EN

Annex III

Horizon Europe

Work Programme 2025

4. Health

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Introduction

Introduction

This work programme part is the first for the Health Cluster under Horizon Europe's new strategic plan for 2025-2027. It reflects a detailed review of the first four years of Horizon Europe (2021-2024), identifying funding gaps, emerging research needs and future challenges. It aligns with the European Commission's Political Guidelines for 2024-2029, focusing on strengthening healthcare resilience, leveraging biotechnology and artificial intelligence, and addressing public health needs. Research and innovation are key to achieving these goals, especially in healthcare.

As outlined in the Horizon Europe strategic plan, the main priorities of the Health Cluster from 2025 to 2027, are geared towards social cohesion, inclusion, and the overall health and wellbeing of Europeans, in line with the European Pillar of Social Rights. These priorities also emphasise the need to modernise healthcare systems and support an innovative, sustainable, and competitive health industry in Europe.

The EU's substantial pre-COVID-19 investments in infectious disease research enabled a swift response to the pandemic, including the development of vaccines. Building on this experience, the establishment of the European Health Emergency Preparedness and Response Authority (HERA) underscores the Commission's commitment to pandemic preparedness. The Health Cluster will continue to invest in this area, supporting the objectives of the European Health Union.

The public health impacts of climate change, pollution, and biodiversity loss (the triple planetary crisis) are increasingly concerning. Research and Innovation investments are essential to understanding and mitigating these effects on human health and healthcare systems. This aligns with EU policies such as the European Green Deal and the EU Climate Adaptation Strategy. Additionally, the surge in mental health issues, exacerbated by the pandemic, climate crisis, and other stressors, highlights the need for further Research and Innovation investments in support of the Commission initiative on a comprehensive approach to mental health.

Further investments are necessary to address Europe's long-term challenges related to an ageing population and non-communicable diseases. The Health Cluster will contribute to initiatives such as “Healthier Together - EU Non-communicable Diseases Initiative” and the Cancer Mission, supporting the policy objectives of Europe’s Beating Cancer Plan.

Europe's healthcare systems, already strained by demographic changes and chronic conditions, face additional pressures from the energy crisis, inflation, and pandemic-related backlogs. The Health Cluster will explore ways to enhance the resilience of these systems, complementing the work of the European Partnership on Transforming Health and Care Systems. This includes promoting greener practices, addressing health inequities, and leveraging digital transformation.

Further investments are also needed to leverage the innovation potential of health data and data-driven approaches. The proposed European Health Data Space (EHDS) Regulation will provide a framework for data-based health Research and Innovation activities, ensuring compliance with the EU's high data protection standards. Critical technologies such as Artificial Intelligence (AI) and biotechnology will be supported to secure EU technological sovereignty in the healthcare sector, in line with the EU "Artificial Intelligence Strategy" and the EU "Biotechnology and Biomanufacturing Strategy".

The Health Cluster work programme part for 2025 will take the first stride in addressing the needs and challenges identified in the strategic plan for 2025-2027 and support the objectives set by the European Commission's Political Guidelines for 2024-2029. It focusses on key areas such as the health impacts from pollution and environmental degradation, supporting policies like the European Green Deal and the Zero Pollution Action Plan. It will also address non-communicable diseases, mental health, pandemic preparedness, and antimicrobial resistance. This includes new treatment options, AI-based tools for pandemic response, and the European Partnership for Brain Health, as well as measures to improve the quality of life for individuals with intellectual disabilities. Furthermore, the programme aims to enhance healthcare efficiency, patient engagement, and trust in AI tools, in line with the European care strategy and the digital transformation of health and care in the EU. It will support biotechnology and AI to improve healthcare, including cellular and cell-free therapeutic approaches, generative AI models for biomedical research, and bridging the gap between pre-clinical and clinical development. Additionally, it will advance manufacturing processes for medical devices, supporting the EU Industrial Policy, ensuring resilience of the single market, fostering industrial competitiveness, and promoting sustainable practices.

In March 2024, the Commission adopted the Strategic Technologies for Europe Platform (STEP) to boost investments in critical technologies in Europe: clean and resource efficient technologies, digital and deep innovation technologies and biotechnologies. STEP will mobilise funding from existing EU programmes to support the development and manufacturing of these critical technologies, while safeguarding and strengthening the respective value chains, as well as associated services and skills critical for and specific to the development and manufacturing of the final products. This work programme part identifies one action in support of STEP objectives, for which proposals meeting the minimum requirements indicated in the specific call conditions will receive a STEP seal[1] (See topic HORIZON-HLTH-2025-01-TOOL-05: "Boosting the translation of biotech research into innovative health therapies").

To realise the potential of new Research and Innovation for society, collaboration between research teams and prospective users of the knowledge and technology developed is paramount. It is therefore essential to involve these users - such as patients, healthy citizens, healthcare professionals, providers and payers, public health authorities, regulators, and innovators from academia and industry - early in the process of knowledge generation and technology development. This involvement can take the form of patient and citizen

[1] https://strategic-technologies.europa.eu/about/step-seal_en

engagement, community involvement, and other social innovation approaches, ensuring that Research and Innovation activities align with the specific expectations, needs, constraints, and potential of users. Furthermore, effective intellectual property management strategies are crucial to maximise the benefits of such cooperation.

It is in the EU's strategic interest to cooperate with countries beyond the EU, particularly for multilateral cooperation on (global) health issues. This includes countries associated to Horizon Europe as well as other partner countries and regions worldwide. In line with the EU's Global Approach to Research and Innovation[2], participation in the Health Cluster of Horizon Europe is open to third countries. Supporting the Global Gateway Strategy[3], projects involving international partners should aim to increase scientific knowledge and facilitate technology transfer among partner countries, addressing global health challenges and fostering sustainable growth and job creation. Such cooperation should be value-based, creating linkages rather than dependencies.

Applicants are encouraged to explore opportunities for synergies between the Health Cluster and other EU programmes[4] to enhance the reach and impact of their projects, such as through broader stakeholder cooperation and follow-on activities. Synergies are in particular foreseen between the Health Cluster and the EU4Health programme to facilitate the uptake, further development and deployment of new knowledge and technologies in fields such as cancer, non-communicable diseases, mental health, pandemic preparedness and antimicrobial resistance, health systems and digital health. Synergies are also foreseen between the Health Cluster and the Digital Europe Programme to leverage Horizon Europe Research and Innovation results, such as deploying digital, privacy-preserving (distributed) data infrastructures, high-performance computing resources, and developing methods and tools for modeling complex phenomena related to human health.

The European Regional Development Fund (ERDF), focuses, amongst others, on the development and strengthening of regional and local Research and Innovation ecosystems and smart economic transformation, in line with regional/national smart specialisation strategies. The programme can e.g., support investment in research infrastructure, activities for applied Research and Innovation, including industrial research, experimental development and feasibility studies, building on Research and Innovation stemming from Horizon Europe[5].

To further strengthen the impact of Research and Innovation efforts, Horizon Europe applicants could consider tapping into complementary activities offered by other relevant initiatives funded under the Horizon Europe programme. These include the innovation ecosystems and service provisions of the Knowledge and Innovation Communities (KICs) of

2 COM(2021) 252 final
3 JOIN(2021) 30 final
4 E.g., the EU4Health programme, the Digital Europe Programme, European Regional Development Fund (ERDF), European Social Fund (ESF+), Structural Reform Support Programme (SRSP), the Just Transition Fund (JTF), the European Maritime and Fisheries Fund (EMFF), the European Agricultural Fund for Rural Development (EAFRD), the European Defence Fund (EDF) or InvestEU.
5 Synergies between Horizon Europe and ERDF programmes (Draft Commission Notice): https://research-and-innovation.ec.europa.eu/news/all-research-and-innovation-news/synergies-guidance-out-2022-07-06_en

the European Institute of Innovation and Technology (EIT), particularly EIT-KIC Health and EIT-KIC Digital, or the interregional networks funded under the European Innovation Ecosystems (EIE) component of Pillar III.

In addition, applicants to the Health Cluster are encouraged to explore opportunities for complementary topics and activities in other Clusters or parts of the Horizon Europe programme that address thematically similar challenges and areas of intervention. This can be in the Clusters of Pillar II, in the European Research Infrastructures work programme part (Pillar I), or in the European Innovation Council work programme (Pillar III). More specifically, beneficiaries of Horizon Europe grants are invited to consider possible collaborations and cross-fertilisation between their project and other projects selected under the same or other relevant calls.

The EU's Recovery and Resilience Facility (RRF) offers support to Member States in financing reforms and investments that improve their resilience and their growth potential, mitigate the economic and social impacts from the COVID-19 crisis, including in the area of health, and support the twin green and digital transitions. For project ideas that go beyond the remits of a Research and Innovation proposal and directly contribute to the objectives of the RRF it is advisable to check access to funding available at national level in line with the Member States' approved recovery and resilience plans for a fast and targeted support.

For topics in this Cluster, consortia could consider voluntarily contributing data, indicators, and knowledge to relevant Joint Research Centre (JRC) platforms. This would help capitalise on the knowledge developed in their projects and enhance their relevance to policymaking[6, 7, 8, 9, 10, 11].

In the context of the Health Cluster work programme part for 2025, FAIR data are data which meet the principles of findability, accessibility, interoperability, and reusability. Data may include, amongst others, exploitation of information, digital research data generated in the action, data from European research infrastructures and programmes such as Copernicus, European Space Agency and the GEO initiative. For further details, see the FAIR principles website[12], the FAIR cookbook[13] and the guides for researchers on how to make your data FAIR[14].

6 https://health.ec.europa.eu/system/files/2022-02/eu_cancer-plan_en_0.pdf

7 The European Cancer Information System (ECIS - https://ecis.jrc.ec.europa.eu) and the European Network of Cancer Registries (ENCR - https://www.encr.eu)

8 European Commission Initiatives on Breast and Colorectal Cancer: https://healthcare-quality.jrc.ec.europa.eu

9 European Cancer Inequalities Registry: https://cancer-inequalities.jrc.ec.europa.eu

10 European Platform on Rare Disease Registration (EU RD Platform - https://eu-rd-platform.jrc.ec.europa.eu/_en) - for rare cancers

11 Health Promotion and Disease Prevention Knowledge Gateway Horizon Europe: https://knowledge4policy.ec.europa.eu/health-promotion-knowledge-gateway_en

12 https://www.go-fair.org/fair-principles

13 https://faircookbook.elixir-europe.org/content/home.html

14 https://www.openaire.eu/how-to-make-your-data-fair

Applicants to calls of the Health Cluster are encouraged to consider, where relevant, the services offered by current and future EU-funded European Research Infrastructures, including those prioritised by the European Strategy Forum on Research Infrastructures (ESFRI)[15], European Research Infrastructure Consortia (ERICs)[16] and the European Open Science Cloud[17]. Moreover, if projects use satellite-based earth observation, positioning, navigation and/or related timing data and services, they must make use of European space technologies and services provided by Copernicus and/or Galileo/EGNOS (other data and services may additionally be used)[18].

In the context of the Health Cluster work programme part for 2025, a clinical study covers clinical studies/trials/investigations/cohorts and is defined as any systematic prospective or retrospective collection and analysis of health data obtained from individual patients or healthy persons in order to address scientific questions related to the understanding, prevention, diagnosis, monitoring or treatment of a disease, mental illness, or physical condition. It includes but it is not limited to clinical studies as defined by Regulation 536/2014 (on medicinal products), clinical investigation and clinical evaluation as defined by Regulation 2017/745 (on medical devices), performance study and performance evaluation as defined by Regulation 2017/746 (on in vitro diagnostic medical devices).

Please note that the European Union (EU) pharmaceutical legislation known as the Clinical Trials Regulation No 536/2014[19] entered into application on 31 January 2022, repealing the Clinical Trials Directive (EC) No. 2001/20/EC and national implementing legislation in the EU Member States, which regulated clinical trials in the EU until the Regulation's entry into application. As a result, from 31 January 2023, all initial clinical trial applications in the European Union (EU) must be submitted via the Clinical Trials Information System (CTIS)[20]. CTIS is now the single-entry point for sponsors and regulators of clinical trials for the submission and assessment of clinical trial data.

The Horizon Europe strategic plan (2025-2027) sets out three Key Strategic Orientations (KSOs) for the last three years of the EU's framework programme for Research and Innovation, namely: KSO 1: "The Green Transition," aiming to support Europe in becoming the world's first climate-neutral continent by 2050, tackling biodiversity loss and pollution; KSO 2: "The Digital Transition," focusing on reinforcing Europe's competitiveness and strategic autonomy through research in core digital technologies; and KSO 3: "A More Resilient, Competitive, Inclusive, and Democratic Europe," aiming to bolster Europe's social

15 https://ri-portfolio.esfri.eu
16 https://www.eric-forum.eu/the-eric-landscape
17 https://research-and-innovation.ec.europa.eu/strategy/strategy-2020-2024/our-digital-future/open-science/european-open-science-cloud-eosc_en
18 European space technology based earth observation, positioning, navigation and timing services provided by: Copernicus, the European Union's Earth observation programme https://www.copernicus.eu/en/copernicus-services; Galileo, the European Global Satellite Navigation System (GNSS) https://www.gsc-europa.eu/galileo/services/galileo-initial-services; and the European Geostationary Navigation Overlay Service (EGNOS) https://www.euspa.europa.eu/eu-space-programme/egnos
19 https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32014R0536
20 https://euclinicaltrials.eu

rights and democratic values, ensuring they are globally promoted. This includes research in civil security, health and wellbeing, a fair economic model, and democratic participation.

The Health Cluster will support these KSOs by enhancing the understanding of climate change impacts on health, developing tools to protect against global health challenges, and reducing the sector's carbon footprint. It will promote technological and digital advancements to improve healthcare systems, focusing on disease prevention, personalised treatment, and equitable access to health services. Additionally, it will foster inclusive and resilient healthcare systems capable of responding to cross-border health threats and demographic changes, leveraging digital technologies such as AI to accelerate health research and improve health outcomes.

More specifically, the Health Cluster will support the KSOs by contributing to the six expected impacts set out for the Health Cluster in the strategic plan 2025-2027, which translate into the following six destinations of the Health Cluster work programme part for 2025:

Destination "Staying healthy in a rapidly changing society": The expected impact is that people of all ages in the EU stay healthy, resilient, and independent even as society changes fast. This will arise from healthier lifestyles and behaviour, healthier diets, healthier environments, improved evidence-informed health policies, and more effective solutions for health and wellbeing promotion, disease prevention and monitoring, and rehabilitation.

Destination "Living and working in a health-promoting environment": The expected impact is that people's living and working environments are health-promoting and sustainable thanks to a better understanding of the environmental, occupational, social, sex and gender-related, and economic determinants of health.

Destination "Tackling diseases and reducing disease burden": The expected impact is that healthcare providers improve their ability to tackle and manage diseases (infectious diseases, including poverty-related and neglected diseases, non-communicable and rare diseases) thereby reducing the disease burden on patients and enabling healthcare systems to perform more effectively. It can be achieved through better understanding, prevention, diagnostics, treatment, management, and cure of diseases and their co- and multi-morbidities, more effective and innovative health technologies and medical countermeasures, better ability and preparedness to manage pandemic and/or epidemic outbreaks, and improved patient safety.

Destination "Ensuring equal access to innovative, sustainable, and high-quality healthcare": The expected impact is that healthcare systems provide equal access to innovative, sustainable and high-quality healthcare thanks to the development and uptake of safe, cost-effective and people-centred solutions. This is to be accompanied by management models focusing on population health, health systems resilience, and health equity and patient safety, and also improved evidence-informed health policies.

Destination "Developing and using new tools, technologies and digital solutions for a healthy society": The expected impact is that health technologies, data, new tools, and digital

solutions are applied effectively thanks to their inclusive, ethically sound, secure and sustainable delivery, integration and deployment in health policies and in health and care systems.

Destination "Maintaining an innovative, sustainable, and competitive EU health industry": The expected impact is that the EU health industry is innovative, sustainable, and globally competitive thanks to improved uptake of breakthrough technologies and innovations (including social innovations) that make the EU with its Member States and Associated Countries more resilient and less reliant on imports of critical health technologies.

Calls

Call - Cluster 1 - Health (Single stage - 2025)

HORIZON-HLTH-2025-01

Overview of this call[21]

Proposals are invited against the following Destinations and topic(s):

Topics	Type of Action	Budgets (EUR million)	Expected EU contribution per project (EUR million)[22]	Indicative number of projects expected to be funded
		2025		
Opening: 22 May 2025 Deadline(s): 18 Sep 2025				
Destination - Tackling diseases and reducing disease burden				
HORIZON-HLTH-2025-01-DISEASE-01: Testing safety and efficacy of phage therapy for the treatment of antibiotic-resistant bacterial infections	RIA	45.00	Around 15.00	3
HORIZON-HLTH-2025-01-DISEASE-03: Development of antibodies and antibody-derived proteins for the prevention and treatment of infectious diseases with epidemic potential	RIA	50.00	Around 10.00	5
HORIZON-HLTH-2025-01-DISEASE-04: Leveraging artificial intelligence for pandemic preparedness and response	RIA	35.00	6.00 to 8.00	5
HORIZON-HLTH-2025-01-DISEASE-05:	CSA	2.00	Around	1

[21] The Director-General responsible for the call may decide to open the call up to one month prior to or after the envisaged date(s) of opening.
The Director-General responsible may delay the deadline(s) by up to two months.
All deadlines are at 17.00.00 Brussels local time.
The budget amounts are subject to the availability of the appropriations provided for in the general budget of the Union for 2025.

[22] Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.

Support for the functioning of the Global Research Collaboration for Infectious Disease Preparedness (GloPID-R)			2.00	
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)	RIA	20.00	3.00 to 4.00	5
Destination - Ensuring equal access to innovative, sustainable, and high-quality healthcare				
HORIZON-HLTH-2025-01-CARE-01: End user-driven application of Generative Artificial Intelligence models in healthcare (GenAI4EU)	RIA	40.00	15.00 to 20.00	2
Destination - Developing and using new tools, technologies and digital solutions for a healthy society				
HORIZON-HLTH-2025-01-TOOL-01: Enhancing cell therapies with genomic techniques	RIA	50.00	8.00 to 10.00	5
HORIZON-HLTH-2025-01-TOOL-02: Advancing cell secretome-based therapies	RIA	40.00	9.00 to 13.00	3
HORIZON-HLTH-2025-01-TOOL-03: Leveraging multimodal data to advance Generative Artificial Intelligence applicability in biomedical research (GenAI4EU)	RIA	50.00	15.00 to 17.00	3
HORIZON-HLTH-2025-01-TOOL-05: Boosting the translation of biotech research into innovative health therapies	RIA	80.00	4.00 to 8.00	10
Destination - Maintaining an innovative, sustainable, and competitive EU health industry				
HORIZON-HLTH-2025-01-IND-01: Optimising the manufacturing of Advanced Therapy Medicinal Products (ATMPs)	IA	40.00	6.00 to 8.00	5
HORIZON-HLTH-2025-01-IND-02: Digitalisation of conformity assessment procedures of medical devices and in vitro diagnostic medical devices	CSA	4.00	Around 4.00	1
HORIZON-HLTH-2025-01-IND-03: Facilitating the conduct of multinational	RIA	40.00	6.00 to 8.00	5

clinical studies of orphan devices and/or of highly innovative ("breakthrough") devices				
Overall indicative budget		496.00		

General conditions relating to this call	
Admissibility conditions	The conditions are described in General Annex A.
Eligibility conditions	The conditions are described in General Annex B.
Financial and operational capacity and exclusion	The criteria are described in General Annex C.
Award criteria	The criteria are described in General Annex D.
Documents	The documents are described in General Annex E.
Procedure	The procedure is described in General Annex F.
Legal and financial set-up of the Grant Agreements	The rules are described in General Annex G.

Call - Partnerships in Health (2025)

HORIZON-HLTH-2025-02

Overview of this call[23]

Proposals are invited against the following Destinations and topic(s):

Topics	Type of Action	Budgets (EUR million)			Expected EU contribution per project	Indicative number of projects
		2025	2026	2027		

[23] The Director-General responsible for the call may decide to open the call up to one month prior to or after the envisaged date(s) of opening.
The Director-General responsible may delay the deadline(s) by up to two months.
All deadlines are at 17.00.00 Brussels local time.
The budget amounts are subject to the availability of the appropriations provided for in the general budget of the Union for 2025.

					(EUR million)[24]	expected to be funded
Opening: 13 May 2025 Deadline(s): 03 Jun 2025						
Destination - Tackling diseases and reducing disease burden						
HORIZON-HLTH-2025-02-DISEASE-01: European Partnership for Brain Health	COFUND	46.00	54.00	50.00	Around 150.00	1
HORIZON-HLTH-2025-02-DISEASE-02: European partnership fostering a European Research Area (ERA) for health research (Phase 2)	COFUND	77.00			Around 77.00	1
Overall indicative budget		123.00	54.00	50.00		

General conditions relating to this call	
Admissibility conditions	The conditions are described in General Annex A.
Eligibility conditions	The conditions are described in General Annex B.
Financial and operational capacity and exclusion	The criteria are described in General Annex C.
Award criteria	The criteria are described in General Annex D.
Documents	The documents are described in General Annex E.
Procedure	The procedure is described in General Annex F.
Legal and financial set-up of the Grant Agreements	The rules are described in General Annex G.

[24] Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.

Call - Cluster 1 - Health (Two stage - 2025)

HORIZON-HLTH-2025-03-two-stage

Overview of this call[25]

Proposals are invited against the following Destinations and topic(s):

Topics	Type of Action	Budgets (EUR million)	Expected EU contribution per project (EUR million)[26]	Indicative number of projects expected to be funded
		2025		
Opening: 22 May 2025 Deadline(s): 18 Sep 2025 (First Stage), 16 Apr 2026 (Second Stage)				
Destination - Staying healthy in a rapidly changing society				
HORIZON-HLTH-2025-03-STAYHLTH-01-two-stage: Improving the quality of life of persons with intellectual disabilities and their families	RIA	40.00	6.00 to 8.00	5
Destination - Living and working in a health-promoting environment				
HORIZON-HLTH-2025-03-ENVHLTH-01-two-stage: The impact of pollution on the development and progression of brain diseases and disorders	RIA	40.00	6.00 to 7.00	6
HORIZON-HLTH-2025-03-ENVHLTH-02-two-stage: Advancing knowledge on the impacts of micro- and nanoplastics on human health	RIA	40.00	7.00 to 8.00	5
Destination - Tackling diseases and reducing disease burden				

[25] The Director-General responsible for the call may decide to open the call up to one month prior to or after the envisaged date(s) of opening.
The Director-General responsible may delay the deadline(s) by up to two months.
All deadlines are at 17.00.00 Brussels local time.
The budget amounts are subject to the availability of the appropriations provided for in the general budget of the Union for 2025.

[26] Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.

HORIZON-HLTH-2025-03-DISEASE-02-two-stage: Advancing innovative interventions for mental, behavioural and neurodevelopmental disorders	RIA	50.00	6.00 to 8.00	7
Overall indicative budget		170.00		

General conditions relating to this call	
Admissibility conditions	The conditions are described in General Annex A.
Eligibility conditions	The conditions are described in General Annex B.
Financial and operational capacity and exclusion	The criteria are described in General Annex C.
Award criteria	The criteria are described in General Annex D.
Documents	The documents are described in General Annex E.
Procedure	The procedure is described in General Annex F.
Legal and financial set-up of the Grant Agreements	The rules are described in General Annex G.

Destinations

Destination - Staying healthy in a rapidly changing society

Topics under this destination are directed towards the Key Strategic Orientation 2 "*The Digital transition*" and Key Strategic Orientation "*A more resilient, competitive, inclusive, and democratic Europe*" of Horizon Europe's strategic plan 2025-2027.

Research and Innovation supported under this destination should contribute to the following expected impact, set out in the strategic plan impact summary for the Health Cluster: *"people of all ages in the EU stay healthy, resilient, and independent even as society changes fast. This will arise from healthier lifestyles and behaviour, healthier diets, healthier environments, improved evidence-informed health policies, and more effective solutions for health and well-being promotion, disease prevention and monitoring, and rehabilitation".*

People´s healthcare needs are different, depending on their age, stage of life and socioeconomic background. Both physical and mental health are shaped not only by personal circumstances but also by the broader societal environment. In 2019, nearly 650,000 premature deaths across the EU [27] could have been prevented with effective primary prevention and public health measures targeting modifiable risk factors such as smoking, alcohol use and lack of physical activity. In addition, an estimated 135 million people in Europe live with a disability[28], highlighting the critical need for healthcare systems that are both accessible and adaptable. With population ageing and the rising prevalence of chronic conditions due to noncommunicable diseases and injuries, this number is set to increase in the future. Upbringing, income, education levels, social and gender aspects play a critical role in shaping health risks as well as in prevention and management of disease. To leave no one behind, reduce health inequalities and support healthy and active lives for all, it is crucial to provide suitable, tailor-made solutions, including for people with specific needs. The prevention and early detection of diseases along with support and empowerment of citizens regarding their own health and wellbeing are at the core of successful public health programmes in the future.

Research and Innovation under this destination should help enhance the dialogue and coordination among stakeholders and policymakers, ensuring integration across different care settings to develop effective cross-sectoral solutions for holistic health promotion and disease prevention. Funded activities should seek to leverage the wealth of data sources, including real-world health data, to develop integrated and personalised health promotion and disease prevention strategies. These activities will benefit from emerging data resources such as the European Health Data Space (EHDS)[29] and European Open Science Cloud (EOSC)[30], and

[27] https://health.ec.europa.eu/document/download/3f9d55be-9e36-43d9-99ad-b96ac63a5b9b_en?filename=2022_healthatglance_rep_en_0.pdf

[28] https://www.who.int/europe/news-room/fact-sheets/item/disability The WHO European Region comprises 53 countries, covering a vast geographical region from the Atlantic to the Pacific oceans.

[29] https://health.ec.europa.eu/ehealth-digital-health-and-care/european-health-data-space_en

contribute to the European care strategy[31] and the digital transformation of health and care in the EU[32]. During the first four years of Horizon Europe (2021-2024), this destination focused on urgent health issues such as obesity prevention, digital health literacy, understanding health-to-disease transitions, and using Artificial Intelligence (AI) to predict chronic disease risks. It also emphasised holistic disease prevention, healthy ageing, life course approaches to physical and mental health from early childhood, and personalised disease prevention.

In this work programme part, the emphasis will be on enhancing the quality of life, autonomy, and empowerment of individuals with intellectual disabilities and their families through innovative medical, technological, and digital solutions. This includes comprehensive and personalised approaches to health promotion, disease prevention, and integrated care. Importantly, this focus addresses habilitation and rehabilitation for disabilities, which have not yet been funded under the Horizon Europe Health Cluster. This aligns with the EU Strategy for the Rights of Persons with Disabilities 2021-2030 and supports Pillar 17 of the European Pillar of Social Rights, which aims to promote the inclusion of people with disabilities.

To increase the impact of EU investments under Horizon Europe, the European Commission encourages collaboration between EU-funded projects to foster synergies through networking, joint workshops, knowledge exchange, best practices, and joint communication activities. Synergies can be explored between projects funded under the same or different topics, Clusters or pillars of Horizon Europe. This includes collaborations between projects funded under Cluster 1 and Cluster 2 for complementary actions, such as promoting social inclusion, health equity (including gender equality and support for marginalised groups), and mental health initiatives in education, work, and daily life (including through culture and the arts).

Expected impacts:

Proposals for topics under this destination should set out a credible pathway to contributing to staying healthy in a rapidly changing society, and more specifically to one or several of the following impacts:

- Citizens adopt healthier lifestyles and behaviours, make healthier choices and maintain longer a healthy, independent and active life with a reduced disease burden, including at old ages or in other vulnerable stages of life.

- Citizens are empowered to effectively manage their physical and mental health and wellbeing, monitor their health status, and interact with healthcare providers to optimise their wellbeing throughout life.

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30 https://research-and-innovation.ec.europa.eu/strategy/strategy-2020-2024/our-digital-future/open-science/european-open-science-cloud-eosc_en

31 Communication from the European Commission on the European care strategy, COM(2022) 440, 7.9.2022

32 Communication from the European Commission on enabling the digital transformation of health and care in the Digital Single Market; empowering citizens and building a healthier society, COM(2018) 233, 25.4.2018

- Children and adolescents are empowered to better monitor and manage their physical, social and mental health with a view to lifelong healthy lifestyles.
- Society benefits from reduced economic and health burdens due to preventable illness and premature mortality, efficiency is increased by targeting scarce resources in appropriate, cost-effective ways, to areas of high social return, contributing to an improvement and optimisation of health and wellbeing of citizens and reduction of health inequalities.
- Citizens' trust in knowledge-based health interventions and in guidance from health authorities is strengthened, including through improved health literacy, resulting in increased engagement in and adherence to effective strategies for health promotion, disease prevention and treatment, while digital literacy inequalities are minimised.
- Health policies and actions for health promotion and disease prevention are knowledge-based, people-centred, personalised and thus targeted and tailored to citizens' needs, and designed to reduce health inequalities.

Proposals are invited against the following topic(s):

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

Call: Cluster 1 - Health (Two stage - 2025)	
Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of between EUR 6.00 and 8.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 40.00 million.
Type of Action	Research and Innovation Actions
Admissibility conditions	The conditions are described in General Annex A. The following exceptions apply: Applicants submitting a proposal under the blind evaluation pilot (see General Annex F) must not disclose their organisation names, acronyms, logos, nor names of personnel in Part B of their first stage application (see General Annex E).
Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: In recognition of the opening of the US National Institutes of Health's programmes to European researchers, any legal entity established in the

	United States of America is eligible to receive Union funding. If projects use satellite-based earth observation, positioning, navigation and/or related timing data and services, beneficiaries must make use of Copernicus and/or Galileo/EGNOS (other data and services may additionally be used).
Award criteria	The criteria are described in General Annex D. The following exceptions apply: For the first stage, the thresholds for each criterion will be 4 (Excellence) and 4 (Impact). The overall threshold applying to the sum of the two individual scores will be set at a level that ensures the total requested budget of proposals admitted to stage 2 is as close as possible to four times the available budget, and not less than three and a half times the available budget. For the second stage, the thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.
Legal and financial set-up of the Grant Agreements	The rules are described in General Annex G. The following exceptions apply: Eligible costs will take the form of a lump sum as defined in the Decision of 7 July 2021 authorising the use of lump sum contributions under the Horizon Europe Programme – the Framework Programme for Research and Innovation (2021-2027) – and in actions under the Research and Training Programme of the European Atomic Energy Community (2021-2025) [33].

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.

[33] This decision is available on the Funding and Tenders Portal, in the reference documents section for Horizon Europe, under 'Simplified costs decisions' or through this link: https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/ls-decision_he_en.pdf

- Policymakers, health and care services, patient organisations, funders, the scientific community, and other relevant bodies are informed of the research advances and best 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'* [34] and under *'20: Developmental anomalies'* [35] including disorders of intellectual development, such as *'LD40: Complete trisomies of the autosomes'*[36] and *'LD90: Conditions with disorders of intellectual development as a relevant clinical feature'* [37] . Moreover, the three types of autism with disorders of intellectual development (6A02.1, 6A02.3 and 6A02.5) under *'6A02: Autism spectrum disorder'* [38] are also within the scope of this topic.

The focus of this topic is human-centred on the persons with long-term intellectual disabilities[39] 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

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34 Disorders of intellectual development are a group of etiologically diverse conditions originating during the developmental period characterised by significantly below average intellectual functioning and adaptive behaviour that are approximately two or more standard deviations below the mean (approximately less than the 2.3rd percentile), based on appropriately normed, individually administered standardised tests. Where appropriately normed and standardised tests are not available, diagnosis of disorders of intellectual development requires greater reliance on clinical judgment based on appropriate assessment of comparable behavioural indicators. See also https://icd.who.int/browse/2024-01/mms/en#605267007

35 https://icd.who.int/browse/2024-01/mms/en#223744320

36 https://icd.who.int/browse/2024-01/mms/en#948835301

37 https://icd.who.int/browse/2024-01/mms/en#775270311

38 https://icd.who.int/browse/2024-01/mms/en#437815624

39 Persons with disabilities include those who have long-term physical, mental, intellectual or sensory impairments which in interaction with various barriers may hinder their full and effective participation in society on an equal basis with others (Art. 1 of the Convention on the Rights of Persons with Disabilities - https://www.ohchr.org/en/instruments-mechanisms/instruments/convention-rights-persons-disabilities).

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 at this 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[40] should provide details of their clinical studies in the dedicated annex using the template provided in the submission system.

[40] Please note that the definition of clinical studies (see introduction to this work programme part) is broad and it is recommended that you review it thoroughly before submitting your application.

Destination - Living and working in a health-promoting environment

Topics under this destination are directed towards the Key Strategic Orientation 1 "*The Green transition*" and Key Strategic Orientation 3 "*A more resilient, competitive, inclusive, and democratic Europe*" of Horizon Europe's strategic plan 2025-2027.

Research and innovation supported under this destination should contribute to the following expected impact, set out in the strategic plan impact summary for the Health Cluster: "*people's living and working environments are health-promoting and sustainable thanks to a better understanding of the environmental, occupational, social, sex and gender-related, and economic determinants of health*".

The environment we live and work in is a major determinant of our health and wellbeing. The World Health Organization estimates that approximately 12.6 million deaths each year (24% of global deaths) are attributable to environmental risk factors and these factors are estimated to account for almost 20% of all deaths in Europe. Pollution in particular leads to more than 10% of annual premature deaths around the world. Environment-related disease burden also has significant economic effects. The environmental factors impacting on both physical and mental health and wellbeing are not well identified nor their effects comprehensively understood and accounted for to support evidence-based policy- and decision-making. Therefore, this destination aims at filling knowledge gaps in the understanding of the impacts on our health and wellbeing of those environmental, occupational and socio-economic risk factors that have the most significant or widespread societal impacts.

In this work programme part, Destination "*Living and working in a health-promoting environment*" focuses on the health impacts of exposures to pollution and environmental degradation in living and working environments. The results will support the EU's environment and health policies and overarching policy frameworks such as the European Green Deal, the Chemical Strategy for Sustainability, the Zero Pollution Action Plan, the 8th Environment Action Programme, the EU Strategic Framework on Health and Safety at Work as well as the WHO European Environment and Health Process (EHP). Strong collaborations across sectors and with other Horizon Europe Clusters dealing with issues such as agriculture, food, environment, climate, biodiversity, mobility, security, urban planning, social inclusion and gender will be needed to ensure that maximal societal benefits are reached. In view of increasing the impact of EU investments under Horizon Europe, the European Commission welcomes and supports cooperation between EU-funded projects to enable cross-fertilisation and create synergies. This could range from networking to joint activities such as the participation in joint workshops, the exchange of knowledge, development and adoption of best practices, or joint communication activities. All topics are open to international collaboration to address global environment and health challenges.

Expected impacts:

Proposals for topics under this destination should set out a credible pathway to contributing to living and working in a health-promoting environment, and more specifically to one or several of the following impacts:

- Policy-makers and regulators are aware and well informed about environmental, socio-economic and occupational risk factors as well as health-promoting factors across society;
- Environmental, occupational, social, economic, and health policies and practices at the EU, national and regional level are sustainable and based on solid scientific evidence.
- The upstream determinants of health are known, understood and reduced;
- The health threats and burden resulting from hazardous chemicals and air, water and soil pollution and contamination are lessened, so that the related number of deaths and illnesses is substantially reduced;
- Living and working environments in European cities and regions are healthier, more inclusive, safer, resilient and sustainable;
- The adaptive capacity and resilience of populations and health systems in the EU to climate and environmental change-related to mental and physical health risks are strengthened;
- Citizens' health and wellbeing are protected and promoted, and premature deaths, diseases and inequalities related to environmental pollution and degradation are prevented;
- Citizens understand better complex environment and health issues, and effective measures to address them and support related policies and regulations.

Proposals are invited against the following topic(s):

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

Call: Cluster 1 - Health (Two stage - 2025)	
Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of between EUR 6.00 and 7.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 40.00 million.
Type of Action	Research and Innovation Actions
Admissibility conditions	The conditions are described in General Annex A. The following exceptions apply: Applicants submitting a proposal under the blind evaluation pilot (see

	General Annex F) must not disclose their organisation names, acronyms, logos, nor names of personnel in Part B of their first stage application (see General Annex E).
Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: In recognition of the opening of the US National Institutes of Health's programmes to European researchers, any legal entity established in the United States of America is eligible to receive Union funding. The Joint Research Centre (JRC) may participate as member of the consortium selected for funding. If projects use satellite-based earth observation, positioning, navigation and/or related timing data and services, beneficiaries must make use of Copernicus and/or Galileo/EGNOS (other data and services may additionally be used).
Award criteria	The criteria are described in General Annex D. The following exceptions apply: For the first stage, the thresholds for each criterion will be 4 (Excellence) and 4 (Impact). The overall threshold applying to the sum of the two individual scores will be set at a level that ensures the total requested budget of proposals admitted to stage 2 is as close as possible to four times the available budget, and not less than three and a half times the available budget. For the second stage, the thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.
Legal and financial set-up of the Grant Agreements	The rules are described in General Annex G. The following exceptions apply: Eligible costs will take the form of a lump sum as defined in the Decision of 7 July 2021 authorising the use of lump sum contributions under the Horizon Europe Programme – the Framework Programme for Research and Innovation (2021-2027) – and in actions under the Research and Training Programme of the European Atomic Energy Community (2021-2025) [41]. 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

[41] This decision is available on the Funding and Tenders Portal, in the reference documents section for Horizon Europe, under 'Simplified costs decisions' or through this link: https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/ls-decision_he_en.pdf

	(and in determining modalities for their implementation and the specific responsibilities of projects). These activities will be included in a dedicated work package, having sufficient budget allocated to it (around 2% of the total requested budget). Depending on the scope of proposals selected for funding, these activities may include: • Attendance of regular joint meetings (e.g., common kick-off meeting and annual meetings). • Periodic report of joint activities (delivered at each reporting period). • Common dissemination and communication activities (which may include, for example: a common dissemination and communication strategy, web portal and visual identity, brochure, newsletters). • Common Data Management Strategy and Common Policy Strategy (including joint policy briefs). • Thematic workshops/trainings on issues of common interest. • Working groups on topics of common interest (e.g. data management and exchange, communication and dissemination, science-policy link, scientific synergies).

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[42] 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.

[42] See definition of FAIR data in the introduction to this work programme part.

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 [43] . 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[44]:

- 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;

[43] For guidance on the diseases and disorders under scope of this topic please consult ICD-11 for Mortality and Morbidity Statistics (who.int): https://icd.who.int/browse/2024-01/mms/en#1516623224 Chapters 6 and 8 specifically on neurodevelopmental disorders and neurocognitive disorders (including accelerated cognitive decline and chronic pain conditions).

[44] For each of the three focus areas, proposals can address one or several diseases or disorders as relevant for the research action proposed.

- 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[45] 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 [46], the EFSA activities under Environmental

[45] See definition of FAIR data in the introduction to this work programme part.
[46] https://research-and-innovation.ec.europa.eu/research-area/health/environment-and-health_en

Neurotoxicants[47] and Developmental neurotoxicity[48] and the Partnership for the Assessment of Risks from Chemicals - PARC[49].

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) [50] 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)[51] or other relevant agency (such as the European Environment Agency - EEA[52]) 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[53].

Applicants invited to the second stage should provide details of their clinical studies[54] 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-ENVHLTH-02-two-stage: Advancing knowledge on the impacts of micro- and nanoplastics on human health

Call: Cluster 1 - Health (Two stage - 2025)

47 https://etendering.ted.europa.eu/cft/cft-display.html?cftId=13967
48 https://www.efsa.europa.eu/en/art36grants/article36/gpefsaed202201-nam-projects-areas-aop-development-and-transcriptomics-risk
49 https://www.eu-parc.eu
50 https://ipchem.jrc.ec.europa.eu
51 https://echa.europa.eu
52 https://www.eea.europa.eu
53 https://research-and-innovation.ec.europa.eu/research-area/health/environment-and-health_en
54 Please note that the definition of clinical studies (see introduction to this work programme part) is broad and it is recommended that you review it thoroughly before submitting your application.

Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of between EUR 7.00 and 8.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 40.00 million.
Type of Action	Research and Innovation Actions
Admissibility conditions	The conditions are described in General Annex A. The following exceptions apply: Applicants submitting a proposal under the blind evaluation pilot (see General Annex F) must not disclose their organisation names, acronyms, logos, nor names of personnel in Part B of their first stage application (see General Annex E).
Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: In recognition of the opening of the US National Institutes of Health's programmes to European researchers, any legal entity established in the United States of America is eligible to receive Union funding. The Joint Research Centre (JRC) may participate as member of the consortium selected for funding. If projects use satellite-based earth observation, positioning, navigation and/or related timing data and services, beneficiaries must make use of Copernicus and/or Galileo/EGNOS (other data and services may additionally be used).
Award criteria	The criteria are described in General Annex D. The following exceptions apply: For the first stage, the thresholds for each criterion will be 4 (Excellence) and 4 (Impact). The overall threshold applying to the sum of the two individual scores will be set at a level that ensures the total requested budget of proposals admitted to stage 2 is as close as possible to four times the available budget, and not less than three and a half times the available budget. For the second stage, the thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.
Legal and financial set-up of	The rules are described in General Annex G. The following exceptions apply:

the Grant Agreements	Eligible costs will take the form of a lump sum as defined in the Decision of 7 July 2021 authorising the use of lump sum contributions under the Horizon Europe Programme – the Framework Programme for Research and Innovation (2021-2027) – and in actions under the Research and Training Programme of the European Atomic Energy Community (2021-2025) [55]. 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 (and in determining modalities for their implementation and the specific responsibilities of projects). These activities will be included in a dedicated work package, having sufficient budget allocated to it (around 2% of the total requested budget). Depending on the scope of proposals selected for funding, these activities may include: • Attendance of regular joint meetings (e.g., common kick-off meeting and annual meetings). • Periodic report of joint activities (delivered at each reporting period). • Common dissemination and communication activities (which may include, for example: a common dissemination and communication strategy, web portal and visual identity, brochure, newsletters). • Common Data Management Strategy and Common Policy Strategy (including joint policy briefs). • Thematic workshops/trainings on issues of common interest. • Working groups on topics of common interest (e.g. data management and exchange, communication and dissemination, science-policy link, scientific synergies).

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;

[55] This decision is available on the Funding and Tenders Portal, in the reference documents section for Horizon Europe, under 'Simplified costs decisions' or through this link: https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/ls-decision_he_en.pdf

- Public authorities and the scientific community have access to FAIR[56] 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:

[56] See definition of FAIR data in the introduction to this work programme part.

- 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[57] 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 [58] 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)[59] or other relevant agency (such as the European Environment Agency - EEA[60]) responsible for the 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[61].

Applicants invited to the second stage should provide details of their clinical studies[62] 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.

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57 See definition of FAIR data in the introduction to this work programme part.
58 https://ipchem.jrc.ec.europa.eu
59 https://echa.europa.eu
60 https://www.eea.europa.eu
61 https://research-and-innovation.ec.europa.eu/research-area/health/environment-and-health_en
62 Please note that the definition of clinical studies (see introduction to this work programme part) is broad and it is recommended that you review it thoroughly before submitting your application.

Destination - Tackling diseases and reducing disease burden

Topics under this destination are directed towards the Key Strategic Orientation 3 "*A more resilient, competitive, inclusive, and democratic Europe*" of Horizon Europe's strategic plan 2025-2027.

Research and Innovation supported under this destination should contribute to the following expected impact, set out in the strategic plan impact summary for the Health Cluster: "*healthcare providers improve their ability to tackle and manage diseases (infectious diseases, including poverty-related and neglected diseases, non-communicable and rare diseases) thereby reducing the disease burden on patients and enabling healthcare systems to perform more effectively. It can be achieved through better understanding, prevention, diagnostics, treatment, management, and cure of diseases and their co- and multi-morbidities, more effective and innovative health technologies and medical countermeasures, better ability and preparedness to manage pandemic and/or epidemic outbreaks, and improved patient safety*".

Communicable and non-communicable diseases cause the greatest amounts of premature death and disabilities and pose a major health, societal and economic threat and burden in the EU and worldwide. Many people are still suffering from these diseases and too often dying prematurely. Although many of these diseases are preventable to a large extend, only around 6% of the healthcare budgets are currently spent on preventive measures[63]. Therefore, there is the urgent need to develop new public health interventions, preventive, diagnostic and therapeutic approaches, alternatives to antimicrobials, as well as to improve existing preparedness and response strategies to create tangible impacts, taking into account sex/gender-related issues. In this regard, Research and Innovation will require international cooperation to pool the best expertise and know-how available worldwide, to access world-class research infrastructures and to leverage critical scales of investments on priority needs through a better alignment with other funders of international cooperation in health Research and Innovation. The continuation of international partnerships and cooperation with international organisations is particularly needed to combat infectious diseases, to address brain health, to respond to public health needs, including the global burden of non-communicable diseases.

In this work programme part, Destination "*Tackling diseases and reducing disease burden*" will focus on major societal challenges linked to the Commission's political priorities such as the fight against non-communicable and communicable diseases, mental health and better treatment of mental, behavioural and neurodevelopmental diseases, preparedness and response to and surveillance of health threats and epidemics, reduction and treatment of the number of antimicrobial-resistant infections. In particular, the topics under this destination will support activities aiming at: i) new effective treatment options for patients suffering from

[63] Preventive healthcare expenditure as a share of the current expenditure on healthcare https://ec.europa.eu/eurostat/statistics-explained/index.php?title=File:Preventive_healthcare_expenditure_as_a_share_of_current_expenditure_on_healthcare,_2021_(%25)_HCE2024.png

antimicrobial resistant (AMR) infections; ii) innovative therapeutic interventions and complementary approaches for patients suffering from mental, behavioural and neurodevelopmental disorders; iii) new prevention and treatment options for infectious diseases with epidemic potential; iv) Artificial Intelligence (AI) based tools and technologies for pandemic preparedness and response; v) implementation research on strengthening health systems in the context of non-communicable diseases; vi) supporting the Global Research Collaboration for Infectious Disease Preparedness; vii) setting up the European Partnership for Brain Health; and viii) supporting efforts of the European Partnership fostering a European Research Area for health research (ERA4Health)[64] in particular in funding large-scale multi-country Investigator-Initiated Clinical Studies (IICS) on various health interventions addressing important public health needs.

In view of increasing the impact of EU investments under Horizon Europe, the European Commission welcomes and supports cooperation between EU-funded projects to enable cross-fertilisation and other synergies. This could range from networking to joint activities such as the participation in joint workshops, the exchange of knowledge, the development and adoption of best practices, or joint communication activities. Opportunities for potential synergies exist between projects funded under the same topic but also between other projects funded under another topic, Cluster or pillar of Horizon Europe (but also with ongoing projects funded under Horizon 2020). In particular, this could involve projects related to European health research infrastructures (under pillar I of Horizon Europe), the EIC strategic challenges on health and EIT-KIC Health (under pillar III of Horizon Europe), or in areas cutting across the health and other Clusters (under pillar II of Horizon Europe). For instance, with Cluster 3 *"Civil security for society"* such as on health security/emergencies (preparedness and response, medical countermeasures, epidemic outbreaks/pandemics, natural disasters and technological incidents, bioterrorism); with Cluster 4 *"Digital, Industry and Space"* such as on AI-based tools and technologies (e.g. detection, management and monitoring of an epidemic at population levels, and the diagnosis, treatment, and prevention at the level of individuals); or with Cluster 6 *"Food, bioeconomy, natural resources, agriculture and environment"* such as on antimicrobial resistance - AMR (e.g. new effective treatment options, alternatives to antibiotics).

Some Research and Innovation actions under this destination should support the mission of the European Health Emergency and Response Authority (HERA) to strengthen Europe's ability to prevent, detect, and rapidly respond to cross-border health emergencies by ensuring the availability and access to key medical countermeasures. Furthermore, synergies will be sought between this destination and the implementation of the EU4Health Programme (2021-2027) [65] . These synergies and complementarities could be achieved, notably through mechanisms based on feedback loops, enabling on the one hand to identify policy needs that should be prioritised in Research and Innovation actions and facilitating on the other hand the

64 https://era4health.eu

65 https://health.ec.europa.eu/funding/eu4health-programme-2021-2027-vision-healthier-european-union_en

implementation of research results into policy actions and clinical practice, thereby providing an integrated response across sectors and policy fields.

Expected impacts:

Proposals for topics under this destination should set out a credible pathway to contributing to tackling diseases and reducing disease burden, and more specifically to several of the following impacts:

- Health burden of diseases in the EU and worldwide is reduced through effective disease management, including through the development and integration of innovative preventive, diagnostic and therapeutic approaches, digital and other people-centred solutions for healthcare.

- Premature mortality from non-communicable diseases is reduced by one third (by 2030), mental health and wellbeing are promoted, and the voluntary targets of the WHO Global Action Plan for the Prevention and Control of NCDs[66] 2013-2020 are attained (by 2025), with an immediate impact on the related disease burden (Disability-Adjusted Life Years - DALYs)[67,68,69].

- Healthcare systems benefit from strengthened Research and Innovation expertise, human capacities and know-how for combatting communicable and non-communicable diseases, including through international cooperation.

- Citizens benefit from reduced (cross-border) health threat of epidemics and AMR pathogens, in the EU and worldwide[70,71].

- Patients and citizens are knowledgeable of disease threats, involved and empowered to make and shape decisions for their health, and better adhere to knowledge-based disease management strategies and policies (especially for controlling outbreaks and emergencies).

Proposals are invited against the following topic(s):

66 Non-communicable diseases
67 https://www.who.int/publications/i/item/9789241506236
68 Including for instance the following voluntary targets (against the 2010 baseline): A 25% relative reduction in the overall mortality from cardiovascular diseases, cancer, diabetes, or chronic respiratory diseases; Halt the rise in diabetes and obesity; An 80% availability of the affordable basic technologies and essential medicines, including generics, required to treat major non-communicable diseases in both public and private facilities.
69 Disability-adjusted life year (DALY) is a quantitative indicator of overall disease burden, expressed as the number of years lost due to ill-health, disability or early death.
70 WHO global action plan on antimicrobial resistance, 2015
71 EU One Health Action Plan against AMR, 2017

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

Call: Cluster 1 - Health (Single stage - 2025)	
Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of around EUR 15.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 45.00 million.
Type of Action	Research and Innovation Actions
Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: In recognition of the opening of the US National Institutes of Health's programmes to European researchers, any legal entity established in the United States of America is eligible to receive Union funding. If projects use satellite-based earth observation, positioning, navigation and/or related timing data and services, beneficiaries must make use of Copernicus and/or Galileo/EGNOS (other data and services may additionally be used). The following exceptions apply: subject to restrictions for the protection of European communication networks.
Award criteria	The criteria are described in General Annex D. The following exceptions apply: The thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.
Legal and financial set-up of the Grant Agreements	The rules are described in General Annex G. The following exceptions apply: Eligible costs will take the form of a lump sum as defined in the Decision of 7 July 2021 authorising the use of lump sum contributions under the Horizon Europe Programme – the Framework Programme for Research and Innovation (2021-2027) – and in actions under the Research and Training Programme of the European Atomic Energy Community (2021-2025) [72].

[72] This decision is available on the Funding and Tenders Portal, in the reference documents section for Horizon Europe, under 'Simplified costs decisions' or through this link: https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/ls-decision_he_en.pdf

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[73] 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[74].

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.

[73] https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance
[74] https://www.who.int/news/item/22-06-2022-22-06-2022-lack-of-innovation-set-to-undermine-antibiotic-performance-and-health-gains

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[75].

Lessons learned from previous clinical trials that failed[76] (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)[77]. 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

75 https://iris.who.int/bitstream/handle/10665/376776/9789240093461-eng.pdf?sequence=1
76 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9598614
77 https://www.ema.europa.eu/en/human-regulatory-overview/research-development/scientific-advice-protocol-assistance

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)[78] 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[79] data principles, adopt wherever relevant, data standards and data sharing/access good practices, and apply good practices for GDPR[80] 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 studies[81] 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

Call: Cluster 1 - Health (Two stage - 2025)	
Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of between EUR 6.00 and 8.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 50.00 million.
Type of Action	Research and Innovation Actions
Admissibility conditions	The conditions are described in General Annex A. The following exceptions apply:

78 https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32003H0361
79 See definition of FAIR data in the introduction to this work programme part.
80 General Data Protection Regulation: https://gdpr-info.eu
81 Please note that the definition of clinical studies (see introduction to this work programme part) is broad and it is recommended that you review it thoroughly before submitting your application.

	Applicants submitting a proposal under the blind evaluation pilot (see General Annex F) must not disclose their organisation names, acronyms, logos, nor names of personnel in Part B of their first stage application (see General Annex E).
Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: In recognition of the opening of the US National Institutes of Health's programmes to European researchers, any legal entity established in the United States of America is eligible to receive Union funding. If projects use satellite-based earth observation, positioning, navigation and/or related timing data and services, beneficiaries must make use of Copernicus and/or Galileo/EGNOS (other data and services may additionally be used). The following exceptions apply: subject to restrictions for the protection of European communication networks.
Award criteria	The criteria are described in General Annex D. The following exceptions apply: For the first stage, the thresholds for each criterion will be 4 (Excellence) and 4 (Impact). The overall threshold applying to the sum of the two individual scores will be set at a level that ensures the total requested budget of proposals admitted to stage 2 is as close as possible to four times the available budget, and not less than three and a half times the available budget. For the second stage, the thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.
Legal and financial set-up of the Grant Agreements	The rules are described in General Annex G. The following exceptions apply: Eligible costs will take the form of a lump sum as defined in the Decision of 7 July 2021 authorising the use of lump sum contributions under the Horizon Europe Programme – the Framework Programme for Research and Innovation (2021-2027) – and in actions under the Research and Training Programme of the European Atomic Energy Community (2021-2025) [82].

[82] This decision is available on the Funding and Tenders Portal, in the reference documents section for Horizon Europe, under 'Simplified costs decisions' or through this link: https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/ls-decision_he_en.pdf

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[83] 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[84] 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.

83 Innovative interventions should be based on new and/or alternative approaches that are aimed at achieving a lasting therapeutic benefit. The innovative intervention should be a combination of a product based on an active substance that is complemented by another multidisciplinary approach.

84 See definition of FAIR data in the introduction to this work programme part.

85 If proposals concern drug addiction, they are encouraged to liaise with the EU Drugs Agency.

The disorders within the scope of this topic fall under Chapter 6 of the International Classification of Diseases[86]. Rare diseases are excluded[87].

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[88], 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[89], EATRIS[90], EBRAINS[91], BBMRI[92], EuroBioImaging[93],

86 International Classification of Diseases 11th Revision (ICD-11), developed by the World Health Organization (WHO); Chapter 6: 'Mental, behavioural or neurodevelopmental disorders'.

87 Rare diseases, as defined by the European Union Regulation on Orphan Medicinal Products (1999), being a disease that affects not more than 1 person per 2000 in the European population (https://www.orpha.net/).

88 Generative AI is a type of AI technology that can generate various forms of new content such as text, images, sounds, and even code, such as for programming or gene sequencing (https://ec.europa.eu/newsroom/dae/redirection/document/101621).

89 https://ecrin.org

90 https://eatris.eu

91 https://www.ebrains.eu

92 https://www.bbmri-eric.eu

93 https://www.eurobioimaging.eu

European Genomic Data Infrastructure[94], 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)[95] 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[96] 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-03: Development of antibodies and antibody-derived proteins for the prevention and treatment of infectious diseases with epidemic potential

Call: Cluster 1 - Health (Single stage - 2025)	
Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of around EUR 10.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 50.00 million.

94 https://gdi.onemilliongenomes.eu
95 https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32003H0361
96 Please note that the definition of clinical studies (see introduction to this work programme part) is broad and it is recommended that you review it thoroughly before submitting your application.

Type of Action	Research and Innovation Actions
Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: In recognition of the opening of the US National Institutes of Health's programmes to European researchers, any legal entity established in the United States of America is eligible to receive Union funding. If projects use satellite-based earth observation, positioning, navigation and/or related timing data and services, beneficiaries must make use of Copernicus and/or Galileo/EGNOS (other data and services may additionally be used).
Award criteria	The criteria are described in General Annex D. The following exceptions apply: The thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.
Legal and financial set-up of the Grant Agreements	The rules are described in General Annex G. The following exceptions apply: Eligible costs will take the form of a lump sum as defined in the Decision of 7 July 2021 authorising the use of lump sum contributions under the Horizon Europe Programme – the Framework Programme for Research and Innovation (2021-2027) – and in actions under the Research and Training Programme of the European Atomic Energy Community (2021-2025) [97].

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.

[97] This decision is available on the Funding and Tenders Portal, in the reference documents section for Horizon Europe, under 'Simplified costs decisions' or through this link: https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/ls-decision_he_en.pdf

- 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)[98] 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.

[98] https://www.who.int/teams/health-product-policy-and-standards/standards-and-specifications/gmp

- 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)[99] 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[100].

Applicants should provide details of their clinical studies[101] 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-04: Leveraging artificial intelligence for pandemic preparedness and response

Call: Cluster 1 - Health (Single stage - 2025)	
Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of between EUR 6.00 and 8.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.

99 https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32003H0361
100 https://isidore-project.eu
101 Please note that the definition of clinical studies (see introduction to this work programme part) is broad and it is recommended that you review it thoroughly before submitting your application.

Indicative budget	The total indicative budget for the topic is EUR 35.00 million.
Type of Action	Research and Innovation Actions
Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: In recognition of the opening of the US National Institutes of Health's programmes to European researchers, any legal entity established in the United States of America is eligible to receive Union funding. If projects use satellite-based earth observation, positioning, navigation and/or related timing data and services, beneficiaries must make use of Copernicus and/or Galileo/EGNOS (other data and services may additionally be used). The following exceptions apply: subject to restrictions for the protection of European communication networks.
Award criteria	The criteria are described in General Annex D. The following exceptions apply: The thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.

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[102] 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 existing and emerging data research infrastructures and the future European Health Data Space (EHDS)[103] and the European Open Science Cloud (EOSC)[104] architectures and research environments, while comprehensively addressing cybersecurity, data privacy, trustworthiness, equity and data quality, interoperability and access modalities.

102 See definition of FAIR data in the introduction to this work programme part.
103 https://health.ec.europa.eu/ehealth-digital-health-and-care/european-health-data-space_en
104 https://research-and-innovation.ec.europa.eu/strategy/strategy-2020-2024/our-digital-future/open-science/european-open-science-cloud-eosc_en

- 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)[105] 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 studies[106] should provide details of their clinical studies in the dedicated annex using the template provided in the submission system.

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

Call: Cluster 1 - Health (Single stage - 2025)	
Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of around EUR 2.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a

105 https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32003H0361

106 Please note that the definition of clinical studies (see introduction to this work programme part) is broad and it is recommended that you review it thoroughly before submitting your application.

	proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 2.00 million.
Type of Action	Coordination and Support Actions
Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: In recognition of the opening of the US National Institutes of Health's programmes to European researchers, legal entities established in the United States of America may exceptionally participate as a beneficiary or affiliated entity, and are eligible to receive Union funding. Coordinators of projects must be legal entities established in an EU Member State or Associated Country. If projects use satellite-based earth observation, positioning, navigation and/or related timing data and services, beneficiaries must make use of Copernicus and/or Galileo/EGNOS (other data and services may additionally be used).
Award criteria	The criteria are described in General Annex D. The following exceptions apply: The thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.
Legal and financial set-up of the Grant Agreements	The rules are described in General Annex G. The following exceptions apply: Eligible costs will take the form of a lump sum as defined in the Decision of 7 July 2021 authorising the use of lump sum contributions under the Horizon Europe Programme – the Framework Programme for Research and Innovation (2021-2027) – and in actions under the Research and Training Programme of the European Atomic Energy Community (2021-2025) [107].

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:

[107] This decision is available on the Funding and Tenders Portal, in the reference documents section for Horizon Europe, under 'Simplified costs decisions' or through this link: https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/ls-decision_he_en.pdf

- 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)[108], 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;

[108] https://www.glopid-r.org

- 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-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)

Call: Cluster 1 - Health (Single stage - 2025)	
Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of between EUR 3.00 and 4.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 20.00 million.
Type of Action	Research and Innovation Actions
Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: In recognition of the opening of the US National Institutes of Health's programmes to European researchers, any legal entity established in the United States of America is eligible to receive Union funding. If projects use satellite-based earth observation, positioning, navigation and/or related timing data and services, beneficiaries must make use of Copernicus and/or Galileo/EGNOS (other data and services may additionally be used).
Award criteria	The criteria are described in General Annex D. The following exceptions apply: The thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.

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)[109]. 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[110]. 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

109 https://www.gacd.org

110 Kruk ME, Pate M, Mullan Z. Introducing The Lancet Global Health Commission on High-Quality Health Systems in the SDG Era. Lancet Glob Health. 2017 May;5(5):e480-e481.

focused on disease and hospital-based care, to a more holistic model, involving communities and primary care, and focused on maintaining health[111,112]. 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[113].

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).

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111 Hunter DJ, Bengoa R, Meeting the challenge of health system transformation in European countries, Policy and Society, Volume 42, Issue 1, March 2023, Pages 14–27.

112 The WHO has produced a series of recommendations for strengthening health systems, to improve capacity and services to tackle NCDs, with an eye to understanding how the service improvement will be scaled up system-wide; https://apps.who.int/gb/ebwha/pdf_files/WHA66-REC1/A66_R1_ANX4-en.pdf

113 Health equity is achieved when everyone can attain their full potential for health and wellbeing.

Proposals should address all the following activities[114]:

- 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)[115], 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.

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114 The following types of proposals are not in the scope of this topic: i) proposals with the primary aim of informing the development and/or selection of an intervention for a given context, where the implementation component will be explored in a future project (i.e. standalone feasibility projects);ii) epidemiological cohorts; iii) etiological work, mechanistic, or epidemiological research, unless an essential component of a focused study to develop implementation research approaches; iv) clinical trials, validation studies, or intervention efficacy studies for a new or established pharmacological agent or behavioural intervention.

115 https://www.who.int/health-topics/universal-health-coverage

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)[116,117].

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

116 Examples of frameworks include (this list is not exclusive): i) Consolidated Framework for Implementation Research (CFIR); ii) the context enhanced (RE-AIM) Reach, Effectiveness, Adoption, Implementation, Maintenance); iii) Practical Robust Implementation and Sustainability Model (PRISM) frameworks.

117 The following are potential interventions or strategies that applicants may consider in their implementation plan (please note that this is not an exhaustive list): i) Strengthening within the workforce including: training; task shifting within healthcare services; multi-disciplinary teams; community outreach; and the care continuum; ii) Changes in health or related facilities, including relationships, engagement and linkages between facility levels (primary, secondary, tertiary), regional specialist care, pharmacies, and community healthcare; iii) Digital or information technologies in health systems to improve condition management; shared records; coordination in continuum of care; self-management and equitable health outcomes; iv) Implementation of new technologies, innovations for screening, earlier diagnosis and better management of NCDs; v) Ensuring equitable access to good quality medicines (priority medicine lists and financing, monitoring; procurement and distribution; charging and fees); vi) Health policy entrepreneurship linked to solving or capitalizing a policy or practice issues/innovations that have a clear link with service delivery or health promotion with NCDs.

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 studies[118] should provide details of their clinical studies in the dedicated annex using the template provided in the submission system.

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

Call: Partnerships in Health (2025)	
Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of around EUR 150.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 150.00 million.
Type of Action	Programme Co-fund Action
Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: In recognition of the opening of the US National Institutes of Health's programmes to European researchers, any legal entity established in the United States of America is eligible to receive Union funding. Because the US contribution will be considered for the calculation of the EU contribution to the partnership, the concerned consortium of research

[118] Please note that the definition of clinical studies (see introduction to this work programme part) is broad and it is recommended that you review it thoroughly before submitting your application.

	funders from eligible EU Members States and Associated Countries must expressly agree to this participation. The following exceptions apply: subject to restrictions for the protection of European communication networks.
Award criteria	The criteria are described in General Annex D. The following exceptions apply: The thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.
Legal and financial set-up of the Grant Agreements	The rules are described in General Annex G. The following exceptions apply: Beneficiaries may provide financial support to third parties. The support to third parties can only be provided in the form of grants. Financial support provided by the participants to third parties is one of the primary activities of the action in order to be able to achieve its objectives. Given the type of action and its level of ambition, which could entail costly pilot clinical studies, the maximum amount to be granted to each third party is EUR 3.00 million. However, if the objectives of the action would otherwise be impossible or overly difficult (and duly justified) the maximum amount may be higher. The funding rate is up to 30% of the eligible costs.
Total indicative budget	The total indicative budget for the topic is EUR 150 million committed in annual instalments over the 3 years, 2025-2027 (EUR 46 million from the 2025 budget, EUR 54 million from the 2026 budget and EUR 50 million from the 2027 budget).

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 health[119], 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

[119] In the context of the partnership, 'brain health' should be interpreted along the lines of the World Health Organisation's (WHO) definition ('Brain health is the state of brain functioning across cognitive, sensory, social-emotional, behavioural and motor domains, allowing a person to realise their full potential over the life course, irrespective of the presence or absence of disorders') and includes both neurological and mental 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[120], as well as to the "Communication on a comprehensive approach to mental health" (COM(2023) 298 final)[121].

The partnership should also contribute from the research and innovation angle to achieving the objectives of the Pharmaceutical Strategy for Europe[122], 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[123].

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)[124], which aims to ensure high quality, affordable and accessible care services for all ages. By fostering data sharing and boosting FAIR[125] and open data, the

120 https://health.ec.europa.eu/publications/eu-non-communicable-diseases-ncds-initiative-guidance-document_en
121 https://health.ec.europa.eu/publications/comprehensive-approach-mental-health_en
122 https://health.ec.europa.eu/medicinal-products/pharmaceutical-strategy-europe_en
123 https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32021R0522
124 https://ec.europa.eu/social/main.jsp?langId=en&catId=89&furtherNews=yes&newsId=10382
125 See definition of FAIR data in the introduction to this work programme part.

partnership should also contribute to the implementation of the European Health Data Space (EHDS)[126].

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[127].

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[128], EATRIS[129], EBRAINS[130], BBMRI[131], EuroBioImaging[132], European Genomic Data Infrastructure[133], 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.

126 https://health.ec.europa.eu/ehealth-digital-health-and-care/european-health-data-space_en
127 https://www.brainhealth-partnership.eu
128 https://ecrin.org
129 https://eatris.eu
130 https://www.ebrains.eu
131 https://www.bbmri-eric.eu
132 https://www.eurobioimaging.eu
133 https://gdi.onemilliongenomes.eu

- 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)[134], (ii) the Network of European Funding for Neuroscience Research (NEURON)[135], and (iii) the Human Brain Project[136] (HBP, a FET Flagship project), as well as the digital research infrastructure EBRAINS[137], which was put in place by HBP, and the Coordination and Support Actions (CSAs) BrainHealth[138] and European Brain Research Area (EBRA)[139].

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

134 https://www.neurodegenerationresearch.eu
135 https://www.neuron-eranet.eu
136 https://www.humanbrainproject.eu/en
137 https://ebrains.eu
138 https://www.brainhealth-partnership.eu
139 https://www.ebra.eu

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'[140], 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)[141].

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.

140 https://research-and-innovation.ec.europa.eu/document/download/846561ef-7696-4957-802a-69d19ea6b739_en?filename=ec_rtd_coherence-synergies-of-ep-under-he.pdf

141 https://research-and-innovation.ec.europa.eu/strategy/strategy-2020-2024/our-digital-future/open-science/european-open-science-cloud-eosc_en

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

Call: Partnerships in Health (2025)	
Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of around EUR 77.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 77.00 million.
Type of Action	Programme Co-fund Action
Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: The proposal must be submitted by the coordinator of the consortium funded under topic HORIZON-HLTH-2022-DISEASE-03-01: "European partnership fostering a European Research Area (ERA) for health research". This eligibility condition is without prejudice to the possibility to include additional partners. The proposed EU contribution of Phase 2 devoted to activities related to funding multi-country Investigator-Initiated Clinical Studies must be between 60% and 70% of the EU contribution of Phase 2. In recognition of the opening of the US National Institutes of Health's programmes to European researchers, any legal entity established in the United States of America is eligible to receive Union funding. Because the US contribution will be considered for the calculation of the EU contribution to the partnership, the concerned consortium of research funders from eligible EU Members States and Associated Countries must expressly agree to this participation.
Award criteria	The criteria are described in General Annex D. The following exceptions apply: The thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.
Procedure	The procedure is described in General Annex F. The following exceptions apply: If the proposal is successful, the next stage of the procedure will be grant agreement amendment preparations. If the outcome of amendment preparations is an award decision, the coordinator of the consortium funded under topic HORIZON-HLTH-

	2022-DISEASE-03-01: "European partnership fostering a European Research Area (ERA) for health research" will be invited to submit an amendment to the grant agreement, on behalf of the beneficiaries.
Legal and financial set-up of the Grant Agreements	The rules are described in General Annex G. The following exceptions apply: This action is intended to be implemented in the form of an amendment of the grant agreement concluded pursuant to Article 24(2) of the Horizon Europe Regulation. For the additional activities covered by this action: • The funding rate is 30% of the eligible costs. • Beneficiaries may provide financial support to third parties (FSTP). The support to third parties can only be provided in the form of grants. 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. Given the novelty of funding multi-country clinical studies which can result in different strategies being implemented (e.g. a few projects with relatively hight budget per partner) and taking into consideration that clinical studies entail very high costs, the maximum amount to be granted to each third party is EUR 10.00 million for the duration of the partnership. However, if the objectives of the action would otherwise be impossible or overly difficult (and duly justified) the maximum amount may be higher. • The starting date of the grant awarded under this topic may be as of the submission date of the application. Applicants must justify the need for a retroactive starting date in their application. Costs incurred from the starting date of the action may be considered eligible (and will be reflected in the entry into force date of the amendment to the grant agreement).
Total indicative budget	The total indicative budget for the duration of the co-funded Partnership is EUR 110 million.

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)[142] 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[143]), 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

142 In this text, IICS means a clinical study in which a health technology (e.g. a medicinal product, a medical device, an *in vitro* diagnostic medical device, a surgical or other medical intervention) is tested in humans, independently from commercial interest and for public health benefits.

143 The Pharmaceutical Strategy for Europe refers to including representative participation of population groups, for example gender and age groups, that are likely to use the medicinal product investigated in the clinical trials to ensure appropriate safety and efficacy.

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 [144] - "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

144 https://era4health.eu

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 [145] 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[146]); 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)[147] for sponsor-delegated activities related to implementation of clinical studies, and Biobanking and Biomolecular Resources Research Infrastructure (BBMRI)[148] 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

145 Wide definition of health intervention: medicinal products, medical devices, surgical or other invasive procedures, other medical interventions including preventative measures.
146 https://www.eppermed.eu
147 https://ecrin.org
148 https://www.bbmri-eric.eu

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.

Destination - Ensuring equal access to innovative, sustainable, and high-quality healthcare

Topics under this destination are directed towards the Key Strategic Orientation 2 "*The Digital transition*" and Key Strategic Orientation 3 "*A more resilient, competitive, inclusive, and democratic Europe*" of Horizon Europe's strategic plan 2025-2027.

Research and Innovation supported under this destination should contribute to the following expected impact, set out in the strategic plan impact summary for the Health Cluster: *"healthcare systems provide equal access to innovative, sustainable and high-quality healthcare thanks to the development and uptake of safe, cost-effective and people-centred solutions. This is to be accompanied by management models focusing on population health, health systems resilience, and health equity and patient safety, and also improved evidence-informed health policies".*

Health systems are affected by limitations in sustainability and resilience, challenges which were reinforced by the COVID-19 crisis that also revealed inequalities in access to high-quality healthcare services. Our health systems need to become more effective, efficient, accessible, fiscally and environmentally sustainable, and resilient in order to cope with public health emergencies, support healthcare workforce, adapt to environmental challenges like climate change, and contribute to social justice and cohesion. The transformation and modernisation of our health systems will remain an important challenge for many years to come, but it also holds a significant opportunity to generate evidence, leverage existing and emerging solutions, implement digital and data-driven innovation and develop more accessible, cost-effective, flexible and equitable health systems.

Research and Innovation under this destination aim to support healthcare systems in their transformation to ensure fair access to high-quality, sustainable healthcare for all citizens. Funded activities should develop innovative, practical, financially sound, and scalable solutions across various dimensions of healthcare systems. These activities should improve governance and provide decision-makers with new evidence, innovative tools and technologies while ensuring long-term fiscal, environmental and climate sustainability, making sure the health sector reduces its carbon footprint and supports sustainable use of resources. A patient-centred approach should be adopted to improve patients' health outcomes, empower patients, foster active dialogue among stakeholders (e.g., citizens, patients, caregivers, healthcare providers), and encourage social innovation. Support to healthcare professionals and providers, with an adequate allocation of resources according to citizen's needs and preferences, are key in these Research and Innovation actions.

Research and Innovation should help deliver solutions that are scalable and transferable between different types of healthcare systems in different national, regional, and local contexts. It should also provide knowledge that supports the transfer of solutions between countries, including measures to address health inequalities. Research and Innovation activities under this destination will contribute to, among other things, the European care

strategy[149], the digital transformation of health and care in the EU[150], the EU digital strategy, the EU Artificial Intelligence Strategy[151], the strategic investment framework in trustworthy Artificial Intelligence for the Union[152], the EU strategy on adaptation to climate change[153], and the European Green Deal. They can also build upon and contribute to the Europe's Beating Cancer Plan[154] and Cancer Mission under Horizon Europe.

In this work programme part, the focus of this destination will be on:

- Enhancing healthcare efficiency and cost-effectiveness with Generative Artificial Intelligence (AI) solutions, augmented by other AI tools that aim to support healthcare professionals in decision making, offer improved personalised care, and to develop sustainable practices, by leveraging the availability of the different types of health data.

- Improving patient engagement and empowerment by increasing public knowledge, trust and acceptance of AI tools, leading to better understanding of medical information and to improved patient outcomes, while also improving the communication between patients and healthcare providers, as well as between healthcare providers.

To increase the impact of EU investments under Horizon Europe, the European Commission encourages and supports cooperation among EU-funded projects to foster cross-fertilisation and synergies. This includes networking, joint activities such as workshops, knowledge exchange, best practices development, and joint communication activities. Synergies can be explored not only between projects funded under the same topic, but also between projects funded under other topics, Clusters or pillars of Horizon Europe. For instance, collaborations may arise between projects related to European health research infrastructures (under Pillar I), the EIC strategic challenges on health (under Pillar III), or across the Clusters of Pillar II such as Cluster 2 "Culture, Creativity and Inclusive Society" focusing e.g., on the long-term sustainability of public health systems (e.g., economic and organisational models and measures for cost effectiveness and fiscal sustainability), or Cluster 4 "Digital, Industry and Space" focusing on the digitalisation of the health sector, including the use of AI.

Expected impacts:

149 Communication from the European Commission on the European care strategy, COM(2022) 440, 7.9.2022

150 Communication from the European Commission on enabling the digital transformation of health and care in the Digital Single Market; empowering citizens and building a healthier society, COM(2018) 233, 25.4.2018

151 Commission Communication on Artificial Intelligence for Europe; COM(2018) 237 final: https://digital-strategy.ec.europa.eu/en/policies/european-approach-artificial-intelligence; https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=COM:2018:237:FIN

152 Communication on boosting startups and innovation in trustworthy artificial intelligence | Shaping Europe's digital future (europa.eu): https://digital-strategy.ec.europa.eu/en/library/communication-boosting-startups-and-innovation-trustworthy-artificial-intelligence

153 Commission Communication on Forging a climate-resilient Europe - the new EU Strategy on Adaptation to Climate Change COM(2021) 82 final: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52021DC0082

154 Communication from the European Commission on Europe's Beating Cancer Plan, COM(2021) 44, 3.2.2021

Proposals for topics under this destination should set out a credible pathway to contributing to ensuring access to innovative, sustainable and high-quality healthcare, and more specifically to one or several of the following impacts:

- Health and social care services and systems have improved governance mechanisms, making them more effective, efficient, accessible, resilient, trusted and sustainable, both fiscally and environmentally. This includes shifting from hospital-centred to community-based, people-centred and integrated healthcare structures, embedding technological innovations and prioritising health promotion and disease prevention.

- Healthcare providers are trained and equipped with the skills and competences needed for future healthcare systems that are modernised, digitally transformed and equipped with safe innovative tools, technologies and digital solutions for healthcare. This will involve better patient management, improved patient engagement, reorganised workflows, and improved resource management.

- Citizens play a key role in managing their own healthcare, informal carers (including unpaid carers) are fully supported (e.g. by preventing overburdening and economic stress) and the specific needs of vulnerable groups are recognised and addressed. This includes improved access to healthcare services, financial risk protection, timely access to quality healthcare services including essential medicines and vaccines.

- Health policy and systems adopt a holistic approach - considering individuals, communities, organisations, society - in evaluating health outcomes, public health interventions, healthcare organisation, and decision-making. They benefit from evidence based, scalable and transferable healthcare solutions (e.g., between countries and healthcare settings) including for addressing health inequalities and ensuring environmental and climate sustainability in the health sector.

The actions resulting from the topics under this destination will also create strong opportunities for synergies with actions stemming from the EU4Health programme, in particular contributing to the goals under the general objective "*protecting people in the Union from serious cross-border threats to health*" and specific objective 4 "*to strengthen health systems, their resilience and resource efficiency*".

Proposals are invited against the following topic(s):

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

Call: Cluster 1 - Health (Single stage - 2025)	
Specific conditions	
Expected EU contribution per	The Commission estimates that an EU contribution of between EUR 15.00 and 20.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and

project	selection of a proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 40.00 million.
Type of Action	Research and Innovation Actions
Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: In recognition of the opening of the US National Institutes of Health's programmes to European researchers, any legal entity established in the United States of America is eligible to receive Union funding. The Joint Research Centre (JRC) may participate as member of the consortium selected for funding. If projects use satellite-based earth observation, positioning, navigation and/or related timing data and services, beneficiaries must make use of Copernicus and/or Galileo/EGNOS (other data and services may additionally be used). The following exceptions apply: subject to restrictions for the protection of European communication networks.
Award criteria	The criteria are described in General Annex D. The following exceptions apply: The thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.

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)[155] 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.

[155] Generative AI is a type of AI technology that can generate various forms of new content such as text, images, sounds, and even code, such as for programming or gene sequencing (https://ec.europa.eu/newsroom/dae/redirection/document/101621).

- 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[156].

    - Appropriate solutions to identify and mitigate potential bias and confounding[157] 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[158], when relevant and in accordance with the specific access terms and conditions.

The proposals should adhere to the FAIR[159] data principles and apply GDPR[160] 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

156 Ethics Guidelines for Trustworthy AI, published by the European Commission's High Level Expert Group on Artificial Intelligence: https://ec.europa.eu/futurium/en/ai-alliance-consultation.1.html

157 Guidelines on the responsible use of generative AI in research developed by the European Research Area Forum: https://research-and-innovation.ec.europa.eu/news/all-research-and-innovation-news/guidelines-responsible-use-generative-ai-research-developed-european-research-area-forum-2024-03-20_en

158 https://digital-strategy.ec.europa.eu/en/policies/ai-factories

159 See definition of FAIR data in the introduction to this work programme part.

160 General Data Protection Regulation: https://gdpr-info.eu

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[161], European Genomic Data Infrastructure[162], Cancer Image Europe[163], European Open Science Cloud[164], EBRAINS[165] 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[166], 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

161 https://health.ec.europa.eu/ehealth-digital-health-and-care/european-health-data-space_en
162 https://gdi.onemilliongenomes.eu
163 https://cancerimage.eu
164 https://research-and-innovation.ec.europa.eu/strategy/strategy-2020-2024/our-digital-future/open-science/european-open-science-cloud-eosc_en
165 https://www.ebrains.eu
166 https://digital-strategy.ec.europa.eu/en/policies/ai-factories

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[167] should provide details of their clinical studies in the dedicated annex using the template provided in the submission system.

167 Please note that the definition of clinical studies (see introduction to this work programme part) is broad and it is recommended that you review it thoroughly before submitting your application.

Destination - Developing and using new tools, technologies and digital solutions for a healthy society

Topics under this destination are directed towards the Key Strategic Orientation 2 "*The Digital Transition*" and Key Strategic Orientation 3 "*A More Resilient, Competitive, Inclusive, and Democratic Europe*" of Horizon Europe's strategic plan 2025-2027.

Research and Innovation supported under this destination should contribute to the following expected impact, set out in the strategic plan impact summary for the Health Cluster: "*Health technologies, data, new tools, and digital solutions are applied effectively thanks to their inclusive, ethically sound, secure and sustainable delivery, integration and deployment in health policies and in health and care systems.*"

The Health Cluster will continue work to develop and stimulate the uptake of new technologies and digital solutions to improve healthcare and health systems. This includes using technology to help people better understand and use health information, promote healthier lifestyles, improve pandemic/epidemic preparedness, prevent diseases, provide better diagnoses and more personalised treatments and care solutions, and improve access to health and care systems while making sure that even groups with limited access to good healthcare can benefit. The Cluster will help the EU ensure leadership in breakthrough health and medical technologies and achieve open strategic autonomy in essential medical supplies and digital innovations. By collecting and analysing health data across borders and creating human-centred health technologies, including the use of Artificial Intelligence (AI), research can improve and personalise medical care for different patients, increasing patient safety and leading to better health outcomes and wellbeing.

Support for Research and Innovation is needed on the large spectrum of tools and technologies for biomedical research, prevention, diagnosis, therapy and health monitoring. This includes enabling technologies not least innovative biotechnological approaches. The emergence of the European Health Data Space will create an additional boost to cross-border, data-driven approaches and innovation, e.g. for personalised medicine or patient safety. High-quality health data (incl. real world data) combined with digital technologies, modelling and AI tools, have a high potential for advancing biomedical Research and Innovation. Emerging and disruptive technologies using tools like new genomic techniques and AI tools, offer big opportunities for transforming healthcare, but also depend on the capacity to collect, integrate and interpret large amounts of data and on their compatibility with appropriate regulatory frameworks. Such technologies can provide better and more cost-efficient solutions with high societal impact, tailored to the specific healthcare needs of the individual. However, novel tools, technologies and digital approaches face specific barriers and hurdles in piloting, implementing and scaling-up before reaching the patient, encountering additional challenges such as public acceptance and trust. The development and uptake of new technologies for high-quality healthcare will need to draw on multiple disciplines and require cross-sectoral cooperation among all those concerned, including end-users (patients, healthcare providers and workforce, researchers, regulatory bodies, policymakers, and funders). These interactions will help address unmet needs via integrated tools, hybrid health technologies and digital

solutions (including those with limited commercial interest). It will also support the design and development of health products and services tailored to the needs of specific population groups, thereby improving patient outcomes and reducing health inequalities.

This destination aims to promote the development of novel tools, technologies and digital solutions for prevention, diagnosis and therapy with the goal to improve health outcomes, while taking into consideration the rights of the individual, safety, effectiveness, appropriateness, accessibility, comparative value-added and fiscal sustainability as well as issues of ethical, legal and regulatory nature.

In this work programme part, Destination "*Developing and using new tools, technologies and digital solutions for a healthy society*" is driven by two key Commission policies, the "Biotechnology and Biomanufacturing Strategy [168] " and the "Artificial Intelligence Strategy[169]" and will focus on the development and use of innovative biotechnological tools for the improvement of the therapeutic arsenal of healthcare against diseases where there are currently no or only insufficient therapeutic strategies, on the development of Generative Artificial Intelligence models to help researchers in their activities to deliver new knowledge for advancing biomedical research and on the technology transfer of biotechnology-derived therapeutics from discovery to approved products. In particular, the topics under this destination will support activities aiming at: cellular and cell-free therapeutic approaches employing either genetic modifications or more classical techniques for improving the safety and therapeutic performance of these therapies, including their testing in clinical studies; development of generative AI models based on large-scale multi-modal health data for better understanding of diseases and their management thanks to the enhancement of biomedical discoveries and more personalised treatment solutions; bridging the gap between pre-clinical and clinical development stages of therapeutics developed through biotechnological methods and giving special emphasis on small and medium-sized enterprises (SMEs). In this context, specific attention is given to support the objectives of the Strategic Technologies for Europe Platform (STEP), adopted by the Commission in March 2024, which aims to boost investments in critical technologies in Europe (see introduction to this work programme part).

Under this destination, actions will support interdisciplinary Research and Innovation activities involving a broad spectrum of actors from different sectors, who will strive for the convergence of health technologies, combining medical technologies, pharmaceuticals, Advanced Therapy Medicinal Products (ATMPs) and digital health technologies, that will lead to integrated health solutions for the benefit of healthcare providers and patients.

In view of increasing the impact of EU investments under Horizon Europe, the European Commission welcomes and supports cooperation between EU-funded projects to enable cross-fertilisation and other synergies. This could range from networking to joint activities

[168] Commission Communication on Building the future with nature: Boosting Biotechnology and Biomanufacturing in the EU; COM(2024) 137 final: https://research-and-innovation.ec.europa.eu/document/download/47554adc-dffc-411b-8cd6-b52417514cb3_en

[169] Commission Communication on Artificial Intelligence for Europe; COM(2018) 237 final: https://digital-strategy.ec.europa.eu/en/policies/european-approach-artificial-intelligence; https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=COM:2018:237:FIN

such as the participation in joint workshops, the exchange of knowledge, the development and adoption of best practices, or joint communication activities. Opportunities for such activities and potential synergies exist between projects funded under the same topic but also between other projects funded under another topic, Cluster or pillar of Horizon Europe (but also with ongoing projects funded under Horizon 2020). In particular, this could involve projects related to European health research infrastructures (under pillar I of Horizon Europe), the EIC strategic challenges on health, the European Innovation Ecosystems (EIE) interregional networks on health and EIT-KIC Health (under pillar III of Horizon Europe) or in areas cutting across the health and other Clusters (under pillar II of Horizon Europe), like, for instance, with Cluster 4 "Digital, Industry and Space" on digitalisation of the health sector or key enabling technologies.

Expected Impacts:

Proposals for topics under this destination should set out a credible pathway towards the development and use of new tools, technologies and digital solutions for a healthy society, and more specifically to one or several of the following impacts:

- Europe's scientific and technological expertise and know-how, its capabilities for innovation in new tools, technologies and digital solutions, and its ability to take-up, scale-up and integrate innovation in healthcare is world-class.
- Citizens benefit from targeted and faster research resulting in safer, more sustainable, efficient, cost-effective and affordable tools, technologies and digital solutions for improved (personalised) disease prevention, diagnosis, treatment and monitoring for better patient outcome and wellbeing, in particular through increasingly shared health resources (interoperable data, infrastructure, expertise, citizen/patient driven co-creation)[170].
- The EU gains high visibility and leadership in terms of health technology development, including through international cooperation.
- The burden of diseases in the EU and worldwide is reduced through the development and integration of innovative diagnostic and therapeutic approaches, personalised medicine approaches, digital and other people-centred solutions for healthcare.
- Both the productivity of health Research and Innovation, and the quality and outcome of healthcare is improved thanks to the use of health data and innovative analytical tools, such as artificial intelligence (AI) supported decision-making, in a secure and ethical manner, respecting individual integrity and underpinned with public acceptance and trust.
- Citizens trust and support the opportunities offered by innovative technologies for healthcare, based on expected health outcomes and potential risks involved.

[170] Commission Communication on the digital transformation of health and care; COM(2018) 233 final

Proposals are invited against the following topic(s):

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

Call: Cluster 1 - Health (Single stage - 2025)	
Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of between EUR 8.00 and 10.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 50.00 million.
Type of Action	Research and Innovation Actions
Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: In recognition of the opening of the US National Institutes of Health's programmes to European researchers, any legal entity established in the United States of America is eligible to receive Union funding. The Joint Research Centre (JRC) may participate as member of the consortium selected for funding. If projects use satellite-based earth observation, positioning, navigation and/or related timing data and services, beneficiaries must make use of Copernicus and/or Galileo/EGNOS (other data and services may additionally be used).
Award criteria	The criteria are described in General Annex D. The following exceptions apply: The thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.
Procedure	The procedure is described in General Annex F. The following exceptions apply: Proposals under this topic may address any of the therapeutic areas mentioned in the scope. In order to ensure a balanced project portfolio with regard to the therapeutic area targeted, grants will be awarded to

	proposals not only in order of ranking but also to the highest ranked proposal within each[171] of the therapeutic areas, under the condition that the applications attain all thresholds.

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.

[171] Subject to available budget. Some therapeutic areas may not be funded as the number of targeted therapeutic areas is broader than the indicative number of projects expected to be funded.

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 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[172] 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

Call: Cluster 1 - Health (Single stage - 2025)	
Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of between EUR 9.00 and 13.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 40.00 million.
Type of Action	Research and Innovation Actions
Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: In recognition of the opening of the US National Institutes of Health's programmes to European researchers, any legal entity established in the United States of America is eligible to receive Union funding. The Joint Research Centre (JRC) may participate as member of the consortium selected for funding. If projects use satellite-based earth observation, positioning, navigation and/or related timing data and services, beneficiaries must make use of Copernicus and/or Galileo/EGNOS (other data and services may

[172] Please note that the definition of clinical studies (see introduction to this work programme part) is broad and it is recommended that you review it thoroughly before submitting your application.

	additionally be used).
Award criteria	The criteria are described in General Annex D. The following exceptions apply: The thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.

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[173] 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[174]), 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.

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[173] Good Manufacturing Practice (GMP): https://www.who.int/teams/health-product-policy-and-standards/standards-and-specifications/gmp

[174] Investigational Medicinal Product Dossier - European Medicines Agency: https://www.ema.europa.eu/en/requirements-quality-documentation-concerning-biological-investigational-medicinal-products-clinical-trials-scientific-guideline

- 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[175]. 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[176] 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[177] 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-03: Leveraging multimodal data to advance Generative Artificial Intelligence applicability in biomedical research (GenAI4EU)

Call: Cluster 1 - Health (Single stage - 2025)
Specific conditions

175 Blood, tissues, cells and organs - European Commission (europa.eu): https://health.ec.europa.eu/blood-tissues-cells-and-organs_en

176 Diseases with a high frequency (e.g.: incidence or prevalence) or high DALY (Disability-Adjusted Life Years)

177 Please note that the definition of clinical studies (see introduction to this work programme part) is broad and it is recommended that you review it thoroughly before submitting your application.

Expected EU contribution per project	The Commission estimates that an EU contribution of between EUR 15.00 and 17.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 50.00 million.
Type of Action	Research and Innovation Actions
Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: In recognition of the opening of the US National Institutes of Health's programmes to European researchers, any legal entity established in the United States of America is eligible to receive Union funding. The Joint Research Centre (JRC) may participate as member of the consortium selected for funding. If projects use satellite-based earth observation, positioning, navigation and/or related timing data and services, beneficiaries must make use of Copernicus and/or Galileo/EGNOS (other data and services may additionally be used). The following exceptions apply: subject to restrictions for the protection of European communication networks.
Award criteria	The criteria are described in General Annex D. The following exceptions apply: The thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.

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

[178] Generative AI is a type of AI technology that can generate various forms of new content such as text, images, sounds, and even code, such as for programming or gene sequencing (https://ec.europa.eu/newsroom/dae/redirection/document/101621).

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[179].
- Appropriate solutions to identify and mitigate potential bias and confounding[180] 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[181] data principles and apply GDPR[182] 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

179 Ethics Guidelines for Trustworthy AI, published by the European Commission's High Level Expert Group on Artificial Intelligence: https://ec.europa.eu/futurium/en/ai-alliance-consultation.1.html

180 Guidelines on the responsible use of generative AI in research developed by the European Research Area Forum: https://research-and-innovation.ec.europa.eu/news/all-research-and-innovation-news/guidelines-responsible-use-generative-ai-research-developed-european-research-area-forum-2024-03-20_en

181 See definition of FAIR data in the introduction to this work programme part.

182 General Data Protection Regulation: https://gdpr-info.eu

Joint Programme of Rare Diseases[183] etc. Moreover, the applicants are encouraged to leverage available and emerging European data infrastructures (e.g., the European Health Data Space[184], European Genomic Data Infrastructure[185], Cancer Image Europe[186], European Open Science Cloud[187], EBRAINS[188] 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[189], 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[190] should provide details of their clinical studies in the dedicated annex using the template provided in the submission system.

183 https://www.ejprarediseases.org/what-is-the-virtual-platform
184 https://health.ec.europa.eu/ehealth-digital-health-and-care/european-health-data-space_en
185 https://gdi.onemilliongenomes.eu
186 https://cancerimage.eu
187 https://research-and-innovation.ec.europa.eu/strategy/strategy-2020-2024/our-digital-future/open-science/european-open-science-cloud-eosc_en
188 https://www.ebrains.eu
189 https://digital-strategy.ec.europa.eu/en/policies/ai-factories
190 Please note that the definition of clinical studies (see introduction to this work programme part) is broad and it is recommended that you review it thoroughly before submitting your application.

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

Call: Cluster 1 - Health (Single stage - 2025)	
Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of between EUR 4.00 and 8.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 80.00 million.
Type of Action	Research and Innovation Actions
Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: In order to prove that the investigational product is ready for clinical testing, proposals must provide evidence of regulatory approval in the EU already in place for phase I clinical study. The proposed EU contribution going to small and medium-sized enterprises (SMEs) must be 50% or more of the total EU contribution to the project as a whole. In addition to the eligibility conditions as described in General Annex B, the consortium must be composed of at most 5 legal entities as beneficiaries. If projects use satellite-based earth observation, positioning, navigation and/or related timing data and services, beneficiaries must make use of Copernicus and/or Galileo/EGNOS (other data and services may additionally be used).
Award criteria	The criteria are described in General Annex D. The following exceptions apply: The thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.
Procedure	The procedure is described in General Annex F. The following exceptions apply: Eligible proposals submitted under this topic and exceeding all the evaluation thresholds will be awarded a STEP Seal[191].

[191] https://strategic-technologies.europa.eu/about/step-seal_en

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.

192 https://research-and-innovation.ec.europa.eu/document/download/47554adc-dffc-411b-8cd6-b52417514cb3_en

193 https://go.bio.org/rs/490-EHZ-999/images/ClinicalDevelopmentSuccessRates2011_2020.pdf

- 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 studies[194] 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.

194 Please note that the definition of clinical studies (see introduction to this work programme part) is broad and it is recommended that you review it thoroughly before submitting your application.

Destination - Maintaining an innovative, sustainable, and competitive EU health industry

Topics under this destination are directed towards the Key Strategic Orientation 3 "*A more resilient, competitive, inclusive, and democratic Europe*" of Horizon Europe's strategic plan 2025-2027. In addition, Key Strategic Orientation 2 *"The Digital Transition"* and Key Strategic Orientation 1 "*The Green Transition*" are supported.

Research and Innovation supported under this destination should contribute to the following expected impact, set out in the strategic plan impact summary for the Health Cluster: *"the EU health industry is innovative, sustainable, and globally competitive thanks to improved uptake of breakthrough technologies and innovations (including social innovations) that make the EU with its Member States and Associated Countries more resilient and less reliant on imports of critical health technologies*".

The health industry is a key driver for growth and has the capacity to provide health technologies to the benefit of patients and providers of healthcare services. The relevant value chains involve a broad variety of key players from supply, demand and regulatory sides. In addition, the path of innovation in health is long and complex. The development of novel health technologies is generally associated with uncertainties and market barriers due to expensive and risky development (e.g., high attrition rate in pharmaceutical development), high quality and security requirements (e.g., clinical performance, safety, data privacy and cybersecurity) and market specificities (e.g., strong regulation, pricing and reimbursement issues). In addition, the growing concern about environmental issues is putting more pressure on this industry. Therefore, there is a need for Research and Innovation integrating various stakeholders to facilitate market access of innovative health technologies (medical technologies, pharmaceuticals, biotechnologies, digital health technologies).

In this work programme part, Destination "*Maintaining an innovative, sustainable and competitive EU health industry*" focuses on collaborative efforts to advance manufacturing processes and activities to ensure increased knowledge on and a faster uptake of medical devices and *in vitro* diagnostic medical devices in the current EU regulatory context. The results will support the EU Industrial Policy, with a focus on strengthening the resilience of the single market, addressing the EU's strategic dependencies, gaining technological sovereignty and accelerating the green and digital transitions. In addition, the results will further strengthen the single market, by implementing the Digital Single Market strategy, providing evidence and guidelines for stakeholders and regulators to ensure take-up of innovations, supporting environmental, fiscal and socio-economic sustainability while fostering healthcare access and reducing health inequities. The results will also support the implementation of the Regulations on Medical Devices (MDR) and *In Vitro* Medical Devices (IVDR) and the Pharmaceutical Strategy for Europe, especially aspects related to the importance of ensuring industry competitiveness, innovation and sustainability and the development of high quality, safe, effective, and greener medicines.

In view of increasing the impact of EU investments under Horizon Europe, the European Commission welcomes and supports cooperation between EU-funded projects to enable

cross-fertilisation and other synergies. This could range from networking to joint activities such as the participation in joint workshops, the exchange of knowledge, development and adoption of best practices, or joint communication activities. All topics are open to international collaboration to address global environment and health challenges.

In particular, the topics under this destination will support activities aiming at: i) optimising the manufacturing of Advanced Therapy Medicinal Products (ATMPs) with the ultimate aim that healthcare providers, researchers and patients get faster access to ATMPs with demonstrated health benefits for unmet medical needs; ii) advance digitalisation of conformity assessment procedures in the context of medical device and *in vitro* diagnostic medical device development; iii) facilitating and enabling improved knowledge on the conduct of multinational clinical studies of orphan devices and/or highly innovative ("breakthrough") devices.

Expected impacts:

Proposals for topics under this destination should set out a credible pathway to contributing to maintaining an innovative, sustainable and competitive EU health industry, and more specifically to one or several of the following expected impacts:

- Health industry in Europe and Associated Countries is more competitive and sustainable, assuring European leadership in breakthrough health technologies and open strategic autonomy in essential medical supplies and (digital) technologies, contributing to job creation and economic growth, in particular with small and medium-sized enterprises (SMEs).

- Health industry is supported by cross-sectoral Research and Innovation in the context of convergence of health technologies (integrating medical technologies, pharmaceuticals, biotechnologies, digital health, and e-health technologies) while strengthening key market positions.

- Health industry is working more efficiently along the value chain from the identification of needs to the scale-up and take-up of solutions at national, regional or local level, including through early engagement with patients, healthcare providers, health authorities and regulators ensuring suitability and acceptance of solutions.

- Citizens, healthcare providers and health systems benefit from a swift uptake of innovative health technologies and services through the provision of evidence and guidelines for stakeholders, policymakers and regulators. These efforts offer significant improvements in health outcomes, also potentially strengthening access to healthcare for all and reducing health inequities while health industry benefits from decreased time-to-market.

- Citizens, healthcare providers and health systems benefit from increased health security in Europe and Associated Countries due to reliable access to key manufacturing

capacity, including timely provision of essential medical supplies and technologies of particularly complex or critical supply and distribution chains.

Legal entities established in China are not eligible to participate in Innovation Actions in any capacity. Please refer to the Annex B of the General Annexes of this Work Programme for further details.

Proposals are invited against the following topic(s):

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

Call: Cluster 1 - Health (Single stage - 2025)	
Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of between EUR 6.00 and 8.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 40.00 million.
Type of Action	Innovation Actions
Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: In recognition of the opening of the US National Institutes of Health's programmes to European researchers, any legal entity established in the United States of America is eligible to receive Union funding. The Joint Research Centre (JRC) may participate as member of the consortium selected for funding. If projects use satellite-based earth observation, positioning, navigation and/or related timing data and services, beneficiaries must make use of Copernicus and/or Galileo/EGNOS (other data and services may additionally be used).
Award criteria	The criteria are described in General Annex D. The following exceptions apply: The thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.
Legal and financial set-up of the Grant Agreements	The rules are described in General Annex G. The following exceptions apply: Eligible costs will take the form of a lump sum as defined in the Decision of 7 July 2021 authorising the use of lump sum contributions

	under the Horizon Europe Programme – the Framework Programme for Research and Innovation (2021-2027) – and in actions under the Research and Training Programme of the European Atomic Energy Community (2021-2025) [195].

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[196] in ATMPs.

Scope: New pioneering treatments called Advanced Therapy Medicinal Products (ATMPs)[197], 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,

195 This decision is available on the Funding and Tenders Portal, in the reference documents section for Horizon Europe, under 'Simplified costs decisions' or through this link: https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/ls-decision_he_en.pdf

196 A centre of excellence refers to a team with a clear focus on a particular area of research; such a centre may bring together faculty members from different disciplines and provide shared facilities.

197 ATMPs as classified by the European Medicines Agency (EMA): https://www.ema.europa.eu/en/human-regulatory-overview/advanced-therapy-medicinal-products-overview

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[198], 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[199] 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

Call: Cluster 1 - Health (Single stage - 2025)	
Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of around EUR 4.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 4.00 million.
Type of Action	Coordination and Support Actions
Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: In recognition of the opening of the US National Institutes of Health's programmes to European researchers, legal entities established in the United States of America may exceptionally participate as a beneficiary or affiliated entity, and are eligible to receive Union funding. Coordinators of projects must be legal entities established in an EU

198 https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/how-to-participate/org-details/999999999/project/101137206/program/43108390/details, https://cordis.europa.eu/project/id/101137206

199 Please note that the definition of clinical studies (see introduction to this work programme part) is broad and it is recommended that you review it thoroughly before submitting your application.

	Member State or Associated Country. If projects use satellite-based earth observation, positioning, navigation and/or related timing data and services, beneficiaries must make use of Copernicus and/or Galileo/EGNOS (other data and services may additionally be used).
Award criteria	The criteria are described in General Annex D. The following exceptions apply: The thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.
Legal and financial set-up of the Grant Agreements	The rules are described in General Annex G. The following exceptions apply: Eligible costs will take the form of a lump sum as defined in the Decision of 7 July 2021 authorising the use of lump sum contributions under the Horizon Europe Programme – the Framework Programme for Research and Innovation (2021-2027) – and in actions under the Research and Training Programme of the European Atomic Energy Community (2021-2025) [200].

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 [201] 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

[200] This decision is available on the Funding and Tenders Portal, in the reference documents section for Horizon Europe, under 'Simplified costs decisions' or through this link: https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/ls-decision_he_en.pdf

[201] For the purpose of this topic, the reference to 'devices' includes both medical devices and *in vitro* diagnostic medical devices, unless otherwise specified.

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 market[202]. 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;

[202] Study commissioned by the European Commission's Directorate-General for Health and Food Safety via the European Health and Digital Executive Agency (results not yet published): https://health.ec.europa.eu/study-supporting-monitoring-availability-medical-devices-eu-market_en

- 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

Call: Cluster 1 - Health (Single stage - 2025)	
Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of between EUR 6.00 and 8.00 million would allow these outcomes to be addressed appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.
Indicative budget	The total indicative budget for the topic is EUR 40.00 million.
Type of Action	Research and Innovation Actions
Eligibility conditions	The conditions are described in General Annex B. The following exceptions apply: In recognition of the opening of the US National Institutes of Health's programmes to European researchers, any legal entity established in the United States of America is eligible to receive Union funding. The Joint Research Centre (JRC) may participate as member of the consortium selected for funding. If projects use satellite-based earth observation, positioning, navigation and/or related timing data and services, beneficiaries must make use of Copernicus and/or Galileo/EGNOS (other data and services may additionally be used). The following exceptions apply: subject to restrictions for the protection of European communication networks.
Award criteria	The criteria are described in General Annex D. The following exceptions apply: The thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.

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[203] 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[204] of orphan devices[205] 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[206] aim to address unmet medical needs. 'Unmet medical needs'

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203 For the purpose of this topic, the reference to 'devices' includes both medical devices and *in vitro* diagnostic medical devices, unless otherwise specified.

204 See definition of clinical studies in the introduction to this work programme part.

205 A device should be regarded as an 'orphan device', if it meets the following criteria: i) the device is specifically intended to benefit patients in the treatment, diagnosis, or prevention of a disease or condition that presents in not more than 12.000 individuals in the European Union per year and ii) at least one of the following criteria are met:
- there is insufficiency of available alternative options for the treatment, diagnosis, or prevention of this disease/condition, or
- the device will offer an option that will provide an expected clinical benefit compared to available alternatives or state of the art for the treatment, diagnosis, or prevention of this disease/condition, taking into account both device and patient population-specific factors. MDCG 2024-10 Guidance on clinical evaluation of orphan medical devices: https://health.ec.europa.eu/document/download/daa1fc59-9d2c-4e82-878e-d6fdf12ecd1a_en?filename=mdcg_2024-10_en.pdf.

206 See Appendix 8 to MEDDEV 2.7/1 revision 4 (https://ec.europa.eu/docsroom/documents/17522/attachments/1/translations) or the FDA's Breakthrough Devices Program (https://www.fda.gov/medical-devices/how-study-and-market-your-device/breakthrough-devices-program).

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[207]. 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

[207] Based on Article 4(2) of Commission Regulation 507/2006 which defines the term 'unmet medical needs' in the field of medicinal products.

the 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[208] 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[209], 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[210] the co-funded European Partnership on Rare Diseases proposed under Horizon Europe[211], 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.

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208 'Clinical benefit' is defined in the Medical Device Regulation (EU) 2017/745, Article 2(53) as follows: Clinical benefit means the positive impact of a device on the health of an individual, expressed in terms of a meaningful, measurable, patient-relevant clinical outcome(s), including outcome(s) related to diagnosis, or a positive impact on patient management or public health.

209 EMA pilots scientific advice for certain high-risk medical devices - European Medicines Agency (EMA): https://www.ema.europa.eu/en/news/ema-pilots-scientific-advice-certain-high-risk-medical-devices

210 'European Rare Diseases Research Alliance', https://erdera.org, https://cordis.europa.eu/project/id/101156595

211 https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/topic-details/horizon-hlth-2023-disease-07-01

Applicants should provide details of their clinical studies[212] 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.

212 Please note that the definition of clinical studies (see introduction to this work programme part) is broad and it is recommended that you review it thoroughly before submitting your application.

Other Actions not subject to calls for proposals

Grants to identified beneficiaries

1. Grant to the Global Alliance for Chronic Diseases (GACD)

Expected Outcome: Proposals should set out a credible pathway to contributing to one or several expected impacts of destination "Tackling diseases and reducing disease burden".

Project results are expected to contribute to the following expected outcome: enable the European Commission to take part in GACD[213], which brings together leading health research funding agencies of key countries (currently Australia, Brazil, Canada, India, Japan, New Zealand, South Africa, Thailand, UK and USA) to coordinate research activities addressing on a global scale the prevention and treatment of chronic, non-communicable diseases such as cardiovascular diseases, diabetes, mental and neurological diseases, lung diseases and cancer.

Scope: Recommendations of GACD are expected to have a fundamental value for future orientation of public health research policy. This will also contribute to the implementation of the Union's strategy for international cooperation in research and innovation.

Award criteria:

The criteria are described in General Annex D. The following exceptions apply: The thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.

Procedure:

The evaluation committee will be composed fully by representatives of EU institutions.

Legal and financial set-up of the Grant Agreements:

The funding rate will be 100%.

Legal entities:

GACD Action, Wellcome Building, 215 Euston Road, London NW1 2BE, United Kingdom

Form of Funding: Grants not subject to calls for proposals

Type of Action: Grant to identified beneficiary according to Financial Regulation Article 198(e) - Coordination and support action

The general conditions, including admissibility conditions, eligibility conditions, award criteria, evaluation and award procedure, legal and financial set-up for grants, financial and operational capacity and exclusion, and procedure are provided in parts A to G of the General Annexes.

213 https://www.gacd.org

Indicative timetable: Fourth Quarter of 2025

Indicative budget: EUR 0.60 million from the 2025 budget

2. Presidency event - Cyprus. Advancement of Treatments for Rare Diseases

This action will cover the organisation of a high-level conference by the Cypriote presidency on the advancement of treatments for Rare Diseases within the EU.

Rare Diseases (RDs), often called orphan diseases, are a large (>7000) and diverse group of disorders that collectively pose a substantial disease burden and affect approximately 30 million people in the EU. The proposed conference should align with the goal of making Europe a world leader in RD research and innovation, addressing the challenges faced by patients with RDs and improving their access to effective treatments and care across Europe. It should aim to engage stakeholders in the RD community to support concrete health benefits to patients through the development of innovative treatments.

The conference should be informed by key EU initiatives on RDs both on healthcare and research sides, such as:

- The European Reference Networks (ERNs)[214], their registries, their Joint Action JARDIN[215] (all funded under the EU4Health programme) and their clinical research coordination platform ERICA[216] (funded under Horizon 2020).
- The Horizon Europe European Partnership on Rare Diseases, namely the European Rare Diseases Research Alliance (ERDERA)[217], and its predecessor the European Joint Program co-fund on Rare Diseases (EJP RD)[218].
- Public-private projects under the Innovative Health Initiative (IHI) such as Conect4Children[219] (pan-European collaborative pediatric network for high quality clinical trials in children), Screen4Care[220] and RealiseD.
- EU policies and regulations to incentivise the development of orphan drugs, the encouragement of member states to develop national plans and strategies for treatment of RD.

The conference should aim to address the following goals:

- Raise national profiles, for example by leveraging tools offered by the ERDERA Partnership and enhance awareness, knowledge exchange, collaboration and coordination between stakeholders in RD treatments.

214 https://health.ec.europa.eu/rare-diseases-and-european-reference-networks/european-reference-networks_en
215 https://jardin-ern.eu
216 https://cordis.europa.eu/project/id/964908, https://erica-rd.eu
217 https://cordis.europa.eu/project/id/101156595, https://erdera.org
218 https://cordis.europa.eu/project/id/825575, https://www.ejprarediseases.org
219 https://cordis.europa.eu/project/id/777389, https://conect4children.org
220 https://cordis.europa.eu/project/id/101034427, https://www.screen4care.eu

- Promote innovation and research that accelerates the translation of scientific findings into new therapies as well as repurposing of already approved drugs for RDs.
- Explore ways to improve the regulatory framework for the approval and equity of access to orphan drugs, ensuring that safe and effective treatments reach patients across all member states.
- Discuss potential solutions to enhance data security, sharing and infrastructure for research and treatment of RDs, recognising the critical role of big data in advancing medical knowledge, enabling AI-based solutions and improving patient outcomes.

The conference should aim to engage with a diverse audience across sectors and disciplines, including representatives from national political, health and research authorities; national research funding agencies; private investors; patients and advocacy groups; EU institutions and agencies; healthcare providers, clinicians and researchers. Participants should also include representatives from pharmaceutical and biotechnology companies and from regulatory bodies such as the European Medicines Agency (EMA), technology and data specialists, NGOs, media professionals, health technology assessment (HTA) experts, legal and ethical experts.

The inclusion of these key stakeholders should ensure the relevance and actionability of the conference's conclusions which are expected to be summarised in a report. This report should provide a comprehensive framework for addressing the challenges and opportunities related to RDs in Europe.

Award criteria:

The criteria are described in General Annex D. The following exceptions apply: The thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.

Procedure:

The evaluation committee will be composed fully by representatives of EU institutions.

Legal and financial set-up of the Grant Agreements:

The funding rate will be 100%.

Subcontracting is not restricted to a limited part of the action.

Legal entities:

The Cyprus Institute of Neurology and Genetics, 6 Iroon Avenue, 2371 Nicosia, Cyprus

Form of Funding: Grants not subject to calls for proposals

Type of Action: Grant to identified beneficiary according to Financial Regulation Article 198(e) - Coordination and support action

The general conditions, including admissibility conditions, eligibility conditions, award criteria, evaluation and award procedure, legal and financial set-up for grants, financial and operational capacity and exclusion, and procedure are provided in parts A to G of the General Annexes.

Indicative timetable: Second Semester of 2025

Indicative budget: EUR 0.30 million from the 2025 budget

3. Supporting European and global efforts to sustain the global biodata ecosystem

Expected Outcome:

Results under this action are expected to contribute to all the following expected outcomes:

- Promote dialogue, exchange and strategic cooperation among public and private research funders in the EU and globally to ensure the long-term sustainability of and access to a robust and open biodata ecosystem for life sciences R&I.
- Enhance knowledge and expertise on global biodata resources, including through analysis on their quality, utility, reliability, interoperability and cost, that would enable funders to make informed decisions about supporting these resources.

The action is expected to contribute to enhanced sustainability of and access to global biodata resources, thus advancing groundbreaking scientific research and innovation with the aim to solving global health challenges.

Scope:

This action continues and builds on an international initiative supporting the long-term sustainability of and access to key biodata resources for life sciences R&I, as executed through an organisation named the Global Biodata Coalition. The experience from this initiative underlines the continued need for global coordination to support and protect the fragile and vulnerable ecosystem of biodata resources that are essential for life sciences, including the ongoing and growing need to enhance the quality, reliability, interoperability and accessibility of biodata. In this context, the proposal should address:

- The establishment of a secretariat supporting the work needed for the achievement of this objective, including through the identification of (and interaction with) global biodata resources. The secretariat provides activities which inform and support the funding community about how best to ensure the health and well-being of the global biodata ecosystem, including providing technical advice and expertise to strengthen institutional and administrative capacity to accelerate financial support for the planning, development and implementation of biodata resources.
- The establishment of a governance framework and the creation of a fora for discussion of strategic funding priorities and strategic decision-making to ensure long-term support and sustainability of the global biodata ecosystem.

The work of the secretariat and governance framework should address global and European needs in biodata sustainability, taking into account specific contexts. The secretariat must establish a working mechanism for ensuring compliance with relevant global ethical and data standards and principles prescribed by international, European and national law.

It is expected that the proposal has a period of implementation of at least seven years.

Award criteria:

The criteria are described in General Annex D. The following exceptions apply: The thresholds for each criterion will be 4 (Excellence), 4 (Impact) and 4 (Implementation). The cumulative threshold will be 12.

Legal and financial set-up of the Grant Agreements:

The funding rate will be 100%.

Subcontracting is not restricted to a limited part of the action.

Legal entities:

EMBL - European Molecular Biology Laboratory, Meyerhofstrasse 1, 69117, Heidelberg, Germany

Form of Funding: Grants not subject to calls for proposals

Type of Action: Grant to identified beneficiary according to Financial Regulation Article 198(e) - Coordination and support action

The general conditions, including admissibility conditions, eligibility conditions, award criteria, evaluation and award procedure, legal and financial set-up for grants, financial and operational capacity and exclusion, and procedure are provided in parts A to G of the General Annexes.

Indicative timetable: Second Semester of 2025

Indicative budget: EUR 5.00 million from the 2025 budget

Other Instruments

1. Studies, conferences, events and outreach activities

A number of specific contracts will be signed in order to: (i) support the dissemination and exploitation of project results; (ii) contribute to the definition of future challenge priorities; (iii) undertake citizen surveys such as Eurobarometers, (iv) carry out specific evaluations of programme parts; and (v) organise conferences, events and outreach activities.

Subject matter of the contracts envisaged: studies, technical assistance, conferences, events and outreach activities.

Form of Funding: Procurement

Type of Action: Public procurement

Indicative timetable: 2025

Indicative budget: EUR 1.27 million from the 2025 budget

2. Subscription to the Human Frontier Science Program Organization

An annual subscription to the international Human Frontier Science Program Organization (HFSPO)[221] will allow researchers from EU non-G7 Member States to fully benefit from the Human Frontier Science Program (HFSP) and contribute to the implementation of the Global Approach to Research and Innovation, Europe's strategy for international cooperation in a changing world[222].

An amount of EUR 1 million in 2025 is set aside in order to enable initiatives to help the affected scientific community in and from areas recently severely ravaged by conflict and/or war on European ground.

Type of Action: Subscription action

Indicative timetable: Second Quarter of 2025

Indicative budget: EUR 6.92 million from the 2025 budget

3. External expertise in relation to EU research and innovation policy issues

This action will support the provision of independent expertise in support of the assessment, design, implementation, evaluation and valorisation of EU research and innovation policies in the areas currently in scope of the Health Cluster.

Individual experts will work on tasks such as, but not limited to: portfolio analysis of projects funded under Horizon Europe or previous European research and innovation programmes; analysis of the contribution of research results (at national, EU and/or international level) to EU policy objectives and emerging issues, including policy recommendations; analysis of the state-of-the-art at European and international level; participation in studies, conferences, events, symposia, etc, including the drafting of papers and reports on their conclusions; assistance for setting-up a research and innovation strategy for selected domains; policy recommendations and options assisting Commission services in elaborating evidence-based and scientifically sound policy proposals; assistance in the evaluation of calls for expression of interest; advice on the valorisation, communication, dissemination and exploitation of research results; identification of innovative solutions as well as potential gaps and synergies

221 The European Commission is a member of the HFSP Organization (HFSPO) and has funded HFSP under previous Framework Programmes

222 Communication from the Commission on the Global Approach to Research and Innovation. Europe's strategy for international cooperation in a changing world, COM(2021) 252, 18.5.2021 (https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=COM%3A2021%3A252%3AFIN).

to be addressed by EU research and innovation policy; advise on promising technologies covered by European and nationally funded projects and on ways to stimulate synergies, etc.

In addition to individual experts, this action could provide for Commission expert groups.

A special allowance of maximum EUR 450/day will be paid to the experts appointed in their personal capacity who act independently and in the public interest.

Form of Funding: Other budget implementation instruments

Type of Action: Expert contract action

Indicative budget: EUR 0.10 million from the 2025 budget

Budget[223] [224]

	Budget line(s)	2025 Budget (EUR million)	2026 Budget (EUR million)	2027 Budget (EUR million)
Calls				
HORIZON-HLTH-2025-01		496.00		
	from 01.020210	*496.00*		
HORIZON-HLTH-2025-02		123.00	54.00	50.00
	from 01.020210	*123.00*	*54.00*	*50.00*
HORIZON-HLTH-2025-03-two-stage		170.00		
	from 01.020210	*170.00*		
Other actions				
Grant awarded without a call for proposals according to Financial Regulation Article 198(e)		5.90		
	from 01.020210	*5.90*		
Public procurement		1.27		
	from 01.020210	*1.27*		
Subscription action		6.92		
	from 01.020210	*6.92*		
Expert contract action		0.10		
	from	*0.10*		

223 The budget figures given in this table are rounded to two decimal places.
The budget amounts are subject to the availability of the appropriations provided for in the general budget of the Union for 2025.

224 The contribution from Cluster 1 for the year 2025 is EUR 129.14 million for the Missions work programme part and EUR 23.55 million for the New European Bauhaus Facility work programme part.

	01.020210			
Estimated total budget		803.19	54.00	50.00