an innovation, it is important to consider all relevant legislative frameworks including MDR[440] and IVDR[441], the proposed SoHO-Regulation[442], and AI Act[443] among others.

Proposals are encouraged to consider, where relevant, the data, expertise and services offered by European research infrastructures especially those active in the health domain, such as EATRIS ERIC[444], and also the findings of previous EU-projects (e.g.: CORE-MD[445]).

HORIZON-HLTH-2027-01-IND-01: Development of cell-free protein synthesis platforms for discovery and/or production of biologicals

Call: Cluster 1 - Health (Single stage - 2027/1)	
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 24.50 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). Subject to restrictions for the protection of European communication networks.

440 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices: https://eur-lex.europa.eu/eli/reg/2017/745/oj

441 Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices: https://eur-lex.europa.eu/eli/reg/2017/746/oj

442 Regulation (EU) 2024/1938 of the European Parliament and of the Council of 13 June 2024 on standards of quality and safety for substances of human origin intended for human application: https://eur-lex.europa.eu/eli/reg/2024/1938/oj

443 https://digital-strategy.ec.europa.eu/en/policies/regulatory-framework-ai, https://eur-lex.europa.eu/eli/reg/2024/1689/oj

444 European Infrastructure for Translational Medicine: https://www.eatris.eu

445 Improved methods for clinical investigation and evaluation of high-risk medical devices: https://www.core-md.eu

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 "Maintaining an innovative, sustainable, and competitive EU health industry". 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:

- Biopharmaceutical industries get access to streamlined development and production processes for peptide- or protein-based biologicals.
- Health systems benefit from the availability of enhanced or decentralised production systems for innovative health technologies that involve peptides or proteins, and which improve health and care.
- Citizens and patients will benefit from better access, availability and affordability of pharmaceuticals based on biologicals.

Scope: Cell-Free Protein Synthesis (CFPS) has been employed in fundamental biological research for decades, however, interest for the approach as a viable means for drug development and production has only emerged in recent years. The advantages that CFPS provides in terms of efficiency, simplicity, flexibility, cost- and time savings outweigh the hurdles that are still to be overcome for CFPS to become a routine manufacturing system for peptide- or protein-based biologicals.

Currently, there are several CFPS systems used that are either based on prokaryotic or eukaryotic cell lysates (including mammalian) or fully synthetic systems consisting of all the molecular machinery necessary to create functional proteins. The choice of a specific lysate is dictated by the target protein and the end-use application. Proteins that require post-translational modification are generally produced using lysates of mammalian cells. Hence systems based on mammalian cells are of particular interest as they combine properties inherent to eukaryotic cells and their ability to produce human-like glycosylated proteins with the advantages of cell-free synthesis. These proteins include antibody fragments, antigens, virus-like particles, cytokines, enzymes, antimicrobial peptides and proteins containing non-natural amino acids. The benefits of CFPS are manifold, from ease of handling and scalability, on-demand launch of production, ability to rapidly switch products, simplified purification to facilitated

standardisation and quality control. CFPS needs less energy resources, the manufacturing footprint is less complex and smaller than in cell cultivation and it enables production of proteins that have toxic effects on cells. In addition, CFPS has the potential as an enabling technology for personalised medicines and is amenable to decentralised manufacturing. CFPS has gained even more interest in the recent past owing to advances in synthetic biology and thanks to the rise of Machine-Learning/Artificial Intelligence (ML/AI). The use of generative deep learning and artificial intelligence has high potential in the de-novo design of biomolecules with specific properties of therapeutic and/or preventive nature. CFPS offers here great opportunities to increase the throughput in screening of the de-novo created biomolecules.

The application of synthetic biology, potentially also combined with generative AI, and cell-free biosynthesis open up new avenues for the design, discovery and manufacture of therapeutics not only against infectious diseases, but also non-communicable diseases and equally for vaccines.

Proposals should address at least two of the following elements:

- Address the bottlenecks that currently hamper the large-scale deployment of CFPS, i.e. the lack of a quality-by-design approach, the need to fully characterise the underlying cell lysates and their critical quality attributes and the need for better understanding of the correlations between specific cell lysate properties and CFPS process parameters, specific product quality attributes (such as protein folding), and CFPS platform performance.

- Use synthetic biology techniques for the design of de-novo biomolecules with specific desired properties (antimicrobial, immunogenic, angiogenic, etc.) and develop suitable cell-free systems for the high-throughput screening of the designed biomolecules.

- Develop novel or optimise existing CFPS platforms for the production of the targeted biomolecule to a Good Manufacturing Practices (GMP)[446] conform process, producing clinical-grade material that can be tested in clinical trials.

The demonstration of the superiority of the developed CFPS platform as compared to the current state-of-the art production system for a specific therapeutic peptide or protein would be an asset and participation of start-ups, micro, small and medium-sized enterprises (SMEs)[447] is encouraged.

Applicants envisaging to include clinical studies[448] should provide details of their clinical studies in the dedicated annex using the template provided in the submission system.

446 https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-4_en

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

448 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.