Destination 6. Maintaining an innovative, sustainable and globally competitive health industry

Calls for proposals under this destination are directed towards the Key Strategic Orientation KSO-A *'Promoting an open strategic autonomy by leading the development of key digital, enabling and emerging technologies, sectors and value chains'* of Horizon Europe's Strategic Plan 2021-2024. Research and innovation supported under this destination should contribute to the impact area *'A competitive and secure data-economy'* and in particular to the following expected impact, set out in the Strategic Plan for the health cluster: *'EU health industry is innovative, sustainable and globally competitive thanks to improved up-take of breakthrough technologies and innovations, which makes the EU with its Member States more resilient and less dependent from imports with regard to the access to and supply of critical health technologies'*. In addition, research and innovation supported under this destination could also contribute to the following impact areas: *'Industrial leadership in key and emerging technologies that work for people'*, *'High quality digital services for all'*, and *'Good health and high-quality accessible health care'*.

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 health care 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 order to address these challenges, in particular green and digital transitions and proper supply of health technologies and products, destination 6 will focus on research and innovation activities that aim at:

- Facilitating the production of pharmaceuticals in compliance with the objectives of the European Green Deal.

- Developing methodologies, guidelines and standards, assessment studies, and structuring activities adapted to digital solutions and interventions for GDPR compliant translation into health care practice, including inter-operability, cyber-security and data confidentiality.

- Supporting public authorities with better methodologies and interdisciplinary approaches to assess and value new health technologies and interventions.

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 4 "Digital, Industry and Space" such as on industrial research and innovation infrastructures (pilot plants, testing and simulation facilities, open innovation hubs); additive manufacturing and other production technologies (incl. bio manufacturing); safe, smart and sustainable materials.

Expected Impacts:

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

- Health industry in the EU 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 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, health care providers, health authorities and regulators ensuring suitability and acceptance of solutions.

- European standards, including for operations involving health data, ensure patient safety and quality of healthcare services as well as effectiveness and interoperability of health innovation and productivity of innovators.

- Citizens, health care providers and health systems benefit from a swift uptake of innovative health technologies and services offering significant improvements in health outcomes, while health industry in the EU benefits from decreased time-to-market.

- Health security in the EU benefits from reliable access to key manufacturing capacity, including timely provision of essential medical supplies of particularly complex or critical supply and distribution chains, such as regards vaccines or medical radioisotopes.

The following call(s) in this work programme contribute to this destination:

Call	Budgets (EUR million)		Deadline(s)
	2023	2024	
HORIZON-HLTH-2023-IND-06	56.00		13 Apr 2023
HORIZON-HLTH-2024-IND-06		12.00	11 Apr 2024
Overall indicative budget	56.00	12.00	

Call - A competitive health-related industry (Single stage - 2023)

HORIZON-HLTH-2023-IND-06

Conditions for the Call

Indicative budget(s)[261]

Topics	Type of Action	Budgets (EUR million)	Expected EU contribution per project (EUR million)[262]	Indicative number of projects expected to be funded
		2023		
Opening: 12 Jan 2023 Deadline(s): 13 Apr 2023				
HORIZON-HLTH-2023-IND-06-01	CSA	5.00 [263]	Around 5.00	1
HORIZON-HLTH-2023-IND-06-02	RIA	8.00 [264]	3.00 to 5.00	2
HORIZON-HLTH-2023-IND-06-04	RIA	25.00 [265]	4.00 to 6.00	5
HORIZON-HLTH-2023-IND-06-05	CSA	3.00 [266]	Around 3.00	1
HORIZON-HLTH-2023-IND-06-07	RIA	15.00 [267]	7.00 to 8.00	2
Overall indicative budget		56.00		

General conditions relating to this call	
Admissibility conditions	The conditions are described in General Annex A.

[261] 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 years 2023 and 2024.

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

[263] Of which EUR 2.50 million from the 'NGEU' Fund Source.

[264] Of which EUR 4.00 million from the 'NGEU' Fund Source.

[265] Of which EUR 14.00 million from the 'NGEU' Fund Source.

[266] Of which EUR 1.50 million from the 'NGEU' Fund Source.

[267] Of which EUR 8.00 million from the 'NGEU' Fund Source.

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.

Proposals are invited against the following topic(s):

HORIZON-HLTH-2023-IND-06-01: Supporting the uptake of innovative Health Technology Assessment (HTA) methodology and advancing HTA expertise across EU

Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of around EUR 5.00 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 5.00 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.
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 3

	(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 6 “Maintaining an innovative, sustainable and globally competitive health industry”. To that end, proposals under this topic should aim to deliver results that are directed, tailored towards and contributing to all of the following expected outcomes:

- Identification of the most innovative HTA methods developed by EU-funded projects, which respond to the needs of HTA bodies and are ready to be used in real-life settings. Endorsement by HTA bodies of such innovative methods would allow for advancing HTA methodology and improve evidence-based decision making, and patient access to novel health technologies

- Dissemination among EU HTA bodies of robust innovative HTA methods and tools developed by EU-funded projects.

- Harmonisation of HTA expertise across EU though the development of a training programme developed in collaboration with academia. The training should address HTA expertise in general, as wells as expertise in joint HTA to be carried out at EU level in accordance with Regulation (EU) 2021/2282, based on the methodological guidelines elaborated by the Coordination Group on HTA.

- Contribution to a successful implementation of the HTA Regulation as well as to building an EU methodological HTA framework fit for purpose and fit for the future.

Scope: HTA bodies have the responsibility to assess the added value of new health technologies and advise on its reimbursement and use within a healthcare system. Due to the rapid pace at which technology advance and in order to support decision making in an appropriate manner, HTA experts have to adapt/revise regularly their methodology. Whilst EU-funded projects in the field of HTA have addressed some of the research needs of the HTA bodies (e.g. methods of analysis, use of real-world data, use of patient reported outcomes), translation of their results/recommendations into HTA work remains limited.

Advancing HTA methodology and expertise could benefit from a more systematic dialogue between HTA bodies and academia. Therefore, this action could represent an excellent opportunity for both those generating and those using the evidence to come together and discuss the key HTA methodological issues.

Under the newly adopted Regulation (EU) 2021/2282, the Coordination Group on HTA will have to adopt methodological guidelines for joint HTA work (e.g. joint clinical assessments, joint scientific consultation), to regularly review, and where necessary update them. The project could provide input to issues identified by the Coordination Group as important for future updates/revisions of HTA methodology for joint HTA work.

The topic is divided into two strands of activities, with applicants tackling both in their proposals:

- **Implementation of innovative HTA methods**: EU-funded research projects (e.g. COMED, IMPACT-HTA, HTx, GetReal, EHDEN) developed innovative methods aiming at addressing HTA bodies' needs. Identifying which of these methods are ready to be used in real-life settings is a first crucial step towards broader uptake and dissemination. Successful implementation of innovative methods in actual HTA practices will contribute to provide a timely response to HTA challenges (e.g. use of real-world data in HTA) also providing a sound scientific resource for updates of methodological guidelines by the Coordination Group on HTA for joint activities as requested by the Regulation (EU) 2021/2282. HTA bodies/agencies participating in such activities will gain expertise in those methods that could be later transferred to other bodies/agencies using the training framework developed in the second strand of work.

- **Advancing HTA expertise across the EU and Associated Countries should be carried out through** a training programme tailored to the needs of HTA bodies, which may include twinning activities between HTA bodies/agencies to develop expertise and facilitate knowledge sharing among HTA bodies/agencies in the EU. The training programme is expected to contribute to the harmonisation of HTA practices in the EU that will in turn contribute to a greater consistency of health technology assessments across the EU and Associated Countries. Thus, the training programme should also support the engagement of HTA experts from Member States and EEA countries in carrying out joint HTA work starting January 2025 (i.e. implementation date of the Regulation on HTA), with the aim to produce high-quality and robust joint clinical assessments. The training programme should include all the necessary elements for carrying out robust assessments at national and EU level. Regarding the latter, the training programme should also promote the dissemination of the methodological guidelines to be adopted by the Coordination Group on HTA (based on the methodology developed and fine-tuned by EUnetHTA joint actions and EUnetHTA21 service contract).

The proposals should address all of the following activities:

- Identification of innovative methods and tools, in particular those developed in EU-funded projects able to address HTA bodies' needs (in different areas: relative effectiveness assessment, cost-effectiveness assessment, etc.)

- Identifications of barriers to the uptake of these methods (and potential associated tools, e.g. open-source software to run cost-effectiveness analyses)

- Use cases (based on the needs identified by HTA bodies) to facilitate the endorsement by HTA bodies of innovative methods

- Development of an implementation plan including supporting tools and training modules (by researchers, alone or in collaboration with HTA bodies, to be delivered to HTA bodies/agencies)

- Recommendations for broader dissemination.

HORIZON-HLTH-2023-IND-06-02: Expanding the European Electronic Health Record exchange Format to improve interoperability within the European Health Data Space

Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of between EUR 3.00 and 5.00 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 8.00 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.
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 3 (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 6 "*Maintaining an innovative, sustainable and globally competitive health industry*". More specifically, this topic aims at supporting activities that are contributing to the following impact area: "*High quality digital services for all."* To that end, proposals under this topic should aim to deliver results that are directed, tailored towards and contributing to all of the following expected outcomes, and provide appropriate qualitative and quantitative indicators to measure their progress and specific impact:

- European Health Record (EHR) stakeholders (e.g. developers, suppliers, integrators, and operators) have at their disposal and use fit-for-purpose standards, guidelines, and toolsets for prioritised health information domains to address interoperability of EHRs in

line with the principles set in the EEHRxF Recommendation[268], contributing also to security and privacy.

- Stakeholders have at their disposal better quality and better integrated health datasets within the European Health Data Space,[269] to foster innovations in the health sector and leverage the potential of new analytics solutions such as AI and big data, get new insights and detect trends from aggregated data, including for cross-border health threats.

- Citizens are provided with an expanded access to their health data, also across borders, and innovative digital services for high-quality health and care across the EU.

Scope: EHR interoperability has yet to become a reality in a number of use cases and health information domains. It is a complex, multi-dimensional challenge. EHRs across the Member States are diverse; so are languages, cultures, and practices in the health sector. Different technical specifications, technologies and clinical terminologies are used, involving a range of stakeholders, within and across care settings.

Proposals should address all of the following:

- Research, develop and validate harmonised interoperability formats for sharing data in specific priority health information domains that should be selected with reference to the EU policies and priorities. The output formats should enable EHR interoperability across the Member States and address cross-border health data exchange by design and in line with the principles set in the EEHRxF Recommendation.

- Leverage and scale up the potential of EHR through enhanced interoperability to improve the quality, safety, and efficiency of patient care, enforce patients' right to data portability, enhance care coordination, guide crisis planning, reduce medical errors, and lower costs. For example, based on the lessons learnt from COVID-19, enable incorporating EHR data into the early stages of clinical crisis planning and leveraging it to identify potential cross-border health threats based on analysis of patients' data trends.

- Address semantic interoperability for prioritised information domains so that the transmitted health record contains standardised coded data.

- Maximise synergies with relevant initiatives, activities and programmes, building upon previous and linking to on-going actions[270].

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268 Commission Recommendation on a European Electronic Health Record exchange Format (EEHRxF) (C(219)800)

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

270 Such as "Support for European eHealth Interoperability roadmap for deployment" https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/topic-details/sc1-hcc-07-2020; "Prototyping a European interoperable Electronic Health Record (EHR) exchange" https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/topic-details/sc1-dth-08-2018; "Setting up a European Electronic Health Record Exchange Format (EEHRxF) Ecosystem" https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/topic-details/horizon-hlth-2022-ind-13-05

- Closely coordinate and collaborate with various stakeholders, from patients and healthcare professionals to EHR providers, healthcare industry (including SMEs), policymakers and legislators to progress towards a more comprehensive EHR interoperability.

Applicants envisaging to include clinical studies should provide details of their clinical studies in the dedicated annex using the template provided in the submission system. See definition of clinical studies in the introduction to this work programme part.

HORIZON-HLTH-2023-IND-06-04: Modelling and simulation to address regulatory needs in the development of orphan and paediatric medicines

Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of between EUR 4.00 and 6.00 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 25.00 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.
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 3 (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 6 "Maintaining an innovative, sustainable and globally competitive health industry". To that end, proposals under this topic should aim to deliver results that are directed, tailored towards and contributing to all of the following expected outcomes:

- Developers and regulators have access to robust modelling and simulation tools to accelerate the effective development of orphan and/or paediatric medicinal products.

- Clinical researchers, developers and regulators use accurate computational models to improve the statistical robustness in clinical trials intended for small populations and guide cost-effective clinical trial designs.

- Clinical researchers and regulators have access to accurate in-silico tools for assessing the actionable use of real-world data and for successfully estimating the risk-benefit effects in clinical trials for small populations.

- Regulators develop guidance for the use of validated computational models to support a robust extrapolation framework and facilitate the safety and efficacy assessment in the process of regulatory appraisal of orphan and/or paediatric medicinal products.

Scope: In its "Regulatory Science Strategy to 2025", the European Medicines Agency included specific recommendations to optimise the capabilities of modelling and simulation in the medicines development process and in particular to benefit special populations and neglected patient populations.

Orphan drug development faces numerous challenges, including low disease prevalence, patient population heterogeneity and strong presence of paediatric patient populations. Consequently, clinical trials for orphan and/or paediatric medicines are often smaller than traditional large-scale randomised ones and they require the development of efficient trial designs relevant to small.

Model-based approaches are significantly advantageous in small populations, as extrapolation tools for rationalising and increasing the statistical robustness in clinical trial designs and pharmacometric studies.

The topic will support research and innovation activities focusing on the development of diverse modelling and simulation methods, as tools for addressing some of the regulatory needs in the clinical development cycle of new orphan and paediatric medicinal products. The topic is not intended to implement new preclinical/clinical studies but to use the existing knowledge/data for assessing and optimising the performance of mature in-silico models in the regulatory context with the goal of improving the clinical trial designs for small populations. Availability of the relevant data to address the requirements of the topic is an indispensable condition that must be demonstrated at the proposal submission.

Proposals should involve national healthcare product regulatory bodies and the European Medicines Agency (EMA) in order to catalyse an effective collaboration between the researchers and the regulators. The active involvement of patient representatives is required in all phases of the research and innovation activities. Furthermore, SME(s) participation is encouraged with the aim to strengthen their scientific and technological basis.

The proposals should address all of the following activities:

- Establish a multidisciplinary approach for assessing the utility of mature computational models, as tools for supporting the optimal design of innovative clinical trials for small populations and as fit-for-purpose solutions for enabling the regulatory scientific advice and marketing authorisation assessment of orphan and/or paediatric medicines, including their pharmacovigilance follow-up.

- Calibrate and optimise mature computational models for enhancing their clinical performance, by using relevant sources of patient data (e.g. natural history and observational clinical studies, medical records, registries, pharmacovigilance and longitudinal studies etc.). The models should include a variety of modelling methods and in particular hybrid solutions linking quantitative mechanistic modelling with advanced statistical modelling (e.g. quantitative systems pharmacology, disease mechanistic models, physiology-based pharmacodynamic/pharmacokinetic models, Bayesian modelling, artificial intelligence algorithms etc.).

- Assess validated in-silico models for their capability to increase the statistical robustness, improve the risk/benefit assessment in small population clinical trials, and for their accuracy to predict and extrapolate the therapeutic and dose effects, taking into account the patient's genotypes/phenotypes, disease characteristics/stage variables and/or clinical/surrogate endpoints for delivering robust evidence of safety and efficacy of the orphan and paediatric medicines under study. The assessment of the in-silico models should be demonstrated in use cases representing well-justified group(s) of rare and/or paediatric diseases with commonalities, such as shared molecular denominators/disease pathways within the same and/or across different medical areas, excluding cancer and infectious diseases.

- Benchmark of diverse computational models by showcasing their simulation performance in virtual patient cohorts and by demonstrating that the models' synthetic data estimates match to actual clinical trial data. This should lead to an assessment of the performance and credibility of a model simulation in the context of their specific use for regulatory purposes. Benchmark studies should be performed in the use cases mentioned above. Availability of clinical trials data and other relevant data is an indispensable requirement that must be demonstrated at the proposal submission.

- Set-up the criteria for the performance and credibility assessment of any relevant computational models for small population clinical trials to progress on their regulatory qualification and acceptability. Further develop and disseminate standards for the design, performance assessment and reporting of modelling and simulation tools with an emphasis on those of high regulatory value for accelerating the clinical development of orphan and paediatric medicinal products.

The proposals should adhere to the FAIR data[271] principles, adopt data quality standards, data integration operating procedures and GDPR-compliant data sharing/access good practices developed by the European research infrastructures, where relevant. Proposals are invited to consider adopting recommendations for in-silico models construction and validation[272]. Data-intensive proposals, particularly those using data from patient registries, should take stock of the tools and services provided by the European Platform on Rare Disease Registration (EU

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

[272] ISO-paper under development "Recommendations and requirements for predictive computational models in personalized medicine research — Part 1: Guidelines for constructing, verifying and validating models".

RD Platform). For example, retrospective registry data are expected to be made accessible via EU RD platform, if reasonably feasible.

All projects funded under this topic are strongly encouraged to participate in networking and joint activities. 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. This could also involve networking and joint activities with projects funded under other clusters and pillars of Horizon Europe, or other EU programmes. 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. In this regard, the Commission may take on the role of facilitator for networking and exchanges, including with relevant stakeholders.

Applicants envisaging to include clinical studies should provide details of their clinical studies in the dedicated annex using the template provided in the submission system. See definition of clinical studies in the introduction to this work programme part.

HORIZON-HLTH-2023-IND-06-05: Mapping the hurdles for the clinical applications of Advanced Therapy Medicinal Products (ATMPs)

Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of around EUR 3.00 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 3.00 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.
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 3

	(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 6 "Maintaining an innovative, sustainable and globally competitive health industry". To that end, proposals under this topic should aim to deliver results that are directed towards and contributing to all of the following expected outcomes:

- Challenging aspects of regulation, policy, safety, efficacy, manufacturing, organisation, infrastructure, decision-making, and commercialisation are identified for speeding up the equitable clinical applications of ATMPs.
- European regulatory frameworks are adapted to novel scientific progress, especially those related to platform approaches, genome editing, interface with medical devices, artificial intelligence.
- Competent authorities in the Member States can propose adapted pricing and reimbursement schemes that allow European citizens to benefit from novel ATMPs.
- Academic and SME developers and manufacturers of ATMPs have an increased knowledge of the regulatory aspects.
- The decentralised manufacturing of ATMPs is consistent across health care centres.

Scope: New pioneering treatments called Advanced Therapy Medicinal Products (ATMPs), including cell and gene therapies, have the potential to bring new cures to patients affected by diseases with limited or no available treatments. However, several hurdles impede or slow down the access of ATMPs to patients in the EU and Associated Countries. These include e.g. regulatory challenges, underlying scientific uncertainties, differences in assessing the values of ATMPs by the various Health Technology Agencies (HTA), difficulties to perform randomised-controlled clinical trials or to obtain long-term safety and effectiveness data, the lack of harmonised approaches to the reimbursement of the high upfront costs by health systems, manufacturing processes, etc.

The proposals should address all of the following activities:

- Map the regulatory, safety and efficacy assessment, manufacturing, organisational and infrastructural needs to improve the translation of ATMPs from preclinical development to clinical use.
- Address the gaps and uncertainties in regulatory and policy aspects pertinent to complex innovative ATMPs.
- Address predictivity of preclinical data for safety and efficacy testing of ATMPs. Improved novel models could be proposed.

- Tackle decision-making processes relating to ATMPs, such as for instance the assessment of their values, the demonstration of the long-term safety and effectiveness, or new pricing and reimbursement frameworks.
- Propose opportunities for an improved knowledge of the regulatory processes among academic ATMP developers.
- Involve regulatory authorities, Health Technology Agencies (HTA), clinicians, ethics committees, and patients, with the aim to ensure higher clinical use of ATMPs. The findings of the project will be available to competent authorities, ATMP developers and manufacturers as well as to national/regional funding agencies.

HORIZON-HLTH-2023-IND-06-07: Development and harmonisation of methodologies for assessing digital health technologies in Europe

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 15.00 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.
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 3 (Implementation). The cumulative threshold will be 12.

Expected Outcome: This topic aims at addressing digital transition challenges through supporting activities that are enabling or contributing to one or several expected impacts of destination 6 "Maintaining an innovative, sustainable and globally competitive health industry". More specifically, this topic aims at supporting activities that are contributing to the following impact area: "*High quality digital services for all".* To that end, proposals under this topic should aim to deliver results that are directed towards and contributing to all of the following expected outcomes:

- Policymakers in the EU have at their disposal a methodological framework and standardised approaches for assessing digital health technologies, that helps them make evidence-based decisions regarding the introduction of digital health technologies in their health and care systems with added value for patients and society.
- Regulators have access to robust, scientifically underpinned evaluation methodologies.
- EU citizens gain faster access to safe and well-performing person-centred digital technologies and are empowered through these tools.
- Health technology developers are better informed and dispose of more guidance on the evidence needed to demonstrate the added value of digital health technologies and have better insights on market predictability.
- (Digital) Health Industry/digital health technology developers and HTA bodies can contribute to the development of EU harmonised Health Technology Assessment (HTA) rules based on common principles.
- Improved cross-border use and interoperability of digital health tools and services throughout the EU and Associated Countries.
- Increased trust in digital health technologies and better integration of digital health tools and services in health and care systems.

Scope: Digital health technologies have been driving a revolution in health and care ranging from general use of computers to algorithms designed to assist radiologists and radiotherapists in detecting and treating diseases, from robotic surgery to artificial intelligence, machine learning, computer aided decision models, and from mobile apps helping patients to self-manage their disease to electronic health records.

Digital health technologies are expected to further contribute to better people-centred health and care systems and have the vast potential to improve our ability to accurately prevent, diagnose and treat diseases.

However, assessing the added value and health benefits for patients and society pose a number of challenges in particular of methodological and technical nature. Best practice for common approaches in methodology for digital health are lacking, especially in the digital health tools that include artificial intelligence algorithms. A framework for the assessment of the digital transformation of health services and its impact is vital to generate the evidence required for decision-making on stimulating, using and/or funding digital health strategies at various levels in the health and care systems.

The Expert Panel on effective ways of investing in Health (EXPH) recommended in its report 'Assessing the impact of digital transformation of health services[273]', further investment in the

[273] ASSESSING THE IMPACT OF DIGITAL TRANSFORMATION OF HEALTH SERVICES, Report of the Expert Panel on effective ways of investing in Health (EXPH) - https://ec.europa.eu/health/system/files/2019-11/022_digitaltransformation_en_0.pdf

development of assessment methodologies and in a European repository for evaluation methods and evidence of digital health services.

To date, such assessment frameworks are relatively scarce, especially those addressing the transformative aspects of healthcare delivery on the organisational and operational level.

The proposals are expected to develop and harmonise methodologies for assessing digital health technologies (including mhealth apps and telehealth, as well as Artificial Intelligence powered health technologies) in order to facilitate assessment of their added value at individual, health system and society levels and facilitate the cross-border deployment of digital health services within the EU. Existing Health Technology Assessment (HTA) methodology is well developed for health technologies such as medicinal products, but also for some categories of medical devices; however digitalisation raises new methodological challenges to the standardisation of assessment criteria such as privacy, cybersecurity, data storage and handling, interoperability, usability etc. Also including aspects like learning curves, iterative development of innovations, variability between settings, determining optimal timing of evaluations in the development process (maturity) are not yet solved.

Proposals are expected to build on existing frameworks such as (but not restricted to) 'Model for Assessment of Telemedicine' (MAST framework – Kidholm et al., 2012) and the results of previous EU-funded projects in particular (but not restricted to) COMED, project that already identified HTA challenges of telehealth and mhealth, and mHealth hub[274].

Proposals should consider involving the JRC to take advantage of its expertise on assessment frameworks of innovative health technologies and its activities at the interface between research and regulatory aspects and/or in translating assessment results into best practice recommendations anchored in EU policies. In that respect, the JRC is open to collaborate with any successful proposal after its approval.

The proposals should address all of the following activities:

- Develop and/or expand a general methodological framework and standardised approaches to assess digital health technologies with a particular focus on criteria such as privacy, cybersecurity, data quality, data storage and handling, interoperability etc.;
- Comply with the relevant requirements proposed in the European Health Data Space (EHDS) legal provisions;
- Test the robustness of the developed methodologies on minimum 3 different digital health technology use cases;
- Pilot the development of common specifications to the harmonisation of assessment frameworks (pre-market and post-market phases) throughout the EU and Associated Countries;

274 https://mhealth-hub.org/

- Include end-users of digital health technologies (be it professionals, care users or citizens), developers of digital health technologies, producers of health services, regulators and governments;
- Collect best practice for common approaches in methodology for digital health technology assessment and develop an open access European repository for evaluation methods, studies, results and evidence of digital health technologies and services;
- Contribute to a framework to evaluate and monitor whether the uptake and use of digital health services contribute to the overall goals of the health and care system;

Applicants envisaging to include clinical studies should provide details of their clinical studies in the dedicated annex using the template provided in the submission system. See definition of clinical studies in the introduction to this work programme part.

Call - A competitive health-related industry (Single stage - 2024)

HORIZON-HLTH-2024-IND-06

Conditions for the Call

Indicative budget(s)[275]

Topics	Type of Action	Budgets (EUR million)	Expected EU contribution per project (EUR million)[276]	Indicative number of projects expected to be funded
		2024		
Opening: 26 Oct 2023 Deadline(s): 11 Apr 2024				
HORIZON-HLTH-2024-IND-06-08	RIA	10.00	8.00 to 10.00	1
HORIZON-HLTH-2024-IND-06-09	CSA	2.00	Around 2.00	1
Overall indicative budget		12.00		

[275] 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 years 2023 and 2024.

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

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.

Proposals are invited against the following topic(s):

HORIZON-HLTH-2024-IND-06-08: Developing EU methodological frameworks for clinical/performance evaluation and post-market clinical/performance follow-up of medical devices and in vitro diagnostic medical devices (IVDs)

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 10.00 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.
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 3 (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 6 "Maintaining an innovative, sustainable and globally competitive health industry". To that end, proposals under this topic should aim to deliver results that are directed, tailored towards and contributing to all of the following expected outcomes:

- Patients gain faster access to innovative, safe and well-performing medical devices;
- Regulators have access to sound scientific resources for clinical/performance evaluation guidance and development of common specifications as foreseen in Article 9 of the Medical Device Regulation (MDR);
- Notified bodies, by their direct participation to the production of documents, will have a harmonised way of assessing the clinical evidence in the pre-market and post-market phases; furthermore their network[277], will be enhanced;
- Health technology developers gain insight on the evidence needed to demonstrate that their devices meet MDR clinical requirements throughout their lifetime. They will also have more guidance on the use of real-world data for their clinical development strategies.

Scope: The Medical Device Regulation (MDR) and *in vitro* diagnostic medical device Regulation (IVDR) provides a new regulatory framework where reinforcement of clinical/performance evaluation of medical devices and IVDs, and in particular high-risk medical devices, is a key element. The confirmation of conformity with the relevant general safety and performance requirements set out in the MDR and IVDR[278] is based on clinical data and its assessment (clinical/performance evaluation), including the evaluation of the acceptability of the benefit-risk- ratio. Within this new framework, the clinical/performance evaluation should follow a defined and methodologically sound procedure based on the critical evaluation of the relevant scientific literature, a critical evaluation of the results of all available clinical investigations/performance studies, as well as consideration of currently available alternative treatment options for the device under evaluation. Clinical/performance evaluation has to be updated throughout the life cycle of the device. Hence, clinical/performance evaluation can draw on multiple types of data including data from initial clinical investigations/performance studies and data gathered by the manufacturer's post-market surveillance system. To operationalise this new requirement, research is needed to help regulators develop common methodological frameworks (including common specifications[279]) on the clinical evidence needed to demonstrate safety, performance and

277 Article 49 – Coordination Group of notified bodies
278 Annex I General safety and performance
279 Mandatory applicable "technical standards" providing to the manufacturers means of proving conformity with the safety and performance legal requirements, issued by Commission as Implementing Acts.

clinical benefit all along the life cycle of devices taking into account the type of device and clinical intended purpose.

Such methodological frameworks and standardised approaches are particularly needed for high-risk medical devices, e.g. implantable and class III medical devices, class C and D IVDs, medical device software (including AI enabled devices and next generation sequencing) and other highly innovative devices.

In order to address the differences between evidence generation for medical devices and IVDs, the project should be tackled taking into account those differences.

Proposals should address all of the following activities:

- Development of a framework for a life-cycle approach to evidence generation and evaluation of high-risk and innovative medical devices and IVDs. This framework will provide a description of the types of evidence i) that meet safety and performance for market access, and ii) that have to be generated to fulfil post-market responsibilities. When appropriate it would be beneficial to consider to what extent the framework could be relevant to demonstrate relative effectiveness as needed for Health Technology Assessment. As regards highly innovative devices, particular attention may be paid to defining acceptable levels of uncertainty in terms of benefit-risk ratio at market entry as well as the type of post-market follow-up to be implemented to generate additional clinical evidence able to reduce this uncertainty. This could be particularly relevant for devices e.g. having no or little similarities with existing devices in terms of intended purpose, mode of action, materials or, for IVDs, with no existing reference materials.;

- For medical devices, a pilot to support development of common specifications which would set the stage for a common specification ecosystem for medical devices in the EU[280], including the development of standardised/common endpoints and associated health outcomes measures by technology type and where relevant by clinical intended purpose;

- Development of a general methodological approach to define, determine and update the state of the art for different device technologies. The robustness of the developed approach should be evaluated on 3 different medical device types and 3 different IVD types;

- Possible use of registries and other sources of real-world data for demonstration of regulatory compliance both pre- and post-market: minimum requirements for data quality, completeness and data reliability, statistical methods for data analysis, methods for limiting biases, methods for data linkage, determination of what acceptable evidence can be drawn from registries;

- Methodology for bridging studies for devices and IVDs with iterative development: assessment of data coming from previous versions of the device and where relevant

[280] building on previous initiatives such as PARENT, CORE-MD, JAMS

integration of that data into the device's clinical investigation/performance study and gap assessment between the different versions of the device;

- Identification of relevant quantitative and qualitative methodologies for integrating evidence derived from various data sources in the clinical evaluation/performance evaluation;

Proposals should build on relevant completed and ongoing initiatives in the field, in particular (but not restricted to) EU-funded initiatives.[281] Proposals should involve researchers who are specialised in the clinical/performance evaluation of medical devices/IVDs and in the use of real-world data to evaluate medical products. Proposals should involve national competent authorities, notified bodies, IVD laboratories as well as Health Technology Assessment bodies and could involve patients' representatives where relevant.

Applicants envisaging to include clinical studies should provide details of their clinical studies in the dedicated annex using the template provided in the submission system. See definition of clinical studies in the introduction to this work programme part.

HORIZON-HLTH-2024-IND-06-09: Gaining experience and confidence in New Approach Methodologies (NAM) for regulatory safety and efficacy testing – coordinated training and experience exchange for regulators

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 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. The Joint Research Centre (JRC) may participate as member of the

[281] e.g. PARENT (PAtient REgistries iNiTiative) Joint Action, CORE-MD (Coordinating Research and Evidence for Medical Devices) H2020 research project, JAMS (Joint Action on Market Surveillance of Medical Devices) initiative

	consortium selected for funding.
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 3 (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 6 "Maintaining an innovative, sustainable and globally competitive health industry". To that end, proposals under this topic should aim to deliver results that are directed, tailored towards and contributing to all of the following expected outcomes:

- European regulators gain state-of-the-art knowledge on different NAMs that are being proposed for the assessment of the safety and efficacy of chemicals and pharmaceuticals;
- European regulators understand better the shortcomings of the current tools based on animal procedures for the assessment of chemicals and pharmaceuticals;
- European regulators collaborate on a framework on how to assess the safety of chemicals based on NAM-data and how to classify the hazardous properties based on such data;
- European regulators collaborate on a similar framework for assessment of safety and efficacy of pharmaceuticals based on NAM-data;
- Citizens benefit from the supply and use of chemicals and pharmaceuticals that have been assessed through NAMs that are better predicting potential effects in humans than the current assessment methods;
- Industry has an improved competitive position with the availability of harmonised and standardised NAM-based assessment tools that are faster and more flexible;
- European Commission and Member States regulators are responding to the societal demand to move away from animal testing.

Scope: There is increasing scientific evidence pointing to the limitations of animal testing for safety and efficacy assessment of chemicals and pharmaceuticals. Europe is also experiencing a strong societal demand to move away from animal testing. Scientific progress of the past two decades has produced a number of animal-free New Approach Methodologies (NAMs) that have the potential to be used instead of the animal models that are currently employed for such testing. However, knowledge, experience and confidence on how results from the NAM assays could be used is still lacking among regulators, which could limit the industry's use of NAMs because of lack of legal certainty when generating safety and health data requested by EU legislation.

The proposals should focus on alternatives to the use of animals for regulatory safety and efficacy testing. Applicants should propose activities that bring together NAM developers and NAM users with European regulators responsible for the safe use of chemicals (e.g. industrial chemicals, pesticides, biocides and cosmetics) and pharmaceuticals in order to inform on NAM solutions available and to encourage the building of a framework on how these NAMs could be most effectively used in the different decision-making contexts. For NAMs applicable to chemical risk assessment, collaboration with existing initiatives such as the Partnership for the Assessment of Risks from Chemicals (PARC) and the ASPIS cluster of projects (Animal-free Safety Assessment of chemicals: Project cluster for Implementation of novel Strategies) is encouraged.

To build such a framework the proposals should address all of the following:

- develop technical and regulatory readiness criteria
- reflect on how to provide mechanisms to support technology transfer, i.e. bringing promising NAMs to the market (including optimisation and transferability assessment)
- discuss how to standardise NAMs and NAM-based strategies via OECD, CEN, ISO, ICH, VICH and other international organisations, as applicable
- provide technical training for Contract Research Organisations (CROs) applying NAMs for regulatory purposes
- promote dialogue (involving companies, regulatory bodies on EU level, including ECHA, EMA and EFSA and Member States authorities) on how to integrate and interpret data from NAMs and facilitate their uptake for safety and efficacy testing of chemicals (including pesticides) and pharmaceuticals, while addressing the lack of reliability and shortcomings of the current tools based on animal procedures
- identify obstacles in EU legislation for the regulatory use of NAMs and propose options/changes in the EU regulatory framework which address these obstacles and facilitate the uptake and use of NAMs

Proposals should consider involving the JRC to take advantage of its expertise and relevant activities in bridging research and regulatory communities and facilitating uptake of NAMs for regulatory application. In that respect, the JRC is open to collaborate with any successful proposal after its approval.