severe depression, anxiety, schizophrenia, psychosis, post-traumatic stress disorder (PTSD), addictive behaviours (drugs 85 , alcohol, gaming and others), obsessive-compulsive disorder, eating disorders and autism spectrum disorder are a high burden for patients, health systems and society, and remain unmet medical needs. More innovative, safer and more effective therapeutic and relapse-preventing solutions based on active substances are required, as for example for mental disorders many available treatments show modest efficacy, non-negligible side effects, discontinuation problems and high relapse rates. Additionally, other non-invasive multidisciplinary and/or transdiagnostic approaches (e.g. neurostimulation, neuroimaging, digital, non-pharmaceutical, psychotherapy, psychosocial) should be further developed to complement the therapeutic and relapse prevention solutions. These approaches aim to further improve health outcomes, self-determination, autonomy and quality of life in the long-term.

The disorders within the scope of this topic fall under Chapter 6 of the International Classification of Diseases. Rare diseases are excluded.

Proposals should address most of the following aspects:

- Perform rigorous clinical studies into the safety and efficacy of the innovative interventions and their mode of administration, ensuring adequate cohorts/sample sizes with adequate representation of the patient population, including in terms of age, sex and ethnicity.
- Through the clinical studies, gain further insight into the mechanism(s) of action of the innovative therapies and complementary approaches. This could entail analyses of imaging (e.g. MRI, ultrasound, nuclear imaging), as well as physiological, molecular, biochemical or omics signatures revealing potential perturbations prior to the intervention and recovery thereafter, and it could lead to the development of surrogate endpoints. This insight should open the path to more personalised interventions and approaches.
- Use and/or develop technologies, including digital ones (e.g., (generative) Artificial Intelligence - AI, wearable technologies) to help implement and monitor the long-term efficacy of the intervention(s), as well as manage the disorder and/or monitor their progression (e.g. with unobtrusive technologies suitable for patient monitoring at home

and in real-world conditions), whilst also ensuring they are bias-free, inclusive, and ethically sound.
- Exploit existing data, biobanks, registries and/or cohorts, together with the generation of new data that should be managed in line with the FAIR principles.
- Engage all relevant stakeholders (especially patients and patients' representatives for the disorder, caregivers, clinicians, counsellors, regulators, etc.) to design end-user optimised interventions, applying gender-sensitive and intersectional approaches.
- Advance research by leveraging already existing and emerging state-of-the-art research infrastructures (e.g. ECRIN, EATRIS, EBRAINS, BBMRI, EuroBioImaging, European Genomic Data Infrastructure, etc.), as well as results stemming from EU-supported research projects, where applicable.
- Engage with national public health authorities and regulators to ensure a robust development pathway and further uptake of the intervention.

The participation of start-ups, micro, small and medium-sized enterprises (SMEs) is encouraged with the aim of strengthening their scientific and technological foundations, enhancing their innovation potential, and exploring possibilities for commercial exploitation.

Funded projects should liaise with the European Partnership for Brain Health (covered by topic HORIZON-HLTH-2025-02-DISEASE-01) once launched.

The topic requires the effective contribution of social sciences and humanities (SSH) disciplines and the involvement of SSH experts, institutions as well as the inclusion of relevant SSH expertise, in order to produce meaningful and significant effects enhancing the societal impact of the related research activities.

All projects funded under this topic are strongly encouraged to participate in networking and joint activities, as appropriate. Therefore, proposals should include a budget for the attendance to regular joint meetings and may consider covering the costs of any other potential joint activities without the prerequisite to detail concrete joint activities at this stage. The details of these joint activities will be defined during the grant agreement preparation phase.

Applicants invited to the second stage should provide details of their clinical studies in the dedicated annex using the template provided in the submission system. As proposals under this topic are expected to include clinical studies, the use of the template is strongly encouraged.

HORIZON-HLTH-2025-02-DISEASE-01: European Partnership for Brain Health

Budget total : 150M€

Budget par projet : 150M€

Type d'action : Programme Co-fund Action

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination "Tackling diseases and reducing disease burden". To that end, proposals under this topic should aim to deliver results that are directed, tailored towards and contributing to all the following expected outcomes:

- The position of the EU and Associated Countries is strengthened as an internationally recognised driver of research and innovation on brain health119, thereby contributing to the achievement of the Sustainable Development Goals related to neurological and mental health.

- Research funders align, adopt and implement their brain health research policies allowing for the optimal generation and translation of knowledge into tailored health products and interventions to (i) promote brain health throughout the lifetime, (ii) prevent neurological and mental disorders, and (iii) improve diagnosis, treatment and care to enhance the quality of life of those living with brain disorders, as well as their caregivers, whilst also considering cultural, ethical, legal and social aspects.
- Research funders, policymakers, relevant agencies and authorities, researchers, innovators, citizens, people living with brain disorders and their caregivers and advocates enhance their collaboration forming a strong, structured and integrated research and innovation ecosystem with shared evidence, tools and methodologies cutting across sectors.
- The brain health research community at large benefits from and uses an improved comprehensive knowledge framework integrating the EU, national/regional data and information infrastructures to improve transnational research.
- People living with a brain disorder benefit from (i) a more timely, equitable access to accurate diagnosis and tailored care and treatment options in an innovative, sustainable and high-quality healthcare system that is well integrated with the research community, and from (ii) less discrimination and stigma, and social inclusion.
- Public and private actors, including civil society (e.g. Non-Governmental Organisations, charities), establish coordinated and efficient multi-stakeholder collaborations at national level in the EU and Associated Countries, allowing for more effective basic and clinical research and enhanced translation into tailored products and interventions.

Scope: The partnership should contribute from the research and innovation angle to priorities set in the "Healthier Together - EU Non-Communicable Diseases Initiative" (2022-2027), which includes a focus area on mental health and neurological disorders, as well as to the "Communication on a comprehensive approach to mental health" (COM(2023) 298 final).

The partnership should also contribute from the research and innovation angle to achieving the objectives of the Pharmaceutical Strategy for Europe, in terms of fulfilling unmet medical needs (numerous in the fields of neurological and mental disorders) and to ensuring that the benefits of innovation reach patients in the EU and Associated Countries. Moreover, it should support the objectives of the EU4Health Programme.

Additionally, the partnership should contribute from the research and innovation angle to the "Communication on the European Care Strategy" (for caregivers and care receivers; COM(2022) 440 final), which aims to ensure high quality, affordable and accessible care services for all ages. By fostering data sharing and boosting FAIR and open data, the partnership should also contribute to the implementation of the European Health Data Space (EHDS).

Thanks to its capacity to bring together different stakeholders (e.g. research funders, health authorities, citizens, healthcare providers, innovators, policymakers), the partnership will create a critical mass of resources to implement a long-term Strategic Research and Innovation Agenda (SRIA), based on the work of the Coordination and Support Action BrainHealth.

The co-funded European Partnership for Brain Health should be implemented based on the priorities identified in the SRIA and through a joint programme of activities ranging from coordinating and

funding transnational research to integrative activities aimed at structuring and enhancing the broader research and innovation ecosystem and facilitating the way research and innovation is carried out, and also delivering impact. Examples include (i) facilitating the sharing and analysis of data and samples, (ii) promoting harmonisation and standardisation efforts, (iii) providing input to shape the services provided by research infrastructures (based on the needs of the research community), as well as (iv) networking, training and dissemination activities.

It should be structured along the following main objectives:

- Strengthening collaboration, strategic alignment and global dialogue: engage and collaborate with key stakeholders, not only those participating in existing EU-supported brain research initiatives but also beyond them, whilst also seeking alignment with these and international initiatives, including other European partnerships.
- Jointly supporting research and innovation: launch joint transnational calls underpinning the brain health research and innovation priorities, as defined in the SRIA, and based on annual work plans. Calls include research calls, networking calls, and those that relate to ethical, legal and social/societal aspects.
- Facilitating the use of infrastructures and platforms in the EU and Associated Countries: improve access to and use of these infrastructures and platforms (e.g. ECRIN, EATRIS, EBRAINS, BBMR, EuroBioImaging, European Genomic Data Infrastructure, etc.), whilst also providing input for shaping the services for the brain health research and funding community. This also covers the facilitation of data sharing by boosting FAIR and open data and improving interoperability and harmonisation.
- Bridging with healthcare providers, the private sector, regulators, and policymakers: enable the translation of research results into accessible, tailored products, technologies, interventions and policies through collaborations, including with institutionalised European partnerships (e.g., Innovative Health Initiative).
- Empowering citizens, people living with brain disorders and patients, families and caregivers (including informal): enable them to be active in their health trajectories via the dissemination of good practices and scientific outputs, as well as trainings to engage them along the whole spectrum of the research process.
- Capacity building in research: support networking and training of scientists, healthcare practitioners, health policy experts, innovators and other professionals contributing to preserve and improve brain health.

The partnership is open to all EU Member States, as well as to countries associated to Horizon Europe and will remain open to third countries wishing to join. Importantly, the EU contribution will not be increased should countries join after signing of the grant agreement.

The partnership should include or engage with the following actors: (i) Ministries in charge of R&I policy, as well as national and regional R&I and technology funding agencies and foundations; (ii) Ministries in charge of health and care policy, as well as national and regional healthcare authorities, organisations and providers; (iii) academic researchers; (iv) research infrastructures; (v) patients organisations; (vi) industry; (vii) research and technology organisations; (viii) private sector; and (ix) charities.

The partnership may also encourage engagement with other relevant Ministries (e.g., related to employment, education, etc.) and research funders. It should involve other key actors from civil society and end-users, research and innovation community, innovation owners, health and care systems owners/organisers and health and care agencies.

The partnership should build on and go beyond existing and previous initiatives, including the ERA-NET actions under (i) the EU Joint Programme for Neurodegenerative Disease Research (JPND), (ii) the Network of European Funding for Neuroscience Research (NEURON), and (iii) the Human Brain Project (HBP, a FET Flagship project), as well as the digital research infrastructure EBRAINS, which was put in place by HBP, and the Coordination and Support Actions (CSAs) BrainHealth and European Brain Research Area (EBRA).

The partnership's governance structure should engage upfront the relevant actors to coordinate, steer and frame the research and innovation activities, and facilitate the use and uptake of the results. The governance should involve key stakeholders, including but not limited to the research and innovation community, patients and citizens, health and care professionals, formal and informal care organisations, and innovation owners. Transparency in governance should be secured (e.g. in calls, governing bodies, etc.).

To ensure coherence and complementarity of activities and leverage knowledge and investment possibilities, the partnership is expected to establish relevant collaborations with other Horizon Europe partnerships (institutionalised and co-funded) and missions, as set out in the working document on 'Coherence and Synergies of candidate European Partnerships under Horizon Europe' , as well as to explore collaborations with other relevant activities at EU and international level. The proposal should also elaborate on possible synergies with other EU programmes, including EU4Health and the Digital Europe Programme (DIGITAL). The Partnership should align with EU-wide initiatives on open access and FAIR data, including the European Open Science Cloud (EOSC).

To tackle the ambitious challenges, cooperation with international organisations, private sector and non-European institutions and experts may be considered. Participation of third countries is encouraged. Applicants should describe in their proposal the methodology for their collaboration and the aims they want to achieve with this kind of collaboration.

Proposals should pool the necessary financial resources from the participating national research programmes with a view to implementing joint calls for transnational proposals resulting in grants to third parties. Financial support provided by the participants to third parties is one of the activities of this action in order to be able to achieve its objectives.

When defining calls for proposals, this partnership needs to consider the effective contribution of social sciences and humanities (SSH) disciplines and the involvement of SSH experts, institutions as well as the inclusion of relevant SSH expertise, in order to produce meaningful and significant effects enhancing the societal impact of the related research activities. In addition, this partnership needs to integrate robust sex and gender considerations, applying an intersectional lens to investigate variations in mental, neurological and neurodegenerative conditions. This includes examining how characteristics such as gender, age, racial/ethnic background, and disability intersect to influence disease/disorder prevalence, prevention, and outcomes.

The expected duration of the partnership is seven to ten years.

Projects funded by the European Partnership for Brain Health will be strongly encouraged to participate in networking and joint activities with relevant projects at European and national levels.

2. Maladies infectieuses et résistances antimicrobiennes

HORIZON-HLTH-2025-01-DISEASE-03: Development of antibodies and antibody- derived proteins for the prevention and treatment of infectious diseases with epidemic potential

Budget total : 50M€

Budget par projet : 10M€ en lump sum

Type d'action : Research and innovation action

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination "Tackling diseases and reducing disease burden". To that end, proposals under this topic should aim to deliver results that are directed, tailored towards and contributing to all the following expected outcomes:

- The scientific and clinical communities have a better understanding of prophylactic and treatment options complementary to low molecular weight antiviral therapeutics for viruses with epidemic potential.
- The scientific and clinical communities have access to experimental antibodies and antibody-derived proteins for the prevention and treatment of emerging or re-emerging viral infections, as well as for further clinical investigation.
- Candidate antiviral therapies, including potentially those of broad spectrum are available for emerging and re-emerging viral infections, increasing therapeutic options for clinical deployment in case of an epidemic or pandemic.

Scope: As shown by the COVID-19 pandemic, infectious diseases remain a major threat to health and health security in the EU and globally. Viral disease emergence is expected to accelerate due to among other, climate change, and thus a proactive approach to the development of antiviral prophylactics and therapeutics in preparedness for future infectious disease outbreaks is needed. The availability of antibodies and antibody-derived proteins would provide a critical preparedness measure against future health threats, due to infectious disease epidemics or pandemics.

Proposals should exclusively pursue the development of existing antiviral and prophylactic and therapeutic candidates that are based on antibody and/or antibody-derived proteins targeting at least one of the priority viruses:

- Arenaviridae: Junin mammarenavirus, Lassa mammarenavirus
- Hantaviridae: Hantaan virus, Andes virus, Sin Nombre virus
- Poxviridae: Variola major
- Paramyxo: Hendra, Nipah virus
- Togaviridae: Venezuelan equine encephalitis virus

Proposals are expected to conduct preclinical studies of antibodies and antibody-derived proteins, prepare Good Manufacturing Practice (GMP) quality test batches and carry out first in human clinical

safety studies. Proposals should include a critical discussion of to what extent the antibodies and antibody-derived proteins would be expected to be amenable to production and distribution at an affordable cost and at a scale sufficient to meet demand in a pandemic.

Proposals should thus aim to diversify and accelerate the global prophylactic and therapeutic research and development portfolio for emerging and re-emerging viral infections, and to strengthen the leading role of the EU in prophylactic and therapeutic research and development.

Proposals may focus either on antibody or on antibody-derived proteins, or both.

Proposals should address all the following areas:

- If necessary, finalisation of the in vitro characterisation of the existing antibody and antibody-derived protein candidates with regard to target specificity, epitope recognised, and their ability to impair or inactivate viral functions.
- In vivo tests in at least one animal model or, if available in humanised immune system animal models, to demonstrate the protective function of the antibodies and antibody- derived therapeutics deemed sufficient for moving to first clinical trials.
- If requested by regulators as enablers for clinical studies, in vivo tests in a non-human primate model.
- Production of GMP quality test batches of the most promising candidates for antibodies and antibody-derived proteins in the EU or the European Economic Area.
- First in human clinical safety studies of the antibody and antibody-derived proteins, demonstrating a clear regulatory pathway for market authorisation. Attention should be paid to critical biological and social factors such as sex, age, ethnicity and disability.

Participation of third countries where viruses addressed in the proposal are endemic or where outbreaks have occurred or are ongoing is encouraged.

The participation of start-ups, micro, small and medium-sized enterprises (SMEs) is encouraged with the aim of strengthening their scientific and technological foundations, enhancing their innovation potential, and exploring possibilities for commercial exploitation.

Applicants are expected to engage with regulatory bodies in a timely manner to ensure adequacy of the actions from a regulatory point of view.

Proposals should advance research by leveraging already existing and emerging state-of-the-art research infrastructures such as those having contributed to the services developed under the ISIDORe project.

Applicants should provide details of their clinical studies in the dedicated annex using the template provided in the submission system. As proposals under this topic are expected to include clinical studies, the use of the template is strongly encouraged.

HORIZON-HLTH-2025-01-DISEASE-05: Support for the functioning of the Global Research Collaboration for Infectious Disease Preparedness (GloPID-R)

Budget total : 2M€

Budget par projet : 2M€ en lump sum

Type d'action : Coordination and support action

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination "Tackling diseases and reducing disease burden". To that end, proposals under this topic should aim to deliver results that are directed, tailored towards and contributing to some of the following expected outcomes:

- International research funders are supported by a dynamic and efficient secretariat in their coordination efforts for a rapid research response when a pandemic or a severe epidemic strikes.
- International research funders can rely on a tested framework underpinning a rapid and effective research response, and as such ensure stronger research preparedness and response for public health emergencies, including in cross-cutting areas such as data sharing, social science, clinical trial networks and others.
- Research funders, policymakers and the research community are well informed of the activities of the members of the Global Research Collaboration for Infectious Disease Preparedness (GloPID-R), both as a group and individually.

Scope: Recent history has illustrated the potential extent of threats posed by new or emerging infectious diseases, as well as the central importance of global collaboration and coordination to fight such international challenges. GloPID-R was established in 2013 for this reason, in response to a request for coordination by the Heads of International Research Organisations. GloPID-R now provides a widely recognised platform for infectious disease research funders to work together to better tackle severe epidemics such as Ebola or Zika, as well as global pandemics such as COVID-19.

GloPID-R enables coordination between funders and with relevant global actors such as the World Health Organization (WHO) or the Coalition for Epidemic Preparedness Innovation (CEPI); or promotes exchanges and synergies between funded researchers. The GloPID-R's regional hubs strategy fosters regional research priorities and funder engagement. The network is engaged among others in efforts to strengthen the coordination of clinical trial responses, to track research and evidence on diseases with pandemic potential, or to coordinate funding for cross-cutting research on pandemic preparedness.

Proposals should foresee administrative and technical support through a secretariat to maintain,but above all to support GloPID-R's continuous evolution for an optimal value added.

Proposals are expected to cover all the following activities:

- Provide administrative and organisational support to the Board of GloPID-R, in close collaboration with the European Commission;
- Provide strong scientific support through a transparent process on topics requested by the GloPID-R Board, independent scientific advisors or (working) groups;
- Facilitate the work of the GloPID-R working groups and scientific advisors, using earlier experience in research preparedness and response to infectious disease outbreaks;
- Manage fluid information dissemination and communication between the Board, Members, scientific advisors, working groups, enquiries, and outside stakeholders;
- Ensure strong external communications activities, e.g. through the website, newsletter, and social media;
- Submit an annual work plan to the Commission each year following the annual meeting of GloPID-R, taking into account the conclusions of the annual meeting;

- Ensure a high level of adaptability to respond to rapidly evolving situations, following the guidance of the GloPID-R Board.

HORIZON-HLTH-2025-01-DISEASE-01: Testing safety and efficacy of phage therapy for the treatment of antibiotic-resistant bacterial infections

Budget total : 45M€

Budget par projet : 15M€ en lump sum

Type d'action : Research and innovation action

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination "Tackling diseases and reducing disease burden". To that end, proposals under this topic should aim to deliver results that are directed, tailored towards and contributing to most of the following expected outcomes:

- Researchers and developers make the best use of the state-of-the-art knowledge and resources for an effective development of new treatment options for patients suffering from difficult-to-treat infections.
- Healthcare professionals and people living with difficult-to-treat infections are ultimately provided with the availability of clinically useful phage therapies.
- Regulators are provided with quantifiable, verifiable and replicable data on safety and efficacy of phage therapy for human use and move faster towards market approval of novel phage-based therapies against antimicrobial resistant infections.
- Citizens are engaged and informed on innovative phage-based treatments as alternative therapeutic options complementary to antibiotics.

Scope: Antimicrobial resistance (AMR) has been identified by the United Nations (UN) General Assembly as a health Emergency in 2016. AMR is contributing to morbidity and mortality increasing the burden for society and healthcare costs. This is due to a worrying increase on the number of bacteria resistant to antibiotic treatment, causing chronic and often life-threatening infections such as wound and urinary tract infections. The World Health Organization (WHO) lists AMR among the top 10 threats for global health and recognises that a lack of innovation is set to undermine antibiotic performance and health gains, with a major gap in the discovery of innovative antibacterial treatments.

Hence, there is an urgent need for the development of therapies to treat infections.

Bacteriophages (phages) represent a promising alternative or complement to antibiotics for the treatment of infections that do not respond to conventional treatment options. With the increase of AMR bacteria, both healthcare practitioners and innovators are expressing an increasing interest in the use of phages for the treatment of infections. As a result, the clinical use of phage therapy is expanding in the EU and beyond under different regulatory pathways, approaches and different conditions (e.g. magistral personalised phage preparations and fixed phage cocktails applied via compassionate use, named-patients based or expanded access programmes) despite a lack of large data on the efficacy of phage therapy for human use. So far, a few modest-sized randomised-controlled trials have been conducted providing indications for the safety and efficacy of the phage products, in

agreement with preclinical animal studies. However, they could not always prove the efficacy of phage preparations.

Therefore, proposals should aim to develop phage-based therapies to treat bacterial infections that do not respond to conventional treatment options. For this, applicants should carry out multicenter, multinational randomised controlled clinical trial (RCT) to generate scientific evidence demonstrating safety and efficacy of phage-based therapy as stand-alone or in combination with standard-of-care (such as antibiotic or other innovative non-antibiotic-based treatment) for the treatment of difficult-to-treat bacterial infections.

Both approaches for phage therapy, personalised phage preparations or ready-to-use phage cocktails, are in scope with the call. Innovative study design, aiming at better capturing and evaluating the full potential of the benefit of personalised phage therapy, e.g. using regularly updated phage preparations, is welcome.

The topic is open to any pathogen causing difficult to treat infections mainly due to AMR or to biofilms, for any clinical indication and applying phage treatment in any route of administration. Applicants are encouraged to address pathogens listed in the WHO Bacterial Priority Pathogens List.

Lessons learned from previous clinical trials that failed (e.g. PhagoBurn) should be considered for optimal study design, e.g. inclusions and logistics criteria, to favour success and conclusive results. The proposed trial should be designed with proper patient selection, diagnostic protocols (e.g. phagogram), production protocols (purification, stability, host selection, etc.) and treatment protocols (including dosage, repetition, duration, route of administration).

All available information about the characteristics of the phages to be used in the clinical trial should be provided (e.g. sequence, stability, targeted bacteria, registration in a phage bank or phage registry, etc.). Moreover, any additional indication of the use of phages for other applications than human use in the clinical trial (e.g. veterinary use, surface cleaning, food preservation) should be detailed in the proposal if available.

The use of computational modelling and/or artificial intelligence (AI) tools is encouraged to speed/optimise trial design, implementation and/or the analysis of large data. In the same way, the use of innovative in silico, in vitro or in vivo models to facilitate pre-clinical selection of phages to use in the clinical trial is welcome.

In their proposal applicants should describe how they take into account scientific advice or protocol assistance from the European Medicines Agency (EMA). In addition, they should provide a sound timeline on the trial protocol and a delivery date for the approval(s) from the regulatory body(ies) at 12 months from the start of the project.

Applicants should propose a clear exploitation pathway through the different necessary steps (research, manufacturing, regulatory approvals and licensing, Intellectual Property management, etc.) in order to accelerate marketing authorisation and uptake by the health systems.

The participation of start-ups, micro, small and medium-sized enterprises (SMEs) is encouraged with the aim of strengthening their scientific and technological foundations, enhancing their innovation potential, and exploring possibilities for commercial exploitation.

Proposals should adhere to the FAIR data principles, adopt wherever relevant, data standards and data sharing/access good practices, and apply good practices for GDPR compliant personal data protection.

Sex and gender-related differences should be addressed, where relevant. To ensure that the needs of patients living with chronic infections are adequately addressed and that there is public acceptability and confidence on innovative phage-based therapies, the involvement of patient and/or civil society representatives in all phases of the research and development process is strongly encouraged. For this, the topic requires the effective contribution of social sciences and humanities (SSH) disciplines and the involvement of SSH experts, institutions as well as the inclusion of relevant SSH expertise, in order to produce meaningful and significant effects enhancing the societal impact of the related research activities.

Applicants should provide details of their clinical studies81 in the dedicated annex using the template provided in the submission system. As proposals under this topic are expected to include clinical studies, the use of the template is strongly encouraged.

3. Santé publique et politiques de santé

HORIZON-HLTH-2025-03-STAYHLTH-01-two-stage: Improving the quality of life of persons with intellectual disabilities and their families

Budget total : 40M€

Budget par projet : entre 6 et 8M€ en lump sum

Type d'action : Research and Innovation Action

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination "Staying healthy in a rapidly changing society". To that end, proposals under this topic should aim to deliver results that are directed at, tailored towards and contributing to several of the following expected outcomes:

- Persons with intellectual disabilities and their families enjoy an improved quality of life, are empowered and have more independence through the support of innovative research.
- The scientific community develops innovative solutions - medical, technological, digital or others - to reverse and/or reduce the severity level of the intellectual disability as soon as possible, especially in children, improving the health and autonomy of persons with intellectual disabilities and relieving their carers.
- Policymakers, health and care services, patient organisations, funders, the scientific community, and other relevant bodies are informed of the research advances and best Intelligence Artificielle practices addressing the health and needs of persons with intellectual disabilities and help reduce the impact of those disabilities on individuals, their families and society as a whole.

Scope: The scope of this topic is set by the definitions provided by 'The international classification of diseases' - World Health Organization (WHO) ICD11 under '6A00: Disorders of intellectual development' and under '20: Developmental anomalies' including disorders of intellectual development, such as 'LD40: Complete trisomies of the autosome' and 'LD90: Conditions with disorders of intellectual development as a relevant clinical feature' .Moreover, the three types of autism with disorders of intellectual development (6A02.1, 6A02.3 and 6A02.5) under '6A02: Autism spectrum disorder' are also within the scope of this topic.

The focus of this topic is human-centred on the persons with long-term intellectual disabilities and their formal and informal carers, including families. The life expectancy of persons with intellectual disabilities has increased in the last 20 years, which makes it even more important to analyse the role of their families acting as informal carers (e.g. ageing parents).

The objective of this topic is to explore new ways to improve the quality of life of persons with intellectual disabilities and their families and to reduce to the maximum possible the negative impact of the disability in their daily lives from different perspectives, such as medical, technological, digital or others. A key element to improve their quality of life is to prevent the worsening of the disability or conditions originating it. Thus, research needs to look from different perspectives into finding the causes of the disease(s) originating the disability and/or reducing as much as possible its level of severity. Innovative solutions are needed in order to deliver medicines, diagnoses, treatments, protocols, technologies or digital solutions, etc. that can help in an early stage to prevent the worsening of the intellectual disability and/or related co-morbidities, reverse or reduce it, and to improve the autonomy of affected persons and relieve their carers.

Research actions under this topic should address several of the following areas:

- To properly diagnose as early as possible the disease(s) causing the intellectual disability or conditions worsening them, especially in the case of children, and paying attention to sex and gender-related differences and diagnostic biases.
- Deliver the necessary medical treatments, diagnoses, medicines, protocols, technologies, digital solutions, habilitation and/or rehabilitation services, etc. that can help preventing the worsening of the intellectual disability, reversing it or reducing its severity, while supporting the empowerment of the person with intellectual disabilities. Any health technology or medical intervention developed for human use must comply with the relevant regulatory requirements and be based on sound scientific evidence to ensure safety and efficacy.
- Tackle comorbidities or other disabilities that persons with intellectual disabilities may suffer from, with awareness of sex and gender-related differences.
- Provide evidence-based approaches for transitional care for young adults with intellectual disabilities, addressing also sex and gender-specific challenges and needs, the transition from paediatric to adult care being perceived as complex to navigate.
- Promote the empowerment among persons with intellectual disabilities and their caregivers. If applicable, with the support of assistive technologies and digital solutions, ensure optimal autonomy of persons with intellectual disabilities, facilitate and improve the treatment of persons with intellectual disabilities, and help also the family members and close carers to take better care of the person with intellectual disabilities. Such technologies must adhere to the relevant standards and be grounded in scientific evidence.
- Propose innovative solutions for high quality, accessible - including cognitively accessible - and affordable care services, to allow carers of persons with intellectual disabilities to better balance their work and family lives. The role of informal/unpaid carers, especially family members, is of key importance for persons with intellectual disabilities. For many persons with intellectual disabilities, the lack of care services and insufficient support for families and personal assistance undermines their quality of life and their rights and possibility to live as independently as possible.
- Develop innovative integrated care strategies - strengthening patient-centred care – to improve the Quality of Life of persons with intellectual disabilities of any age, and their families, paying special attention to persons with intellectual disabilities with the highest vulnerability because of their high dependency on carers (formal and/or informal), multiple

disabilities and need of adapted and special care (medical, social, educational and psychological dimensions).

- Develop guidelines in order to provide adequate support and training for caregivers, formal and informal, especially for those providing care for persons with intellectual disabilities and/or living with them, and also addressing the issue of prevention of and protection from violence since persons with intellectual disabilities are both vulnerable to violence and abuse and can be violent towards care givers and family members.

Applicants are encouraged to include patients, their families and carers in the different stages of the research. Likewise, it is encouraged to involve stakeholders from within and outside the intellectual disabilities sector, in particular policymakers and public authorities, citizens and civil society organisations, end-users and service providers.

This topic requires the effective contribution of social sciences and humanities (SSH) disciplines and the involvement of SSH experts, institutions as well as the inclusion of relevant SSH expertise, in order to produce meaningful and significant effects enhancing the societal impact of the related research activities.

All projects funded under this topic are encouraged to participate in networking and joint activities, as appropriate. These networking and joint activities could, for example, involve the participation in joint workshops, the exchange of knowledge, the development and adoption of best practices, or joint communication activities. Therefore, proposals are expected to include a budget for the attendance to regular joint meetings and may consider covering the costs of any other potential joint activities without the prerequisite to detail concrete joint activities atnthis stage. The details of these joint activities will be defined during the grant agreement preparation phase.

Projects are also encouraged to explore potential complementarities with projects funded under the Cluster 2 topic HORIZON-CL2-2025-01-TRANSFO-10: “Good practices for increased autonomy of persons with disabilities, including physical, mental, intellectual and sensory disabilities” are encouraged.

Applicants invited to the second stage and envisaging to include clinical studies should provide details of their clinical studies in the dedicated annex using the template provided in the submission system.

HORIZON-HLTH-2025-03-ENVHLTH-02-two-stage: Advancing knowledge on the impacts of micro- and nanoplastics on human health

Budget total : 40M€

Budget par projet : entre 7 et 8M€ en lump sum

Type d’action : Research and innovation action

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination “Living and working in a health-promoting environment”. To that end, proposals under this topic should aim to deliver results that are directed, tailored and contributing to most of the following expected outcomes:

- Environmental and health policies reducing exposure to micro- and nanoplastics and preventing their health impacts are supported with up-to-date scientific evidence, standards, tools and methodologies;
- Public authorities and the scientific community have access to FAIR data on realistic human exposures to micro- and nanoplastics and their impacts on human health based on real-world scenarios across living and working environments;
- Citizens are informed about the impacts of exposure to micro- and nanoplastics on health and adopt behaviours protecting health and reducing human impacts on the environment;
- Industry is supported in the assessment of products' safety and sustainability;
- Existing major knowledge gaps in the understanding of the health impacts of exposure to micro- and nanoplastics are filled and mitigation measures based on robust evidence are promoted;
- Public authorities and regulators are supported with evidence-based guidance to design health policies.

Scope: Plastics are an important material in our economy that are everywhere in our daily lives but can present negative environmental and health impacts. A significant amount of plastic ends up in the environment, degrading into micro- or nano-sized plastic particles that are defined as micro- or nanoplastics (MNPs). MNPs can be detected in both marine and terrestrial ecosystems worldwide in food, water, air and consumer products. These MNPs have been documented to accumulate in the human body into cells and tissues (e.g. liver, kidney, gastrointestinal track, placenta, testicles) and cause associated adverse biological effects (e.g. inflammatory response, geno-, cyto-, neuro- and nephron-, respiratory and reproductive toxicity). Exposure routes for MNPs into the human body can be through inhalation, ingestion and dermal contact and translocation of nanoplastics and small microplastics through tissues and organs can occur.

Furthermore, it has been documented that MNPs can cause additional harm by releasing specific chemical additives with potentially negative health impacts. However, because microplastics are an emerging contaminant and research on the causality between exposure to MNPs and health impacts is still at a relatively early stage, the evidence on the health risks of exposure to MNPs is scattered and numerous knowledge gaps still persist.

Research activities under this topic should strengthen the evidence on the impacts of micro- and nanoplastics exposure on human health, considering living and working environments and different exposure routes (inhalation, ingestion and dermal exposure). Proposals should focus on realistic concentrations of tested particles and exposures to a variety of sizes, shapes and chemical compositions of MNPs materials and advance in the comparability between studies.

Moreover, research activities should take into account recent policy developments, support relevant policy gaps and needs and support the work on standardisation of analytical methods.

More specifically, research actions under this topic should include several of the following activities:

- Increase comparability and reproducibility between studies by means of a better optimisation, validation and standardisation of the analytical methods, protocols and methodologies to collect MNPs in the environment and detect and quantify the exposure in the human body and in the environment;
- Study the causal mechanisms of action and pathways involved on molecular, cellular and organism level effects from exposure to MNPs;

- Improve the understanding of the drivers of toxicity and other adverse health effects of MNPs, using realistic environmental samples and considering varying sizes, shapes, concentrations and chemical compositions, and interaction with components in the environment;
- Develop suitable and (environmentally) relevant reference materials that can be used to improve robustness and comparability across laboratories;
- Develop better in-vivo, in-silico and in-vitro models, instruments and methods for risk and hazard assessment harmonised across various types of MNPs. These include long-term exposure and monitoring models, mimicking real-world scenarios and dosimetry and observational studies on humans and development of strategies to integrate experimental and in-silico data;
- Strengthen the existing knowledge on human exposure to micro- and nanoplastics through the development of human biomonitoring studies and the use of specific biomarkers and endpoints;
- Generate evidence on the long-term impacts of MNPs on human health, MNPs' fate and systemic effects through well-designed and robust systematic studies;
- Provide robust evidence on the exposures to MNPs at work: identify environments with highest concentrations and focus on improving approaches for assessment, prevention and mitigation of occupational exposures;
- Increase the understanding of the environmental routes of exposure to MNPs, considering real-life exposure routes;
- Propose mitigation measures to reduce population exposure to MNPs including collecting evidence on the health impacts of potential alternative materials developed to replace plastics;
- Gain better insights on the interactions between MNPs (and their additives) with other pollutants and/or biological agents and the combined impacts of these interactions on human health (considering also the understanding of individual toxicity effects);
- Gain better insights on the delivery mechanisms and study the elimination process of MNPs in the human body and the microbiome capacity to degrade (or accelerate degradation of) ingested MNPs;
- Promote exchange of knowledge and experiences across MS and policies and engage with regulators and public authorities to ensure suitability and further uptake of relevant results.

Gender and sex related differences should be addressed, where appropriate.

Applicants are encouraged to consider the use of experimental methods not using live animals,where relevant and allowing to obtain data of comparable validity.

This topic requires the effective contribution of social sciences and humanities (SSH) disciplines and the involvement of SSH experts, institutions as well as the inclusion of relevant SSH expertise, in order to produce meaningful and significant effects enhancing the societal impact of the related research activities. Proposals should adhere to the FAIR data principles and adopt wherever relevant, data standards and data sharing/access good practices.

Proposals could consider the involvement of the European Commission's Joint Research Centre (JRC) with respect to the value it could bring in providing an effective interface between research activities and regulatory aspects and/or in translating research results into harmonised test methods and strategies fit for regulatory purpose. In that respect, the JRC will consider collaborating with any

successful proposal and this collaboration, when relevant, should be established after the proposal's approval. Proposals should ensure that chemical monitoring including human biomonitoring data are shared in IPCHEM through involvement with the European Commission's Joint Research Centre (JRC), and/or in the future Common Data Platform for Chemicals, through involvement with the European Chemicals Agency (ECHA) or other relevant agency (such as the European Environment Agency - EEA) responsible forthe specific domain.

In order to maximise synergies and increase the impact of the projects, all proposals selected for funding from this topic will form a cluster and be required to participate in common networking and joint activities. Without the prerequisite to detail concrete joint activities, proposals should allocate a sufficient budget for the attendance of regular joint meetings and to cover the costs of any other potential common networking and joint activities. Guidance on the potential activities to be developed can be obtained by consulting the clusters of projects ongoing under the Environment, climate and health portfolio.

Applicants invited to the second stage should provide details of their clinical studies in the dedicated annex using the template provided in the submission system. As proposals under this topic are expected to include clinical studies, the use of the template is strongly encouraged.

HORIZON-HLTH-2025-01-DISEASE-06: Implementation research addressing strategies to strengthen health systems for equitable high-quality care and health outcomes in the context of non-communicable diseases (GACD)

Budget total : 20M€

Budget par projet : entre 3 et 4M€

Type d'action : Research and innovation action

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination "Tackling diseases and reducing disease burden". To that end, proposals under this topic should aim to deliver results that are directed, tailored towards and contributing to some of the following expected outcomes:

- Healthcare practitioners and providers in low- and middle-income countries (LMICs) and/or those in high-income countries (HICs) serving disadvantaged populations have access to information allowing to strengthen health systems for equitable high-quality care and health outcomes in the context of non-communicable diseases (NCDs).
- Public health managers and authorities have access to improved insights and evidence on how to decrease the fragmentation of care for patients living with NCDs and ensure continuity of care across all stages of disease progression, including prevention, risk reduction, and timely diagnosis of NCDs. They use this knowledge to design policies to reduce health inequities and to promote equitable health outcomes.
- Researchers, clinicians and authorities have an improved understanding how the proposed interventions for strengthening health systems for equitable high-quality care and health outcomes in the context of NCDs could be adopted in LMICs and/or disadvantaged populations of HICs setting, taking into account specific social, political, economic and cultural contexts.

- Communities, local stakeholders and authorities are fully engaged in implementing and taking up interventions that strengthen health systems for equitable high-quality care and health outcomes in the context of NCDs and thus contribute to deliver better health, improve quality of life across the life course and extend healthy life expectancy.

Scope: The European Commission is a member of the Global Alliance for Chronic Diseases (GACD). The GACD specifically addresses NCDs and supports implementation science to improve health outcomes. This topic is launched in concertation with the other GACD members (international funding agencies) and aligned with the 10th GACD call.

Health systems in many countries have not kept pace with the rapid emergence of NCDs that require costly long-term care and treatment. Resilient, fit for purpose health system should provide high-quality, safe, equitable, accessible healthcare, that reflects the needs of the population, and enables the integration of healthcare across the care continuum, encompassing prevention, screening, diagnosis and long-term management of NCDs. While health systems across the world struggle with these challenges, this is a particular problem in LMICs that have relatively overburdened, poorly resourced and fragile health systems that struggle to cope with the burden of NCDs. Health inequalities (e.g. linked to geographical location, socioeconomic status, sex and/or gender) are often accentuated by structural and/or systemic weaknesses such as lack of staff and appropriate medicines.

The increasing burden of NCDs on healthcare systems has spurred a greater interest in exploring strategies to tackle these conditions, including a move from a healthcare system focused on disease and hospital-based care, to a more holistic model, involving communities and primary care, and focused on maintaining health. These include interventions addressing the integration of and access to care, screening, access to medicines and technologies, task shifting and digital health interventions. Implementing these strategies while retaining a focus on equity is challenging and health systems need to account for geographical disparities as well as reach communities that have traditionally suffered health inequalities. Equity in health requires that resources and processes are designed to promote equalisation of health outcomes for populations experiencing health disparities, to ensure similar health outcomes for all of society.

Evidence for how to strengthen health systems to improve services and ensure equitable health outcomes is emerging, mostly from research in HICs. However, implementing equity-oriented interventions for transformation and/or strengthening of health systems remains challenging and largely unexplored in underserved populations, especially in LMICs. Providing evidence on implementation strategies that can enable effective adaptation and scaling of programmes will be critical to improving survival and quality of life as well as reducing disability, the burden of caretaking on (typically female) family members and costs of healthcare falling on households.

This implementation research topic is therefore focused on strategies to support health system transformation and/or strengthening using evidence-based interventions in the context of NCDs that can be adapted to and implemented in LMICs and/or disadvantaged populations experiencing health disparities in HICs to encourage equitable health outcomes.

The proposed implementation research should be focused on one or more evidence-based interventions (or complex interventions) focused on building equity-orientated health systems change to tackle the growing burden of chronic conditions, including NCDs. The choice of intervention(s) and provision of existing evidence of the intervention's effectiveness, cost- effectiveness, sustainability, scalability and potential for long-term health and other impacts should be justified (and in what context this evidence has been generated). As the evidence underpinning strategies to transform and/or strengthen health systems in the context of NCDs is still emerging, particularly in LMICs, a

limited period of testing the effectiveness of an intervention that the applicant's team has adapted for local implementation is therefore usually appropriate.

Applicants should explore the implementation of proposed intervention(s) for a selected study population(s) taking into account the unique social, political, economic, and cultural context(s) in which the study will take place. Applicants should justify why any adaptation will not compromise the known effectiveness of the selected intervention(s).

Proposals should address all the following activities:

- Provide a research plan using validated implementation research frameworks or hybrid design research;
- Have an appropriate strategy for measuring implementation research outcomes and real-world effectiveness outcomes and indicators. Other health or non-health outcome measures, especially those identified as important by patient participants and/or critical for advancing Universal Health Coverage (UHC), are also welcome;
- Specifically address health equity and the principles of UHC;
- Engage an appropriately expert and skilled research team which can ensure a suitable multidisciplinary approach and that demonstrates equitable partnership and shared leadership between HIC-LMIC, and/or non-Indigenous-Indigenous members of the project team and external stakeholders through a clear governance strategy;
- Provide a stakeholder engagement strategy with evidence of support/engagement from key stakeholders for delivering patient-centred care;
- Ensure that project partners are engaged from the beginning to contribute to the sustainability of the intervention after the end of project. Proposals should demonstrate sustainability of the strategy, beyond the lifespan of the project;
- Provide opportunities for implementation research capacity building for early career researchers and team members from lower resourced environments, such as LMICs or disadvantaged communities;
- Ensure meaningful involvement of early career team members, including at least one early career member as a co-investigator.

The study population may include the general population, people with one or more existing NCDs, those currently without NCDs, or a combination of both. The study population may also include patients with NCDs and chronic infectious disease(s) (e.g., studies that focus on integrating NCD management into an HIV or tuberculosis clinic). With regard to NCDs, applicants are encouraged to explore any chronic non-communicable condition (or combination of conditions), including mental health disorders, neurological disorders and sleep disorders.

Proposals are expected to use an appropriate implementation research design and frameworks for feasibility studies, cluster randomised control trials (cRCTs), before and after studies, and additional implementation science classifications of study designs (e.g. hybrid designs).

Applicants are not limited to use any particular design, however a validated implementation research framework should underpin the study.

Proposals would be expected to generate evidence that is of direct relevance to policymakers, communities and practitioners. Also, proposals will require a strategy to include the relevant policymakers, local authorities, as well as other stakeholders such as community groups, or other individuals or organisations involved in the implementation of the intervention, with co- creation from

the development of the project through to the implementation knowledge translation phase. Applicants should also provide a clear plan for continuing to engage with stakeholders.

Stakeholders also include patients, their family members and carers. Their contributions should be nurtured through meaningful engagement from the outset, not only as participants in the research undertaken. Patient engagement throughout the research project is critical to developing patient-centred models of care.

All stakeholders should be engaged at every stage of the research project, from initial ideation of research questions, throughout the duration of the project, and afterwards during the knowledge translation phase. It is also important to include stakeholders who can help sustain the project's implementation, facilitate scale up, and use the knowledge generated from the project after the grant ends.

Poverty, racism, gender inequality, ethnic discrimination, and other inequities are directly associated with reduced potential for equitable access to quality care. Proposals should consider the social determinants of health and discuss their potential impact on the effective implementation of the intervention(s). If there is a focus on a particular population (e.g., gender, race and/or ethnicity), then the reason for this should be justified.

In order to promote health equity, proposals should aim to address differences in intervention access, uptake, and effectiveness in socially disadvantaged groups and develop strategies for reducing inequities. To facilitate this process at the data analysis stage, studies should be designed to address such differences. At a minimum, studies should capture and disaggregate data on sex and/or gender differences. If feasible, a plan for capturing intersectional impacts on health outcomes should be included in the analysis strategy.

This topic requires the effective contribution of social sciences and humanities (SSH) disciplines and the involvement of SSH experts, institutions as well as the inclusion of relevant SSH expertise, in order to produce meaningful and significant effects enhancing the societal impact of the related research activities.

All projects funded under this topic are strongly encouraged to participate in networking and joint activities, including internationally, as appropriate. These activities could, for example, involve the participation in joint workshops, the Annual Scientific Meetings of the GACD, the exchange of knowledge, the development and adoption of best practices, or joint communication activities. Therefore, proposals are expected to include a budget for such activities and may consider covering the costs of any other potential joint activities without the prerequisite to detail concrete joint activities at this stage. The details of these joint activities will be defined during the grant agreement preparation phase.

Applicants envisaging to include clinical studies118 should provide details of their clinical studies in the dedicated annex using the template provided in the submission system.

HORIZON-HLTH-2025-02-DISEASE-02: European partnership fostering a European Research Area (ERA) for health research (Phase 2)

Budget total : 77M€

Budget par projet : entre 77M€ en lump sum

Type d'action : Programme Co-funded Action

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of Destination "Tackling diseases and reducing disease burden". To that end, the proposal under this topic should aim to deliver results that are directed, tailored towards and contributing to all the following expected outcomes:

- Based on a trusted governance and effective working modalities, research funders, health policymakers and the research community work together in order to identify and prioritise topics of common interest and European benefit ;
- Research funders and policymakers support the generation of knowledge related, but not limited, to cardiovascular diseases, prevention and public health, diet related diseases and nano medical technologies, and have access to and make use of the evidence on the benefits and drawbacks of health interventions, in particular for optimising clinical management, patient safety, personalised medicine (coordinating with the European Partnership for Personalised Medicine) and avoiding overtreatment;
- In addition to the well-established regular Joint Transnational Calls in the area of pre- clinical research, research funders and policymakers use the funding scheme developed in the Phase 1 of the European partnership fostering a European Research Area (ERA) for health research (ERA4Health) to support testing of health interventions in the clinical setting at European level. Therefore, the research community, independently from private interest, can conduct large-scale multi-country Investigator-Initiated Clinical Studies (IICSs) of various health interventions addressing important public health needs in a seamless way, effectively addressing known challenges and obstacles related to, for example, appropriate study design, ethics (including special patient groups), regulatory and institutional approvals, patient recruitment, management of informed consent, as well as, biobanking of human samples;
- Public health research systems in the ERA are more effective and integrated. Utilisation of health services, preventative measures, technologies, tools and digital solutions are more cost-effective;
- Health and care authorities, policymakers and other stakeholders use the research results to develop evidence-based strategies and policies, and deploy good practices to European countries and regions;
- Patients and citizens are more knowledgeable about disease threats and contribute to a patient-centred decision-making process, assuring better adherence to knowledge-based disease management strategies and policies;
- Countries cooperate better and use context-specific knowledge and evidence to make their health and care systems more sustainable and resilient with respect to upcoming needs and crises (complementary with other current and future co-funded European Partnerships with which strong links will be established).

Scope: There is a need for health research at the EU and Associated Countries level to be more efficient in delivering safer, better and higher-quality solutions for prevention, detection, diagnosis, treatment, and management of diseases, as well as providing better and equal access and affordable healthcare systems to the citizens. Additionally, the high quality of evidence generated by the large multi-country clinical trials comparing to fragmented national or regional efforts confirmed the added value of multinational collaboration, supported by multinational funding schemes. In this regard, a European partnership proposing a new model for impactful multinational collaborations in funding health research is a key initiative to play a central role in addressing public health needs.

ERA4Health - "Fostering a European Research Area for Health Research" - (Grant Agreement: 101095426) is a co-funded European Partnership in health research that aims to increase European transnational collaborative research funding by creating a funding body for joint programming in priority areas addressing European public health needs. It started in November 2022 and brings together 33 entities from 22 countries from the EU as well as Associated and Third countries. During Phase 1 (first 2 years), the main activities of the ERA4Health consortium were:

- Organisation of 4 Joint Translational Calls (JTCs) focused on prevention and public health, nutrition and lifestyle-related diseases, cardiovascular diseases and nanomedicine;
- Analysis of challenges and bottlenecks for investigator-initiated clinical research in the EU and Associated Countries, preparation of the supporting framework and a launch of a pilot JTC on multi-country IICS;
- Developing collaboration on transversal activities, including for instance Responsible Research and Innovation guidelines, enhancing the ERA and health ecosystem, capacity building, patient safety, etc.

Taking into account that the present action is a continuation of the topic HORIZON-HLTH- 2022-DISEASE-03-01 "European partnership fostering a European Research Area (ERA) for health research" and foresees an amendment to the existing grant agreement, the proposal should present the additional activities (including additional partners) to be covered by the award primarily in terms of grant agreement revisions.

The award of a grant to continue the Partnership in accordance with this call should be based on a proposal submitted by the coordinator of the consortium funded under HORIZON-HLTH- 2022-DISEASE-03-01 "European partnership fostering a European Research Area (ERA) for health research" and the additional activities (which may include additional partners) to be funded by the grant should be subject to an evaluation. This evaluation should take into account the existing context and the scope of the initial evaluation as relevant, and related obligations enshrined in the grant agreement.

In this context, based on the funding scheme to support non-commercial clinical research developed during Phase 1, the main activities of the ERA4Health partnership in Phase 2 will mostly focus on additional JTCs on multi-country IICS in well-defined priority areas. In addition, the partnership's activities initiated in Phase 1 will also be continued in Phase 2. The unique composition of the consortium gathering national funders with their competency and experience in funding health research, and links to respective ministries of research and/or health in their home countries or regions guarantees successful continuation of the current partnership via this non-competitive call under an Article 24(2) Horizon Europe Regulation action that allows for the addition of new activities to existing grant agreements (also including new additional partners where relevant).

Phase 2 will benefit from the already established effective governance mechanism to achieve the following additional objectives:

- Bringing together different stakeholders (e.g. research funders, health authorities, health and care institutions, innovators, policymakers), to update and implement the Partnership's long-term Strategic Research and Innovation Agenda that should reflect more extended focus on multi-country IICS in the EU and Associated Countries.
- Using the novel funding mechanism developed during Phase 1, to enlarge the Partnership's activities related to non-commercial clinical studies, including identification of specific topics, pooling of funding, and launching JTCs for EU- and Associated Countries-wide multi-country IICSs on various health interventions addressing important public health needs.

- To continue providing support and building capacity, in particular in conducting multi- country IICSs at European scale.

All types of clinical studies falling under the Clinical Trials Regulation (EU) 536/2014, including low-interventional trials (e.g. pragmatic trials to optimise treatment), may be supported by this Partnership. In particular, proposed multi-country IICSs should i) establish new indications of a given existing health intervention for conditions where alternative solutions do not exist or are sub-optimal (repurposing); ii) optimise or develop new, personalised care pathways (avoiding overlaps with activities of the European Partnership for Personalised Medicine); iii) support the development of new health interventions with clear relative clinical efficacy/effectiveness compared to existing alternatives (including preventative measures); iv) accelerate the uptake of new interventions by healthcare systems.

Support by European research infrastructures, required to perform multinational clinical studies at scale, will, in particular, build on the asset of existing research infrastructures, such as the European Clinical Research Infrastructure Network (ECRIN) for sponsor-delegated activities related to implementation of clinical studies, and Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) for the management of biosamples and linked data that are generated under the studies.

Through pooling existing resources, eliminating redundancies and reducing fragmentation, the implementation of multi-country IICSs supported by this Partnership will benefit from better access to a high number of study participants/patients, medical expertise and facilities, enhanced methodological standards and shared costs, tools and procedures. Additionally, large-scale IICSs generate data on safety and effectiveness of a health intervention, often in real-world settings. They thus provide evidence to answer questions that clinicians face in their day-to-day practice in order to optimise the clinical management of patients beyond the context of marketing authorisation application for medicinal products. All these aspects will contribute to generate robust and reliable clinical evidence, increase the potential for broad implementation of research outcomes; prevent duplication of research efforts and allow broad uptake by health systems.

In the context of new activities of Phase 2, this Partnership will be open to public funders of health research at both national and regional levels in the Member States, countries associated to Horizon Europe and to other health research funders such as philanthropic organisations.

Additional, special attention should be placed on inclusion or engagement with the following actors:

- Ministries in charge of R&I policy, as well as national and regional R&I and technology funding agencies and foundations;
- Ministries in charge of health and care policy, as well as national and regional health and care authorities, organisations and providers.

The Partnership may also encourage engagement with other relevant Ministries and research funders. It will involve other key actors from civil society and end-users, research and innovation community, innovation owners, health and care systems owners/organisers and health and care agencies.

Cooperation with international organisations, and non-European institutions and experts may be considered. Participation of third countries is encouraged. The commitments to the partnership of entities not eligible for funding will not be counted towards the calculation of the EU funding to the partnership. Third country applicants should describe in their proposal the modalities for their collaboration and the aims they want to achieve with this kind of collaboration.

The proposal should pool the necessary financial resources from the participating research programmes with a view to implementing joint calls for transnational proposals resulting in grants to third parties. Financial support provided by the participants to third parties is one of the primary activities of this action in order to be able to achieve its objectives.

When defining calls for proposals, this partnership needs to consider sex and gender-related differences and it needs to consider the effective contribution of social sciences and humanities (SSH) disciplines and the involvement of SSH experts, institutions as well as the inclusion of relevant SSH expertise, in order to produce meaningful and significant effects enhancing the societal impact of the related research activities.

The expected duration of Phase 2 of the partnership should not exceed nine years.

4. Biotechnologies et innovations thérapeutiques

HORIZON-HLTH-2025-01-TOOL-05: Boosting the translation of biotech research into innovative health therapies

Budget total : 80M€

Budget par projet : entre 4 et 8M€

Type d'action : Research and Innovation Action

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination "Developing and using new tools, technologies and digital solutions for a healthy society". To that end, proposals under this topic should aim to deliver results directed towards and contributing to all the following expected outcomes:

- Healthcare providers, researchers and patients get faster access to innovative therapies.
- The European Union benefits from more clinical trials being conducted with new biotech therapeutic approaches.
- The competitiveness of small and medium-sized enterprises (SMEs) from the EU and Associated Countries within the health biotech sector is strengthened.

Scope: The Commission Communication 'Building the future with nature: Boosting Biotechnology and Biomanufacturing in the EU' 192 has recently identified research and technology transfer to the market as a major challenge for the biotechnology sector. This topic aims to speed up the development of innovative biotechnology-based therapies by supporting the initial phases of clinical research. SMEs play a key role in the EU's potential to innovate, with most biotechnology-derived drugs in development being progressed by SMEs and small biotech companies. However, transitioning from drug discovery and development stages to approved products requires substantial investment and sufficient resources in different areas (e.g., manufacturing, clinical trial management, regulatory affairs, etc.), with the time needed for clinical development often exceeding 10 years 193 . This topic targets collaborative multidisciplinary consortia of SMEs, academics, clinicians and research organisations bringing together the necessary expertise to launch the clinical development of novel biotechnology- derived therapeutics. Collaboration with the relevant European research infrastructures is encouraged. This topic does not address the full clinical development needed to bring products to market but aims to support the critical transition phase from preclinical to clinical

development by supporting the early clinical phases. A non-exhaustive list of biotechnology- derived therapies in scope include monoclonal antibodies, (therapeutic) vaccines, recombinant biomolecules, Advanced Therapy Medicinal Products (ATMPs), nano-based drugs, RNA therapies etc. Whole blood, blood components and other substances of human origin are not within the scope of this topic.

Proposals submitted under this topic should include all the following elements :

- A Clinical study either phase I, II or I/II depending on the appropriate stage of development.
- The proposal should convincingly demonstrate a significant economic potential of the final product(s) for the Single Market.
- A clearly defined exploitation plan, with a detailed proposed route to commercialisation, description of the intellectual property ownership and benefit for the SME(s). The plan should include an anti-shelving strategy, commercial forecasts for the product sales & revenue, and strategies for follow-up financing as well as market authorisation. The exploitation strategy should envisage a first deployment in the EU.
- Justification of the patient populations that will benefit directly from the development of the therapies. Clinical indications where potentially large patient populations could benefit will be favoured.

The maximum project duration should not exceed four years.

Applicants should provide details of their clinical studies194 in the dedicated annex using the template provided in the submission system. As proposals under this topic are expected to include clinical studies, the use of the template is strongly encouraged.

HORIZON-HLTH-2025-01-IND-01: Optimising the manufacturing of Advanced Therapy Medicinal Products (ATMPs)

Budget total : 40M€

Budget par projet : entre 6 et 8M€

Type d'action : Innovation Action

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination "Maintaining an innovative, sustainable, and competitive EU health industry". To that end, proposals under this topic should aim to deliver results that are directed, tailored towards and contributing to most of the following expected outcomes:

- Academic and industrial developers advance processes that support the timely and robust development of Advanced Therapy Medicinal Products (ATMPs);
- Manufacturers integrate improved technologies/processes (including Artificial Intelligence solutions), analytic tools, methods including non-clinical methods and assays for more flexible manufacturing of ATMPs;
- Healthcare providers, researchers and patients get faster access to ATMPs with demonstrated health benefits for unmet medical needs;
- Companies in the EU and Associated countries get a better market position in the field of ATMP manufacturing and improve their knowledge on how to advance process improvements;

- The EU and Associated countries lay the foundations for academic centres of excellence in ATMPs

Scope: New pioneering treatments called Advanced Therapy Medicinal Products (ATMPs), including cell and gene therapies, are at the cutting edge of medicines discovery. Owing to their precise nature, ATMPs embody personalised medicine and reflect a shift in medicine towards potentially one-time curative therapies instead of chronic therapies that mainly cure the symptoms but not the underlying cause of diseases.

ATMPs have undergone important technological advancements that are improving their efficacy, precision, scalability, and safety. Additionally, the disease focus of ATMPs is likely to shift further from rare diseases to more common conditions with larger patient populations. However, the development and manufacturing of ATMPs still faces important challenges, such as long development times, expensive manufacturing processes and a fragmented and dispersed biomanufacturing landscape.

The topic focuses on addressing the challenges of ATMP manufacturing, the need for highly specialised equipment and facilities, including in-process quality control and validation tests, scaling up and batch-to-batch reproducibility, whilst maintaining the efficacy of an ATMP product during the manufacturing process and/or the transition from centralised to decentralised manufacturing.

This topic aims to optimise the ATMP production where the general manufacturing process for a given medicinal product has already been established but has not been sufficiently optimised for its scale-up. Collaboration is crucial to refine the manufacturing of ATMPs, emphasising advancements in processes - including leveraging the potential of digital tools and advanced sensors -, fostering standardisation and enhancing quality controls for more efficient production and deployment of these innovative therapies, ideally covering the entire manufacturing lifecycle.

The proposals should address all the following activities for only one chosen category of ATMP as defined by Regulation 1394/2007 per proposal:

- Design an improved manufacturing process for ATMPs by:
- Exploring the potential of platform technologies in manufacturing, quality control, non-clinical or clinical testing;
- Integrating either computational modelling, automation, robotics or digital/Artificial Intelligence solutions with meaningful and measurable impact;
- Verify the improved performance of the developed process, in comparison to established ones.
- Demonstrate a reduction in the timeframe and costs of manufacturing while maintaining product quality and standardisation.
- Demonstrate the translatability, scalability, and robustness of the process suitable for the flexible manufacturing (centralised or decentralised) and deployment of ATMPs by important stakeholders in a patient-centric manner, including the medical community and hospitals.
- Assess the process and methods developed for their regulatory validity and utility (for example standardised assays including for potency), taking into consideration the potential regulatory impact of the results and, as relevant, develop a regulatory strategy for generating appropriate evidence as well as engaging with regulators in a timely manner.
- Promote green and sustainable industrial production and minimise environmental impact.

Participation of small and medium-sized enterprises (SMEs) is strongly encouraged and proposals should include a commitment for first deployment in the EU.

Where relevant, proposals are warmly invited to liaise with the Coordination and Support Action (CSA) project JOIN4ATMP, in view of creating complementarities and potential synergies.

The Joint Research Centre (JRC) may participate as a member of the consortium selected for funding. Proposals should consider the involvement of the European Commission's JRC regarding its experience in this field and with respect to the value it could bring in providing an effective interface between research activities and pre-normative science as well as strategies and frameworks that address regulatory requirements. In that respect, the JRC will consider collaborating with any successful proposal and this collaboration, when relevant, should be established after the proposal's approval.

Applicants envisaging to include clinical studies should provide details of their clinical studies in the dedicated annex using the template provided in the submission system.

HORIZON-HLTH-2025-01-IND-02: Digitalisation of conformity assessment procedures of medical devices and in vitro diagnostic medical devices

Budget total : 4M€

Budget par projet : 4M€

Type d'action : Coordination and Support Action

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination "Maintaining an innovative, sustainable, and competitive EU health industry". To that end, proposals under this topic should aim to deliver results that are directed, tailored towards and contributing to all the following expected outcomes:

- Device developers and manufacturers have access to digitalised conformity assessment procedures. These procedures will become more efficient, less onerous, and more predictable, which will reduce costs and shorten the time to market access;
- Device developers and manufacturers, in particular small and medium-sized enterprises (SMEs), can direct a larger part of their resources towards the research and development of innovative devices;
- Regulators adopt digitalisation in their conformity assessment procedures thus facilitating device development.

Scope: The regulations on Medical Devices (MDR) and In Vitro Diagnostic Medical Devices (IVDR) have introduced stricter regulatory requirements in view of ensuring a high level of patient safety and public health. While the positive impact on patient safety and public health is well recognised by the various actors in the field, the implementation of the new regulatory requirements still remains a challenge for manufacturers. SMEs face particular challenges as they have limited resources to adapt to the new framework. One of the main issues reported by manufacturers is the complexity and perceived unpredictability of the conformity assessment procedure involving a Notified Body (NB).

The Medical Device Coordination Group (MDCG) assists the Commission and the Member States in ensuring a harmonised implementation of the MDR and IVDR, notably through the development of guidance and templates. Notably, the conformity assessment procedures are still based on continuous exchange of highly complex technical documentation in an electronic format (e.g., pdf or excel files) between the key actors of NBs and manufacturers, requiring several iterations between them. Further digitalisation of this process (from document to data-driven processes) can bring greater efficiency, accuracy, and transparency and lead to a more predictable and harmonised assessment process. This

is expected to reduce the administrative burden as well as certification timelines and facilitate the conformity assessment procedure for manufacturers, particularly SMEs. In turn, this will contribute to maintaining the EU as a business-friendly environment for all manufacturers, which will ultimately benefit patients. For example, digitalisation can lead to simplification through the reduction of administrative burden, use of a single-entry point for all exchange of information. If relevant, applicants may liaise with an ongoing study on supporting the monitoring of the availability of medical devices in the EU market202. Potential improvements related to digitalisation can include pre-defining mandatory data elements, the possibility of getting alerts on whether data is complete, the identification of missing parts and inconsistencies and a reduction of error rates in this regard.

Overall improved communication would be anticipated with digitalisation.

Any actions as part of the proposal will be performed under the current regulatory framework and will not involve changing MDR/IVDR requirements. Proposals should present a major step towards digitalisation in Europe and Associated Countries. Governance of a potential IT infrastructure developed in Europe and Associated Countries is outside the scope of the topic.

The proposals should cover all the following points:

- All steps of the MDR/IVDR procedures, from manufacturer's preparation of technical documentation and other pre-application activities for certification to issuance of a MDR/IVDR certificate by a NB;
- All actors involved in the conformity assessment procedure, including manufacturers, NBs, EU reference laboratories, expert panels of medical devices, as well as agencies involved in the consultation activities;
- A good representation of different NBs, including representation from small and large NBs, public and private NBs and a representative mix focusing on medical devices and in vitro diagnostic medical devices. The proposal should put a strong focus on consensus building activities between the different stakeholders involved.

The proposals should address all the following activities:

- Feasibility study
    - Review existing initiatives aimed at digitalising MDR/IVDR conformity assessment procedures, or part thereof, and investigate digitalisation of conformity assessment/approval procedures for devices in other jurisdictions (e.g., US Food and Drug Administration). Consider lessons learned from digitalising conformity assessment procedures in other areas than medical devices.
    - Examine basic processes/workflows established by individual NBs.
    - Identify main steps of the conformity assessment procedure to be digitalised, actors involved, and essential elements and requirements to be considered prior to digitalisation.
    - Collect and analyse feedback from main stakeholders on challenges and feasibility of the digitalisation process, identify interoperability with existing workflows used by manufacturers and/or NBs.
    - Determine technical specifications required for the digitalisation as well as the possible options regarding digital transformation platforms.
    - Analyse facilitating factors, main challenges, possible solutions and required resources
- Pilot

    - Develop a pilot for the whole or part of the MDR/IVDR conformity assessment procedure, including Key Performance Indicators (KPI). This will involve collaboration with relevant stakeholders, including NBs, manufacturers, the European Commission and other involved parties.
    - Develop a dedicated platform to run the pilot or identify an existing platform suitable for the pilot.
- Roadmap towards digitalisation
    - Based on the lessons learned from the pilot, identify different steps to scale-up the pilot in order to digitalise MDR/IVDR conformity assessment procedures, or part of them. Identify associated challenges and possible solutions to address these.
    - Present a roadmap to the piloted approach, including possible alternatives, covering actors involved and resources needed.

HORIZON-HLTH-2025-01-IND-03: Facilitating the conduct of multinational clinical studies of orphan devices and/or of highly innovative ("breakthrough") devices

Budget total : 40M€

Budget par projet : entre 6 et 8M€

Type d'action : Research and Innovation Actions

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination "Maintaining an innovative, sustainable, and competitive EU health industry". To that end, proposals under this topic should aim to deliver results that are directed, tailored towards and contributing to all the following expected outcomes:

- Healthcare providers increase their hands-on experience regarding the clinical use of orphan devices and/or of highly innovative ("breakthrough") devices and get timely access to such devices with demonstrated clinical benefits;
- Developers and manufacturers collect and obtain scientific evidence on their proposed intervention/ approach with the device under investigation;
- Patients benefit from the development, studies and use of orphan devices and/or of highly innovative ("breakthrough") devices;
- Companies in the EU and associated countries get a better market position in this field and improve their knowledge on how to conduct multinational clinical studies for these devices.

Scope: The focus of this topic is on multinational clinical studies of orphan devices and/or of highly innovative ("breakthrough") devices, including digital and Artificial Intelligence (AI) based tools and techniques.

The emphasis within rare disease research and innovation has predominantly centred on pharmaceuticals, leaving a noticeable gap in the support for developing orphan devices. Orphan devices are specifically intended for use in rare diseases or conditions or in specific indications for rare cohorts of patients with an otherwise non-rare disease or condition. As, by their nature, orphan devices are intended for use in a small number of individuals each year, often infants and children, generating clinical data within an appropriate period of time and conducting clinical investigations is especially challenging due to low patient recruitment volumes.

Besides orphan devices, also highly innovative ("breakthrough") devices are in the scope of this topic if they are expected to provide major clinical benefits for the treatment, diagnosis or prevention of a life threatening, seriously debilitating or serious and chronic disease or condition, regardless of whether they target small patient populations. Highly innovative ("breakthrough") devices aim to address unmet medical needs. 'Unmet medical needs' should be understood as a condition for which there exists no satisfactory method of diagnosis, prevention or treatment in the EU or, even if such a method exists, in relation to which the device concerned will be of major advantage to those affected. Those may include devices using digital tools and AI based technologies.

Developers of such devices often face challenges to generate clinical data in the pre-market phase in a timely manner.

Time and cost of clinical data collection can adversely affect public health by significantly delaying the availability of devices needed to treat or diagnose rare diseases or conditions or that may improve patient care or public health. Many devices are used off-label to respond to this unmet need. Nonetheless, a high level of clinical evidence based on thorough clinical data is needed to ensure patient safety.

Clinical development strategies for implementing multinational clinical studies have the potential to offer improved efficiency and to reach larger patient samples. Challenges may arise from the potential uncertainty regarding how regional disparities in regulatory, clinical, business, ethical and cultural practices may affect study design, conduct, data interpretation and various other outcomes.

This topic targets those challenges by supporting multinational studies aiming to gather pre- or post-market clinical data to demonstrate the device's safety and performance (including determination of any undesirable side-effects and their acceptability when weighed against the expected clinical benefits).

The proposals should demonstrate that they address all the following activities for a device that is an orphan device or a highly innovative "breakthrough" device (or both), at any point of the pre-or post-market stage, including the development stage, with the overall purpose to generate data in support of CE marking under the Regulations on medical devices (MDR) or in vitro diagnostic medical devices (IVDR):

- Design and conduct multinational clinical studies in a minimum of two different countries in the EU or Associated Countries, with a focus on orphan devices and/or highly innovative ("breakthrough") devices, with a view to demonstrate the safety and clinical performance of the device(s) subject to the study.
- Present a sound clinical study feasibility plan, including an appropriate patient selection and realistic recruitment plans at different sites, justified by scientific publications or preliminary results. Proposals should adopt a gender-sensitive and intersectional approach, considering individual characteristics such as gender, sex, disability and age. Additionally, socioeconomic, lifestyle and behavioural factors should be taken into account. For this, the topic requires the effective contribution of social sciences and humanities (SSH) disciplines and the involvement of SSH experts, institutions as well as he inclusion of relevant SSH expertise, in order to produce meaningful and significant effects enhancing the societal impact of the related research activities.
- Demonstrate potential clinical benefit for patients and healthcare providers, including quality of life and consideration of patient-reported outcomes when relevant.

- Involve patients, patient organisations, carers and healthcare professionals in the design of the clinical studies.
- Identify, collect and record relevant good practices and experiences related to the design, conduct, sample handling, data analysis and results reporting of multinational clinical studies. In addition, provide appropriate recommendations and lessons learned.
- For multinational clinical studies, authorisation for the study approval by more than one national competent authority may be necessary. Develop a regulatory strategy and interaction plan for generating appropriate evidence as well as engaging with regulators and other relevant bodies (e.g., European Medicines Agency (EMA), EMA expert panels, national regulators, Health Technology Assessment bodies, etc.) in a timely manner. Consider also the potential for future regulatory impact of the results.

Proposals may include multiple devices, but the minimum expected is one device.

Participation of small and medium-sized enterprises (SMEs) is strongly encouraged.

For orphan devices or highly innovative devices relevant to rare disease patients, applicants should look for complementarities and potential synergies with actions implemented under ERDERA the co-funded European Partnership on Rare Diseases proposed under Horizon Europe, as well as synergies with actions implemented under the EU4Health programme.

The Joint Research Centre (JRC) may participate as a member of the consortium selected for funding. Proposals should consider the involvement of the European Commission's JRC regarding its experience in this field and with respect to the value it could bring in providing an effective interface between research activities and pre-normative science as well as strategies and frameworks that address regulatory requirements. In that respect, the JRC will consider collaborating with any successful proposal and this collaboration, when relevant, should be established after the proposal’s approval.

Applicants should provide details of their clinical studies in the dedicated annex using the template provided in the submission system. As proposals under this topic are expected to include clinical studies, the use of the template is strongly encouraged.

HORIZON-HLTH-2025-01-TOOL-01: Enhancing cell therapies with genomic techniques

Budget total : 50M€

Budget par projet : entre 8 et 10M€

Type d’action : Research and Innovation Actions

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination “Developing and using new tools, technologies and digital solutions for a healthy society”. To that end, proposals under this topic should aim to deliver results directed towards and contributing to several of the following expected outcomes:

- Biomedical scientists dispose of tools that allow them to engineer cells with specific therapeutic features.
- Improved methods and assays are available for biopharmaceutical developers.

- Clinicians will get access to innovative therapeutic approaches enabling them to treat conditions, where there are currently no or only insufficient therapeutic strategies.
- Cell engineering will be enriched and pave the way for novel personalised therapy options.

Scope: Therapies based on cells, stem cells or somatic cells, have been shown to be highly effective as therapeutics for a variety of health conditions. However, bottlenecks remain which currently hamper their safe and efficient application on a large scale. Genome- and epigenome editing have great potential to overcome some of these bottlenecks and to lead to the next- generation of cell-based therapies. Advancing the frontier of cell-based therapy with these tools and further translation of such research into clinically viable solutions may open up a new era of innovative therapies.

This topic aims at the design of engineered cells to address the current limitations of cellular therapies, such as delivery efficiency, patient safety, in vivo persistence, desired therapeutic effect, immune tolerance and manufacturing workflows. The chosen approach should enable to control the characteristics, fate and function of the engineered cells from gene level onwards and thus lead to customised cells with improved therapeutic features.

The use of genetic engineering and in particular gene editing tools should be a key element in the design of the engineered cells. The therapeutic action should be based on the endogenous capabilities of the cells; the exogenous loading of cells with drugs (using the cells as drug carrier) is not in scope.

The engineered cells should be derived from human cells. Either stem cells or somatic cells may be used, but of allogeneic origin, thereby opening up the development of “off-the-shelf” cell therapeutics.

Applicants should explicitly state in their proposal which of the following therapeutic areas is targeted and the proposed work should address only this specific therapeutic area:

i. Cancer and oncology

ii. Nervous and sensory system

iii. Cardiovascular and circulatory system

iv. Endocrinology and metabolic system

v. Musculoskeletal system

vi. Digestive system

vii. Infectious diseases

viii. Respiratory system

ix. Dermatology

x. Immune system and auto-immune diseases

xi. Other

The activities should comprise all the following elements:

- Engineering of synthetic genetic circuits acting as switches to modulate the desired function(s) and their integration in the chosen cells, with the help of new genomic techniques. Next to new genomic techniques like genome and epigenome editing, also synthetic biology introducing transgenes or artificial genes may be used to endow the engineered cells with improved therapeutic properties and achieve the desired cell phenotype. The applicants

should use gene control systems, including transcriptional, translational and/or post-translational control, or other approaches which install on-off switches and control systems, like e.g. a “sense-and-respond” mechanism in the engineered cells, sometimes also referred to as “theranostic cells”.

- For the efficient construction and acceleration of the design-build-test cycles of the engineered cells containing the programmed functionalities state of the art tools including digital ones (e.g. Computer-Aided Design - CAD - and similar tools) should be used.
- Suitable in-vitro and ex-vivo systems should be used for testing and demonstration of function and performance of the engineered cells. Their added value, safety and efficacy should be ensured in appropriate pre-clinical models for one specific therapeutic area. Any disease, dysfunction or health impairment may be selected as therapeutic area.
- Applicants should show that the engineered cells are safe and exert the desired therapeutic effect in-vivo. Engagement and interaction with regulatory authorities during the project is essential for qualification of the developed cell-based therapy and in view of the conduct of clinical studies. The demonstration of the feasibility of the proposed cell-based therapy in first in-human studies would be an asset.

Sex differences should be taken into consideration, both with regard to the parent cells and for the targeted therapeutic application. Collaboration with relevant European research infrastructures and findings from EU-supported research projects should be considered.

Participation of small and medium-sized enterprises (SMEs) is strongly encouraged.

Proposals should consider the involvement of the European Commission's Joint ResearchCentre (JRC) as a potential interface between research activities and pre-normative regulatoryscience and in relation to the potential validation of test methods fit for regulatory purpose. Inthat respect, the JRC will consider collaborating with any successful proposal and this collaboration, when relevant, should be established after the proposal’s approval.

Applicants should provide details of their clinical studies in the dedicated annex using the template provided in the submission system. As proposals under this topic are expected to include clinical studies, the use of the template is strongly encouraged.

HORIZON-HLTH-2025-01-TOOL-02: Advancing cell secretome-based therapies

Budget total : 40M€

Budget par projet : entre 9 et 13M€

Type d’action : Research and Innovation Actions

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination “Developing and using new tools, technologies and digital solutions for a healthy society”. To that end, proposals under this topic should aim to deliver results directed towards and contributing to several of the following expected outcomes:

- Researchers and biopharmaceutical developers work together with clinicians striving to translate innovative therapeutic approaches into healthcare solutions.
- Producers of innovative health technologies use standardised manufacturing processes.

- Healthcare providers get access to a new type of innovative therapies with demonstrated health benefits as compared to traditional treatments.
- Patients benefit from innovative therapies for conditions for which there are currently no or only insufficient therapeutic strategies.
- Health systems ultimately benefit from improved patient outcomes, superior to the current standard of care.

Scope: Secretome-based therapies have emerged as a promising alternative to cell-based therapies. The secretome of cells is defined as the repertoire of molecules and biological factors that are secreted into the extracellular space and has been shown to be a key factor for therapeutic activity due to its paracrine effects. The potential to manufacture, store and use secretome factors as off-the-shelf products, while maintaining the therapeutic benefits of cells but with fewer safety concerns, has placed the secretome at the forefront of regenerative medicine. Different cell secretomes or parts thereof have been the subject of clinical trials, but there is currently no regulatory-approved secretome-based therapy owing to several challenges. Currently, for the majority of secretome-based therapies, the main bottlenecks are: the incomplete understanding of their mode of action, their reproducibility due to a lack of standardised manufacturing processes and a lack of potency- and quality assurance assays. Additional limitations are the characterisation of the bioactive factors and the optimisation of the delivery strategies.

Proposals submitted under this topic should tackle the above-mentioned issues and pave the way to secretome-based therapies that are safe, efficacious, and regulatory-approved for human use. The activities should cover secretomes or their parts that are derived from human cells and comprise all the following elements:

- The selection of a secretome-based therapy whose main mechanism of action has been elucidated in in-vitro and/or in-vivo models prior to the start of the proposed work. The selected secretome or its chosen bio-active components (extracellular vesicles, trophic factors, organelles, RNA, proteins, peptides, etc.), including those that are potentially harmful, should have been characterised and its/their therapeutic activity should already have been demonstrated in relevant pre-clinical models. All types of human cells may be used as underlying parent cells.
- All activities that are necessary to ensure regulatory and ethical approvals enabling the conduct of the clinical study. This may comprise the full characterisation, standardised analytical methods, further pre-clinical studies in relevant models (pertinent to the targeted disease or disorder) and appropriate quality assurance assays including computational approaches, organoids and organ-on chips/microfluidic systems.
- Establishment of a manufacturing protocol for the selected secretome or its components, including all the steps of the biogenesis: parent cells selection, their pre-conditioning and bio-processing (isolation, expansion, cultivation in bioreactors), processing of the conditioned media, the extraction of the secretome or its components (isolation, purification, storage, distribution) and its/their delivery to target site in the human body (mode of administration, final formulation).
- Definition of relevant quality criteria for and establishment of a fully GMP-conform production process that enables to carry out clinical trials of the proposed secretome-based therapy.
- Carrying out of all the above-mentioned activities in close interaction with and in compliance with all requirements of the relevant competent authorities, allowing to perform clinical trials.

- Conduct of an interventional randomised controlled clinical trial comprising phase 1 and phase 2 to generate scientific evidence demonstrating safety and efficacy of the proposed secretome-based therapy.
- Applicants are expected to deliver no later than at month 12 of the project the documentation needed for the GMP-conform production (e.g. SOP - Standard Operating Procedures) and no later than at month 24 the documentation needed for the conduct of the clinical trial (e.g. IMDP), enabling to get the regulatory approval for the clinical trial. The overall goal is to perform and finalise the phase 1 and phase 2 clinical trials during the lifetime of the project and further achieve authorization of the proposed secretome-based therapy.
- Optionally and if essential for the chosen secretome-based therapy, the work should also include an engineering step of the secretome to achieve the desired profile for increased safety and improved therapeutic effect. To this end, the secretome or its bioactive component(s) may be modified either pre- or post-biogenesis, by use of classical methods on the parent cells, except their genetic modification, or by physico-chemical modification of the bio-active secretome component. The effected modifications of the secretome should lead to the improvement of the functional properties/features and/or of the delivery to target site (organ, tissue, etc.) for the bioactive secretome component. All these modifications should not alter the main mechanism of action and retain the proposed secretome-based therapy within the boundaries of substances of human origin. The therapeutic effect of the secretome or its components should come from its/their endogenous capabilities and functionalities; exogenous loading with drugs (using the secretome or its components as drug carrier), be it pre- or post-biogenesis, is not in scope.

All types of diseases, dysfunctions or health impairments may be targeted, preference should be given to conditions that affect larger patient populations and/or represent a high burden on public health systems.

Sex differences should be taken into consideration, both with regard to the parent cells and for the targeted therapeutic application. Participation of small and medium-sized enterprises (SMEs) is strongly encouraged and if an exploitation strategy is developed, it should commit to a first deployment in the EU.

Proposals should consider the involvement of the European Commission's Joint Research Centre (JRC) as a potential interface between research activities and pre-normative regulatory science and in relation to the potential validation of test methods fit for regulatory purpose. In that respect, the JRC will consider collaborating with any successful proposal and this collaboration, when relevant, should be established after the proposal's approval.

Applicants should provide details of their clinical studies in the dedicated annex using the template provided in the submission system. As proposals under this topic are expected to include clinical studies, the use of the template is strongly encouraged.

5. Intelligence Artificielle

HORIZON-HLTH-2025-01-DISEASE-04: Leveraging artificial intelligence for pandemic preparedness and response

Budget total : 35M€

Budget par projet : entre 6 et 8M€

Type d'action : Research and Innovation Action

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination "Tackling diseases and reducing disease burden". To that end, proposals under this topic should aim to deliver results that are directed, tailored towards and contributing to all the following expected outcomes:

- The potential of Artificial Intelligence (AI) is used in all aspects that determine optimal pandemic preparedness and response, and fast learning systems are supported, to the benefit of scientists, public health responders and policymakers. This includes using the full potential of available quality data for research and innovation to transform the development of medical, social or logistical countermeasures, as well as the detection, management and monitoring of emergencies at population levels, and the diagnosis, treatment, and prevention at the level of individuals.
- European pandemic preparedness and response benefits from readily available, trustworthy and ethical AI-based tools and technologies that enable it to act fast and in a targeted manner, to timely detect and understand emerging infectious threats, to respond adequately and proportionally to identified threats, and to control such threats effectively and efficiently.
- Different data types from multiple sources and disciplines across the EU and globally can be accessed, integrated and analysed by scientists, public health responders and policymakers, using trustworthy and ethical AI-based tools and technologies that support pandemic preparedness and response.

Scope: The COVID-19 pandemic underscored the need of finding innovative approaches to pandemic preparedness and response, including digital solutions leveraging AI technologies. AI is a fast-developing field, holding an enormous potential in using the multitude of data from an equally vast range of sources, which should be used for improving preparedness and response to epidemics or pandemics in the EU and Associated Countries.

Examples from the COVID-19 pandemic response illustrate how advanced AI tools can enable efficient data use to support areas like forecasting, infectious disease surveillance and monitoring, development of medical interventions, timely diagnosis of infection, disease prognosis, or real-time monitoring of adherence to public health recommendations. New technologies with potentially high impact like air or wastewater real-time monitoring systems have also emerged.

These experiences and advances hold great potential for the future, but additional development and expansion of novel AI-based tools and technologies (including generative AI) is needed, while also further improving and testing existing ones. The use of AI on diverse datasets, as well as on their combinations within and across disciplines, can greatly increase the accuracy of assessments and predictions of medical (pharmaceutical or non-pharmaceutical) interventions in preparedness for, and response to epidemics and pandemics.

Research actions under this topic should include several of the following activities:

- Develop new, or improve existing AI-based tools, methods and technologies, geared towards greater safety, efficiency and impact of medical, societal or logistical countermeasures aiming at the prevention, containment or control of infectious disease epidemics or improved response management of health systems.

- Scout, assemble and prepare appropriate FAIR datasets generated across the EU and Associated Countries (e.g. COVID-19, Influenza, etc.), for the development, training and testing of targeted AI-supported generative assessment and prediction tools, in support of evidence-based policy and decision making for pandemic preparedness and response; in areas like surveillance and monitoring of infectious disease and disease dynamics, facilitating differential diagnosis, triage and risk group predictions, predicting drug response and disease progression, etc.
- Leverage the capacities of the e.xisting and emerging data research infrastructures and the future European Health Data Space (EHDS) and the European Open Science Cloud (EOSC) architectures and research environments, while comprehensively addressing cybersecurity, data privacy, trustworthiness, equity and data quality, interoperability and access modalities.
- Identify and address the current technical, operational, and social limitations related to the (cross-border) access to quality data and to the smooth implementation of AI-driven solutions in the societal and legal context of the EU and Associated Countries.
- Engage with end-users, policymakers, regulatory bodies and authorities, and other stakeholders in the development, improvement, testing and validation of trustworthy and ethical AI-based tools and technologies, to propose options for the validation and uptake of the novel AI tools in real-world settings taking into consideration aspects like training needs, responsible use, users' trust, energy consumption, etc.

The participation of start-ups, micro, small and medium-sized enterprises (SMEs) is encouraged with the aim of strengthening their scientific and technological foundations, enhancing their innovation potential, and exploring possibilities for commercial exploitation.

Proposals selected for funding under this topic are expected to participate in joint activities as appropriate, which can take the form of project clustering, workshops, joint dissemination activities, etc. Applicants should anticipate budget to cover this collaboration.

This topic requires the effective contribution of social sciences and humanities (SSH) disciplines and the involvement of SSH experts, institutions as well as the inclusion of relevant SSH expertise, in order to produce meaningful and significant effects enhancing the societal impact of the related research activities.

Particular attention should be paid to detecting and mitigating gender, ethnicity and other biases, aiming to develop AI models that are fair, trustworthy, and beneficial for all. Proposals are encouraged to explore potential synergies with the projects funded under the topic HORIZON-CL4-2021-HUMAN-01-24: “Tackling gender, race and other biases in AI (RIA)”, as well as under the topic SC1-PHE-CORONAVIRUS-2020-2C: “Behavioural, social and economic impacts of the outbreak response”.

Applicants envisaging to include clinical studies106 should provide details of their clinical studies in the dedicated annex using the template provided in the submission system

HORIZON-HLTH-2025-01-CARE-01: End user-driven application of Generative Artificial Intelligence models in healthcare (GenAI4EU)

Budget total : 40M€

Budget par projet : entre 15 et 20M€

Type d'action : Research and Innovation Action

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination "Ensuring equal access to innovative, sustainable, and high-quality healthcare". To that end, proposals under this topic should aim to deliver results directed towards and contributing to all the following expected outcomes:

- Healthcare professionals, at all stages of healthcare provision, have access to user-centric, robust and trustworthy virtual assistant solutions based on Generative Artificial Intelligence (AI) models and other AI tools to support them towards the provision of safer, more efficient and personalised care.
- Healthcare professionals benefit from cross-country applicable methodologies with the aim to facilitate acceptability, healthcare uptake and public trust of virtual assistant tools based on Generative AI models.
- Patients benefit from enhanced outcomes, more personalised care, and increased engagement with their healthcare professionals, leading to improved safety, quality of care, access to appropriate healthcare information and patient-doctor communication.
- Healthcare systems benefit from improved cost-effective patient outcomes, superior to standard of care in terms of accuracy, safety, and quality, and from cost-savings through advancements in highly accurate, transparent, traceable, and explainable solutions.

Scope: Healthcare professionals face important challenges related to efficiency, patient safety and provision of quality care with limited health systems' resources. Multimodality of health data resources combined with the available high-performance computing capacities have the potential to empower effective and accurate use of trustworthy and ethical Generative AI-based solutions, augmented by other AI tools to address these challenges. Generative AI can benefit patients, healthcare professionals and health systems.

This topic will contribute to advancing and generating research to better understand and improve Generative AI-based virtual assistant solutions and their applicability in healthcare settings by improving patient health outcomes, fostering personalised healthcare and support the resilience, sustainability, and efficiency of the healthcare systems. In addition, the topic aims to also cover the understanding and mitigation of possible shortcomings (biases) and frameworks for monitoring and overseeing these solutions' use.

Research actions under this topic should include all the following activities, ensuring multidisciplinary approaches and a broad representation of stakeholders in the consortia (e.g.industry, academia, healthcare professionals, patients):

- Develop virtual assistant solutions based on new or optimised trustworthy and ethical Generative AI models, augmented by other AI tools to support healthcare professionals. The models should leverage extensive and diverse multimodal health and research data, public knowledge, and reliable healthcare systems information relevant for healthcare settings. Examples can include electronic health records, medical imaging, genomics, proteomics, molecular data, laboratory results, patient information (including on safety), and/or unstructured health data (the applicants may choose any type of available large-scale data). The development and training of the models should take place in multinational consortia and federated governance approaches should be considered. The applicants should demonstrate

how the project goes beyond combining existing data and generates new specific knowledge to improve clinical decision making.

- Demonstrate the added-value and clinical utility of the virtual assistant solutions in at least two healthcare use cases in different medical fields and unmet needs showing e.g.improved care management and efficiency, prediction of potential patient-specific therapeutic strategies and outcomes, etc. The applicants should provide evidence of high maturity technology for the use cases and assess the relative effectiveness of the solutions compared with standard of care, including on why these solutions would be superior to other AI tools and would deliver better outcomes. They should actively engage healthcare professionals as end users, and other stakeholders such as patients, caregivers in the development and testing of the solutions, ensuring that diverse perspectives and intersectional considerations are integrated throughout the process. Training and education activities for healthcare professionals should be organised.
- Develop a regulatory strategy/interaction plan with regulators (including Health Technology Assessment) for generating evidence, where relevant, in a timely manner. Consider also the potential for future regulatory impact of the results and sustainability aspects.
- Develop or adapt existing methodologies for continuous assessment of the developed solutions. The methodologies should demonstrate technical robustness, healthcare utility and trustworthiness of the Generative AI-based solutions, by adopting:
    - Appropriate performance metrics for evaluating and testing the technical robustness and clinical utility, as well as model intelligibility and alignment with ethical principles in view of ensuring AI trustworthiness.
    - Appropriate solutions to identify and mitigate potential bias and confounding of the models (e.g., representativeness of the data, bias of the trainer, bias of training and validation data, algorithmic bias, gender bias etc.).
    - Methods to systematically address and assess ELSI (Ethical, Legal and Societal Implications), including data privacy concerns and risk of discrimination/bias (sex/gender, age, disability, ethnicity, minority and/or vulnerable groups). Implication of medical errors originated from AI-assisted decision-making and the effects on potential legal liability for healthcare professionals should be explored.
    - Appropriate techniques to discover cause-and-effect relationships and explainability of the model reasoning to increase users' trust. Causal understanding mechanisms can predict what's happening inside the AI model, addressing the black box element, increasing transparency and model explainability.

All proposals should demonstrate EU added value by focusing on the development and/or use of trustworthy Generative AI models developed in the EU and Associated countries, involving in the consortium EU industrial developers, including leading-edge startups when possible. An open-source approach is encouraged when technically and economically feasible. Successful proposals are encouraged to utilise the resources offered by the AI factories, when relevant and in accordance with the specific access terms and conditions.

The proposals should adhere to the FAIR data principles and apply GDPR compliant processes for personal data protection based on good practices of the European research infrastructures, where relevant. The proposals should promote the highest standards of transparency and openness of models, as much as possible going well beyond documentation and extending to aspects such as assumptions, code and FAIR data management.

Proposals are encouraged to exploit potential synergies with the projects funded under the topic HORIZON-CL4-2021-HUMAN-01-24, as well as with other projects funded under Horizon Europe and Digital Europe Programmes. When the use cases are relevant to diseases covered by specific Horizon Europe Partnerships or missions (e.g., European Partnership on Rare Diseases, European Partnership on transforming health and care systems, the Cancer Mission, etc.), the proposals should adopt the federated data-management and data access recommendations already developed. Moreover, the applicants are encouraged to leverage available and emerging data infrastructures (e.g., European Health Data Space, European Genomic Data Infrastructure, Cancer Image Europe, European Open Science Cloud, EBRAINS etc.), whenever relevant. Adopting EOSC recommendations and services for high-quality software is also encouraged. The expansion of health data and/or existing or under development AI infrastructures is not in the scope of this topic.

When possible, the developed models should be trained with multimodal data in different EU languages, to ensure accessibility and inclusivity.

Successful proposals are encouraged to utilise the resources offered by the AI factories, when relevant and in accordance with the specific access terms and conditions.

This topic requires the effective contribution of social sciences and humanities (SSH) disciplines and the involvement of SSH experts and institutions as well as the inclusion of relevant SSH expertise, to produce meaningful and significant effects enhancing the societal impact of the related research activities. The active engagement of healthcare professionals as end users, patients, and their caregivers is central to achieving targeted outcomes in the development and testing of the Generative AI virtual assistant solutions.

Proposals should consider the involvement of the European Commission's Joint Research Centre (JRC) based on its experience and with respect to the value it could bring in providing an effective interface between research activities and preliminary regulatory science as well as strategies and frameworks that address fit for regulatory requirements. In that respect, the JRC will consider collaborating with any successful proposal and this collaboration, when relevant, should be established after the proposal’s approval.

All proposals selected for funding under this topic are strongly encouraged to collaborate, for example by participating in networking and joint activities, exchange of knowledge, developing and adopting best practices, as appropriate. Therefore, proposals are expected to include a budget covering the costs of any other potential joint activities without the prerequisite to detail concrete joint activities at this stage. The details of these joint activities will be defined during the grant agreement preparation phase.

Applicants envisaging to include clinical studies should provide details of their clinical studies in the dedicated annex using the template provided in the submission system

HORIZON-HLTH-2025-01-TOOL-03: Leveraging multimodal data to advance Generative Artificial Intelligence applicability in biomedical research (GenAI4EU)

Budget total : 50M€

Budget par projet : entre 15 et 17M€

Type d’action : Research and Innovation Action

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination "Developing and using new tools, technologies and digital solutions for a healthy society". To that end, proposals under this topic should aim to deliver results directed towards and contributing to all the following expected outcomes:

- Researchers, including clinical researchers, have access to robust, trustworthy and ethical Generative Artificial Intelligence (AI)178 models able to effectively advance biomedical research towards predictive and personalised medicine.
- Researchers, including clinical researchers, know how to use Generative AI models to synthesise the available scientific information and large-scale multimodal data and how to apply the necessary precautions, in order to deliver new knowledge and breakthrough scientific discoveries.
- Research community benefits from advanced methodologies to assess the validity and application of accurate, transparent, traceable, and explainable Generative AI models.

Scope: The availability of large-scale multimodal health data, scientific information, and novel Generative AI models, combined with high-performance computing capacities offer an unprecedented opportunity for researchers to achieve breakthroughs in our understanding of disease development and to develop new predictive models for disease management, personalised treatment solutions and personalised care pathways. The European Commission recognises this potential and considers health research and healthcare, among the priority sectors for building the Union's strategic leadership [COM(2024) 28 final].

This topic will contribute to advancing research and providing new evidence on how these models contribute to and support biomedical research and its applicability towards more predictive and personalised medicine, while also defining use conditions, usability requirements and training needs of the researchers. It aims to cover existing gaps related to Generative AI in biomedical research, addressing both capabilities and existing limitations.

Research actions under this topic should include all the following activities, ensuring multidisciplinary approaches and a broad representation of stakeholders in the consortia (e.g. industry, academia, healthcare professionals):

- Develop new or re-purpose existing Generative AI models for biomedical research across various medical fields and/or therapeutic indications. The models should be robust, based on the use of large-scale, complex, and multimodal high-quality data (real and/or synthetic data), such as but not limited to medical imaging, genomics, proteomics, other molecular data, electronic health records, laboratory results, unstructured health data and/or available scientific and public information relevant to biomedical research. The applicants may choose any type of available large-scale biomedical data and/or their combinations and justify their relevance for training and optimisation of the Generative AI tools.
- Develop a proof of concept with at least two use cases relevant for predictive and personalised medicine in different medical fields to demonstrate the scientific added value compared to currently used methods and/or potential future clinical utility of the Generative AI models in biomedical research. The applicants should actively engage potential end users in the development, adaptation and testing of the new/repurposed models, considering sustainability aspects.
- Develop or revise existing methodologies to assess applicability, limitations, and performance of the developed and/or repurposed Generative AI models and their added value in biomedical research. These methodologies should demonstrate the technical, scientific, and

potential future clinical utility, robustness and trustworthiness of the developed or repurposed Generative AI models, in particular:

- Appropriate performance metrics for continuous evaluation and testing of scientific and technical robustness and relevance of the Generative AI models.
- Appropriate metrics for model intelligibility, robustness, alignment with ethical principles and approaches for ethical evaluation of AI trustworthiness.
- Appropriate solutions to identify and mitigate potential bias and confounding of Generative AI models and include examples from different perspectives (e.g., representativeness of the data, bias of the trainer, bias of training and validation data, algorithmic bias, gender bias etc.).
- Methods to systematically address and assess ELSI (Ethical, Legal, and Societal Implications) aspects, including data privacy, risk of discrimination/bias (sex/gender, age, disability, ethnicity, minority and/or vulnerable groups, including disadvantaged groups).
- Appropriate techniques to discover cause-and-effect relationships and explainability of the model reasoning in order to increase users' trust. Causal understanding mechanisms can predict internal processes of the model, addressing the black box element, increasing transparency and model explainability.

All proposals should demonstrate EU added value by developing and/or using trustworthy and ethical Generative AI models developed in the EU and Associated countries, involving in the consortium EU industrial developers of Generative AI solutions, including leading-edge startups when possible. An open-source approach is encouraged when technically and economically feasible.

The proposals should adhere to the FAIR data principles and apply GDPR compliant processes for personal data protection based on good practices developed by the European research infrastructures, where relevant. The proposals should promote the highest standards of transparency and openness of models, as much as possible going well beyond documentation and extending to aspects such as assumptions, code and FAIR data management.

Proposals are encouraged to exploit potential synergies with other relevant projects funded under Horizon Europe and/or Digital Europe Programmes. When the use cases are relevant to diseases covered by specific Horizon Europe Partnerships or missions (e.g., the European Partnership on Rare Diseases, the Cancer Mission, etc.), the proposals should leverage the knowledge/data platforms already developed, such as the Virtual Platform of the European Joint Programme of Rare Diseases etc. Moreover, the applicants are encouraged to leverage available and emerging European data infrastructures (e.g., the European Health Data Space, European Genomic Data Infrastructure, Cancer Image Europe, European Open Science Cloud, EBRAINS etc.), whenever relevant. In addition, adopting EOSC recommendations and services for high-quality software is also encouraged, if applicable. The creation and expansion of health data and/or AI infrastructures or large-data curation initiatives, existing or under development, are not in the scope of this topic.

This topic requires the effective contribution of social sciences and humanities (SSH) disciplines and the involvement of SSH experts and institutions as well as the inclusion of relevant SSH expertise, in order to produce meaningful and significant effects enhancing the societal impact of the related research activities.

Successful proposals are encouraged to utilise the resources offered by the AI factories, when relevant and in accordance with the specific access terms and conditions.

Proposals should consider the involvement of the European Commission's Joint Research Centre (JRC) with respect to the value it could bring in providing an effective interface between research activities and pre-normative regulatory science as well as strategies and frameworks that address regulatory requirements. In that respect, the JRC will consider collaborating with any successful proposal and this collaboration, when relevant, should be established after the proposal’s approval.

All proposals selected for funding under this topic are strongly encouraged to collaborate, for example by participating in networking and joint activities, exchange of knowledge, developing, and adopting best practices, as appropriate. Therefore, proposals are expected to include a budget for the attendance to regular joint meetings and may consider covering the costs of any other potential joint activities without the prerequisite to detail concrete joint activities at this stage. The details of these joint activities will be defined during the grant agreement preparation phase.

Applicants envisaging to include clinical studies should provide details of their clinical studies in the dedicated annex using the template provided in the submission system.