Priority should be given to bio-printing approaches that either target vital internal organs followed by surgical grafting or employ in-situ approaches depositing the cell-laden bioink directly from the printhead or endoscope on the defect target site in the body.

Regulatory knowledge of the field is desired and should be documented through contacts with relevant national or international European regulatory authorities. A good understanding of the different steps involved and the inherent risks in each of these steps will be a basis to identify appropriate safety and quality requirements. Requirements from the different established EU frameworks on Substances of Human Origin (SoHO), medical devices and pharmaceuticals including Advanced Therapy Medicinal Products (ATMPs) should be considered for manufacturing/preparation as well as for clinical outcome monitoring. A combination of requirements from different frameworks might be most appropriate to allow for responsible and fast uptake.

Proposals under this topic may address any therapeutic area, i.e. any disease, dysfunction or defect. Sex differences at the cellular level should be taken into consideration.

Preclinical stage and clinical development are eligible. The involvement of small and medium-sized enterprises (SMEs)[400] is encouraged.

The European Commission's Joint Research Centre (JRC) may contribute to the proposals selected for funding with work on strategic technologies for economic security and innovative industrial ecosystems, particularly activities on innovation in vitro biotechnologies.

Applicants should provide details of their clinical studies[401] 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-2027-03-TOOL-04: Virtual Human Twins (VHTs) for integrated clinical decision support in prevention and diagnosis

Call: Cluster 1 - Health (Single stage - 2027/2)	
Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of between EUR 10.00 and 12.00 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 39.30 million.
Type of Action	Research and Innovation Actions

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

401 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.

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). 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: The granting authority may, up to 4 years after the end of the action, object to a transfer of ownership or to the exclusive licensing of results, as set out in the specific provision of Annex 5.

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 that are directed at, tailored towards and contributing to all the following expected outcomes:

- Healthcare professionals have access to multi-scale[402], multi-organ models of individual patients that aim to improve prevention and diagnosis in high disease burden areas.
- Health professionals benefit from enhanced knowledge of complex diseases and co-morbidities by recourse to multi-scale, multi-organ models.
- Patients with diverse characteristics (e.g. of any sex, age group, racial or ethnic origin[403]) benefit from improved, integrated and personalised prevention and diagnostics tools.
- Health professionals and patients benefit from the use of "Virtual Human Twin" (VHT) models which enable integration of other preventive and diagnostic tools and modalities.

[402] In the context of this topic, multi-scale refers to modelling at different levels of human anatomy, e.g. at (sub-)cellular, tissue, organ or organ system level.

[403] The use of the term 'racial or ethnic origin' does not imply an acceptance of theories that attempt to determine the existence of separate human races.

Scope: VHTs are digital representations and in-silico models of an individual's health and disease state at different levels of anatomy. Multi-scale, multi-organ VHT solutions have a potential for tailored prevention and diagnosis, particularly in areas of high disease burden, and can significantly benefit citizens' health and the efficiency of EU health systems.

Proposals should take into account the work of projects funded under topic HORIZON-HLTH-2023-TOOL-05-03: "Integrated, multi-scale computational models of patient patho-physiology ('virtual twins') for personalised disease management", which had a predominant focus on disease management, and focus on high-potential multi-disciplinary approaches at greater complexity (multiscale, multiorgan, longitudinal), strengthening their deployment in health and care, including the integration into care pathways and links with other decision support tools.

The proposals should address all the following activities:

- Select clinical use cases to deliver multi-disciplinary, high impact solutions requiring multi-organ, multi-scale approaches to modelling complex pathophysiology over time, as a basis from where prevention and diagnosis of diseases with high morbidity and mortality could be enhanced. Proposals can put forward use cases in any areas of high disease burden; examples include co-morbidities, chronic cardiovascular conditions, infection and (auto)immunity, inflammation and cancer, diabetes and related conditions, rare diseases, degenerative diseases (including their interaction with mental health conditions), the exposome and its impact on human health and disease.

- Building on current approaches, standards, data repositories (e.g. biobanks, environmental data, others) and modelling assets (e.g. those of the EDITH CSA[404] and the Platform for Advanced VHT Models[405]), and new data if relevant, design, develop, extend and validate multi-organ, multi-scale, dynamic computational models that accurately simulate a person's health and disease states, as necessary.

- Evaluate, select, extend and validate diverse modelling methodologies, resulting in integrated, advanced, interoperable, patient-specific VHT models that can integrate diverse data sources and methodologies, addressing the chosen clinical use case requirements. Methodologies may include and are not limited to biophysics-based modelling, artificial intelligence (AI) that should be interpretable or allow explainability of outcomes, generative AI and in-silico modelling, agent-based and network physiology approaches. Evaluation, selection and extension of these should be documented during the design phase. Availability and integration of the multi-modal data should be documented, and the ethical and sex dimensions be investigated.

- Demonstrate integration of these models with other advanced preventive and diagnostic modalities, tools and techniques enabling integration across pathways.

404 See the "European Virtual Human Twin" Coordination and Support Action EDITH, funded under the Digital Europe Programme: https://www.edith-csa.eu

405 Funded under the Digital Europe Programme, procedure identifier EC-CNECT/LUX/2024/OP/0014: https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/tender-details/16cc3c6a-844a-42d4-9746-dcc7444b8001-CN

- Generate evidence, including clinical validation, that the solutions deliver clinically meaningful decision support, addressing use case requirements. Document lessons-learned for broader application. Gather evidence via health economic and/or feasibility studies in real-world healthcare settings confirming cost-effectiveness vis-à-vis current practice (e.g. cost-effectiveness analysis). Produce an exploitation plan on regulatory compliance[406] and intellectual property.

Proposals should be multidisciplinary; solution design and development should be end-user-focused and draw on user and non-user input. Best practice in VHT software development including responsible AI development should be followed (e.g. risk assessment and management, requirements definition process).

Participation of small and medium-sized enterprises (SMEs)[407] is encouraged.

Proposals should contribute to the objectives of the European VHT Initiative[408] and to the Platform for Advanced VHT Models, with project assets made available on the Platform and interoperable with its technical specifications[409]; relevant consortia members should join its User Community. Budget should be reserved for these activities. Projects are expected to collaborate with other EU-funded projects on VHTs[410] and align with relevant EU initiatives funded under Horizon Europe, the Digital Europe Programme [411] and the EU4Health Programme (2021-2027)[412], e.g. European Cancer Imaging Initiative[413], 1+Million Genomes Initiative [414], Intensive Care Unit Data Space [415], co-funded European Partnership for Personalised Medicine[416], and projects on advancing AI in health where relevant.

This topic requires the effective contribution of social sciences and humanities (SSH) disciplines and 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[417] 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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406 For example with Regulation (EU) 2017/745 on medical devices: http://data.europa.eu/eli/reg/2017/745/oj, Regulation (EU) 2017/746 on in vitro diagnostic medical devices: http://data.europa.eu/eli/reg/2017/746/2025-01-10, Regulation (EU) 2024/1689 laying down harmonised rules on artificial intelligence: http://data.europa.eu/eli/reg/2024/1689/oj

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

408 https://digital-strategy.ec.europa.eu/en/policies/virtual-human-twins

409 No contact with the developer of the Platform is required at proposal stage.

410 Including the projects funded under topic HORIZON-HLTH-2023-TOOL-05-03: "Integrated, multi-scale computational models of patient patho-physiology ('virtual twins') for personalised disease management"

411 https://digital-strategy.ec.europa.eu/en/activities/digital-programme

412 https://commission.europa.eu/funding-tenders/find-funding/eu-funding-programmes/eu4health_en

413 https://digital-strategy.ec.europa.eu/en/policies/cancer-imaging

414 https://digital-strategy.ec.europa.eu/en/policies/1-million-genomes

415 https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/topic-details/digital-2023-cloud-ai-04-icu-data

416 https://cordis.europa.eu/project/id/101137129, https://www.eppermed.eu

417 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.