Inhaltsverzeichnis

Destination 1 – Staying healthy in a rapidly changing society

HORIZON-HLTH-2021-STAYHLTH-01-02: Towards a molecular and neurobiological understanding of mental health and mental illness for the benefit of citizens and patients

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 60.00 million.
Type of Action	Research and Innovation Actions

Expected Outcome: This topic aims at supporting activities that are enabling or contributing to one or several impacts of destination 1 "*Staying healthy in a rapidly changing society*". To that end, proposals under this topic should aim for delivering results that are directed, tailored towards and contributing to one or several of the following expected outcomes:

- Researchers, health care professionals and developers of medical interventions have a much better understanding of how genetic, epigenetic and environmental risk and resilience factors interact to drive or prevent the transition from mental health to mental illness throughout the life course. Developers of medical interventions make use of this understanding to develop novel classes of medications and non-pharmaceutical interventions for the prevention and treatment of mental illnesses (including relapse prevention).

- Mental health professionals have access to different types of validated biomarkers for making more accurate diagnoses (beyond current symptom-based criteria) and for optimising and personalising preventive and therapeutic treatment decisions. As a result, patients receive more targeted therapies and relapse less frequently. They experience less stigma due to more accurate and objective diagnoses and increased public awareness about the molecular and neurobiological basis of mental health and mental illness.

- Citizens have the possibility to undergo laboratory testing for assessing their mental health and their predisposition to mental illnesses, and are given timely evidence-based guidance on personalised preventive measures that underpin their active engagement and adherence to effective strategies for promoting their mental health.

- Public health authorities and policy makers have access to comprehensive clinical trial data on the effectiveness of different types of pharmacological and non-pharmacological strategies for the promotion of mental health and prevention of mental illnesses, helping them draft evidence-based clinical guidelines and best practices as well as design tailor- made prevention policies and campaigns.

Scope: Mental illnesses represent a huge and growing burden for Europe, both at individual and societal level. There is an enormous stigma and they often remain undetected as diagnoses largely depend on symptom-based criteria without any biological markers linked to causative mechanisms. Currently available medications are primarily used by trial and error (rather than in a targeted and personalised manner) and they are all very similar in their mechanisms of action with rather little breakthrough innovation in the last few decades. There is further a lack of evidence base on the optimal use of different pharmacological and non-pharmacological prevention strategies. A deeper molecular and neurobiological understanding of the interplay between genetic, epigenetic and environmental risk and resilience factors, including neural circuit alterations, is critical for the development of objective biomarkers and evidence-based interventions that will significantly improve mental health outcomes.

Accordingly, the proposed research is expected to deliver on several of the following:

- Significantly advance the molecular and neurobiological understanding of how genetic, epigenetic and environmental risk and resilience factors (such as psychosocial experiences, diet, sleep, natural and artificial light, use or abuse of drugs, infections and other exposures) interact to drive or prevent the transition from mental health to mental illness[1] throughout the life course as well as how such molecular and neurobiological changes could be reversed. The use of computational modelling and/or artificial intelligence tools is encouraged for the analysis of big, complex and heterogeneous data[2].
- Develop relevant predictive models through federated analysis of large European cohorts of psychiatric disorders and investigate the biological and neural basis of pathogenetic mechanisms and symptoms shared by different disorders. If relevant to the disorders studied, develop neurobiologically-grounded models of cognition and social behaviour and apply these models and their simulation potential to the understanding and improved management of mental health conditions associated with behavioural or emotional dysfunction.
- Identify, validate and document different types or combinations of biomarkers for all of the following purposes:
    - development of robust quantitative, clinical measures of mental health;
    - identification of signatures, for example genetic and epigenetic blueprints, conferring susceptibility to and protection against mental illnesses;
    - establishment of more objective diagnostic and monitoring criteria (complementing current symptom-based criteria) to improve patient outcomes and reduce the stigma associated with mental illness;
    - prediction of treatment response and risk of relapse for better, more scientifically-guided and targeted use of currently available preventive and therapeutic interventions

[1] This may include any mental and behavioural disorder(s) according to ICD-10 Chapter V (https://icd.who.int/browse10/2019/en#/V) except dementia. Neurological disorders are outside the scope of this topic. Psychiatric disorders to be studied may be acute, chronic or relapsing-remitting in nature and applicants are encouraged to also study the molecular/neurobiological changes brought about by interventions and associated with remission.

[2] Data needs to meet the FAIR principles: findable, accessible, interoperable and reusable.

for different population groups.

For biomarker discovery, applicants are encouraged to take stock of advances in disciplines such as for instance neuropsychology, neurophysiology, neuroendocrinology, neuroimaging, electrophysiological monitoring, e-health/m-health, -omics (genomics, epigenomics, transcriptomics, proteomics, metabolomics, lipidomics, exposomics, microbiomics including the role of the microbiota-gut-brain axis), optogenetics, nanomedicine, stem cell biology, neuroimmunology and immunopsychiatry.

- Discover new disease pathways and drug targets (including pathways involved in maintaining mental health) to boost the development of new (or repurposed) classes of safer and more effective medications[3] for the prevention and treatment of mental illnesses (including relapse prevention).

- Establish the molecular and neurobiological effects as well as cognitive and psychological consequences of both pharmacological and non-pharmacological prevention strategies (for example: neurostimulation, neurofeedback, psychotherapy and other psychological/behavioural interventions, light therapy, diet, exercise, lifestyle, mindfulness or a combination of them) and assess their efficacy and side effects as part of clinical trials (also determining windows of opportunity when preventive actions are most effective throughout the life course).

Proposals may cover different stages in the continuum of the innovation cycle (from basic and translational research to the validation of findings in real-world settings) and should ensure strong involvement of end-users, including citizens and patients. Sex and gender differences and the effects of age should be duly taken into account. International cooperation is encouraged and the proposed research is expected to be multidisciplinary, including through the involvement of medical sciences, psychological sciences, social sciences and the humanities.

All projects funded under this topic are strongly 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. This could also involve networking and joint activities with projects funded under other clusters and pillars of Horizon Europe, or other EU programmes, as appropriate. Therefore, proposals are expected to include a budget for the attendance to regular joint meetings and may consider to cover 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, if appropriate.

[3] Going beyond monoaminergic neurotransmitter systems by targeting novel pathways and addressing also the challenge of getting drugs pass through the blood-brain barrier.

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

HORIZON-HLTH-2021-IND-07-01: Green pharmaceuticals

Specific conditions	
Expected EU contribution per project	The Commission estimates that an EU contribution of around EUR 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: The Joint Research Centre (JRC) may participate as member of the consortium selected for funding.

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 for delivering results that are directed, tailored towards and contributing to some of the following expected outcomes:

- Researchers and regulators understand the environmental impact of pharmaceuticals.
- Public authorities inform pharmaceutical strategies and polices based on scientific evidences.
- Researchers, innovators and pharmaceutical industries develop and produce greener pharmaceuticals that are either greener by design, intrinsically less harmful for the environment, and/or use greener and economically more sustainable manufacturing processes for the production of pharmaceuticals.

Scope: The EU needs to address the increasing problem of environmental pollution due to pharmaceuticals throughout their life cycle. This encompass both, the industry need to tackle the pollution due to their manufacturing as well as pollution resulting from the use and disposal of their pharmaceuticals. This topic is part of an EU strategic approach to pharmaceuticals in the environment[4] and the Pharmaceutical strategy for Europe[5] called for diversifying and secure supply chains and environmentally sustainable pharmaceuticals[6]. The purpose of this topic is twofold.

One of the purposes is to encourage taking into account the environmental aspects of pharmaceuticals as regards their use and disposal. The action intends to promote the development

[4] COM(2019) 128 final; Section 5.2
[5] COM(2020) 761
[6] https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:52020DC0761&from=EN

of pharmaceuticals intrinsically less harmful to environment. As regards the pharmaceuticals already in use, more understanding is needed concerning their environmental concentration and resulting levels of risk. In particular, the solid knowledge of the impact of molecules on the environment through the eco-toxicity studies will contribute to management of environmental risk and may be taken into account for designing of new molecules.

The second purpose is to promote the green innovation in the pharmaceutical manufacturing of marketed medicinal products, in particular manufacturing of their active pharmaceutical ingredients (APIs). It will contribute to ensuring supplies of medicinal products and prevent shortages as well as crisis preparedness. The difficulties in ensuring compliance with the high environmental standards in the EU and high costs of such compliance are considered one of the main reason for pharmaceutical manufacturing leaving the EU. This in turn results in vulnerabilities of the supply chains (reduced number of suppliers of critical inputs, lack of geographical diversification of the suppliers, lack of critical manufacturing capacity in the EU). The new, greener and sustainable manufacturing methods, which would for the reason of lowering the environmental impact rely on recycled solvents, would need at the same time to address the risk of impurities.

Applicants should propose activities linked to several of the following elements:

- Research and innovation to support the development of “greener” pharmaceuticals that degrade more readily to harmless substances in waste water treatment plants and the environment;

- Research on the eco-toxicity and environmental fate of pharmaceuticals, in particular those that are not yet subject to environmental risk assessment;

- Propose innovative manufacturing technology that are greener, low in energy consumption and emissions, using less solvent or recycling solvents;

- Propose methods for eliminating carcinogenic impurities in pharmaceuticals (e.g. nitrosamines) process and medicinal products, in particular as complementary technologies to the manufacturing methods relying on recycled solvents;

- Explore innovative uses of digital transformation or robotic for competitive and scalable methods of production.

The projects should favour a multi-stakeholders approach. They should address the industry needs, taking account of SMEs’ specificities, and offer deployable technical solutions and/or relevant data. They should also integrate at the same time the academic and public health perspective.

Proposals could consider the involvement of the European Commission's Joint Research Centre (JRC) in the field of new approach methodologies for ecotoxicity assessment.