



# 2023 Amended Work Programme

In accordance with Article 25 of the Council Regulation (EU) 2021/2085 and with Articles 6 and 33 of the Financial Rules of the IHI JU.

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# 1 Chronology and list of reviews

Version	Date of the adoption by the GB	Items
Version 1 – Work Programme 2023	22.12.2022	n/a
Version 2 – amended Work Programme 2023	24.07.2023	<b>2. List of acronyms, definitions and abbreviations</b> <b>4.2.2 Scientific priorities, challenges and expected impacts</b> <b>4.2.3 Calls for proposals</b> <b>4.2.4 Calls for tenders and other actions</b> <b>4.2.5 Follow-up activities linked to past calls: monitoring, evaluation and impact assessment</b> <b>4.3.2 Procurement and contracts</b> <b>5. Budget 2023</b> <b>6.1 IKAA Plan for 2023</b> <b>6.2 IHI JU call 4</b> <b>6.3 IHI JU call 5</b>

## 2 List of acronyms, definitions and abbreviations

ACRONYM	MEANING
µl	Microliter (measurement unit for volume)
3Rs	Replace, Reduce, Refine
ABAC	Accrual Based Accounting System
AI	Artificial Intelligence
ACS	American Chemical Society
ACT EU	Accelerating Clinical Trials in EU
AD (HR)	Administrator
AER	Average error rate
AI	Artificial Intelligence
AMR	Antimicrobial resistance
API	Application Programming Interface
AST	Assistant
ASTERIX	ASTERIX - Advancing Small Trials for Regulatory Innovation and eXcellence
ATMP	Advanced Therapy Medicinal Products
BOA	Back-office arrangements
BSI	British Standards Institute
c4c	Connect 4 Children
CA (Budget)	Commitment appropriation
CA (HR)	Contractual Agent
CE	Conformité Européene (European Conformity)
CEPI	Coalition for Epidemic Preparedness Innovations
CIP	Cleaning in Place

ACRONYM	MEANING
CMC	Chemistry, Manufacturing and Controls
CO2	Carbon dioxide
COCIR	European trade association representing the medical imaging, radiotherapy, health ICT and electromedical industries. See <a href="https://www.cocir.org/">https://www.cocir.org/</a>
<b>Council Regulation (EU) 2021/2085</b>	Council Regulation (EU) 2021/2085 of 19 November 2021 establishing the Joint Undertakings under Horizon Europe and repealing Regulations (EC) No 219/2007, (EU) No 557/2014, (EU) No 558/2014, (EU) No 559/2014, (EU) No 560/2014, (EU) No 561/2014 and (EU) No 642/2014. See <a href="https://eur-lex.europa.eu/eli/reg/2021/2085">https://eur-lex.europa.eu/eli/reg/2021/2085</a>
CRISPR/Cas9	Clustered Regularly Interspaced Short Palindromic Repeats/CRISPR-associated protein 9
CRO	Contract Research Organization
CT	Clinical Trials
CTIS	Clinical Trials Information System
DG HR	Directorate-General for Human Resources and Security (European Commission)
DG GROW	Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs (European Commission)
DG RTD	Directorate-General for Research and Innovation (European Commission)
DG SANTE	Directorate-General for Health and Food Safety (European Commission)
DMO	Document Management Officer
DPO	Data Protection Officer
EC	European Commission
ECA	European Court of Auditors
EFPIA	European Federation of Pharmaceutical Industries and Associations. See <a href="https://www.efpia.eu/">https://www.efpia.eu/</a>
EFTA	The European Free Trade Association. See <a href="https://www.efta.int/about-efta/european-free-trade-association">https://www.efta.int/about-efta/european-free-trade-association</a>
EHDS	European Health Data Space

ACRONYM	MEANING
EHR	Electronic Health Records
EHS	Environmental Health and Sustainability
EJP RD	European Joint Programme on Rare Diseases
EMA	European Medicines Agency
EP	European Pharmacopeia
EPPO	European Public Prosecutor's Office
ERN	European Reference Networks
ESG	Environment, Social & Governance
ESR	Evaluation Summary Report
EU	European Union
EU4Health	European Union for Health
EUPATI	European Patients' Academy on Therapeutic Innovation
EUR	Euro
EU RD Platform	European Platform on Rare Disease Registration
EuropaBio	European association representing corporate and associate members across sectors, plus national and regional biotechnology associations which, in turn, represent over 2 600 biotech companies, 2 300 out of them are SMEs. See <a href="https://www.europabio.org/">https://www.europabio.org/</a>
Fabs	Antigen-binding fragments
FAIR Committee	Fraud and Irregularities in Research Committee
FC	Financial contributions
Fcs	Crystallisable fragments
FDA	Food and Drug Administration
FG	Function Group
FP7	Seventh Framework Programme for Research and Technological Development

ACRONYM	MEANING
FTE	Full-time equivalent
FP	Full proposal
FWC	Framework contract
GA	Grant Agreement
GAP	Grant Agreement preparation
GB	IHI JU Governing Board
GCI	Green Chemistry Institute
GDPR	General Data Protection Regulation
GH EDCTP3	European and Developing Countries Clinical Trials Partnership Programme 3
GHG	Greenhouse Gas
HCPs	Healthcare providers
HERA	European Health Emergency Preparedness and Response Authority
Horizon Europe	Horizon Europe is the EU's key funding programme for research and innovation. See <a href="https://ec.europa.eu/info/funding-tenders/find-funding/eu-funding-programmes/horizon-europe_en">https://ec.europa.eu/info/funding-tenders/find-funding/eu-funding-programmes/horizon-europe_en</a> .
HR	Human resources
HTA	Health technology assessment (bodies)
IAS	Internal Audit Service of the European Commission
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICT	Information and communications technology
IDEAL	Integrated Development of Effective Advanced Therapies for Rare Diseases
IHI JU	Innovative Health Initiative Joint Undertaking
IHInet	The intranet of IHI JU
IKAA	In-kind contributions to additional activities

ACRONYM	MEANING
IKOP	In-kind contributions to operational activities
IMI1 JU	Innovative Medicines Initiative Joint Undertaking
IMI2 JU	Innovative Medicines Initiative 2 Joint Undertaking
InSPiRe	Innovative Methodology for Small Populations Research
IP	Intellectual Property
IRB	Institutional Review Board
ISO	International Organization for Standardization
IT	Information technology
IVDs	In Vitro Diagnostics
JDRF	Juvenile Diabetes Research Foundation
JUs	Joint undertakings
KDT JU	Key Digital Technologies Joint Undertaking. See <a href="https://www.kdt-ju.europa.eu/">https://www.kdt-ju.europa.eu/</a>
KOL	Key opinion leader
KPI	Key performance indicator
LCA	Life Cycle Assessment
LFS	Legislative Financial Statement of the European Commission's proposal. See <a href="https://eur-lex.europa.eu/resource.html?uri=cellar:7efecf4b-75de-11eb-9ac9-01aa75ed71a1.0001.02/DOC_1&amp;format=PDF">https://eur-lex.europa.eu/resource.html?uri=cellar:7efecf4b-75de-11eb-9ac9-01aa75ed71a1.0001.02/DOC_1&amp;format=PDF</a>
mAbs	Monoclonal antibodies
MDCG	Medical Device Coordination Group
MedTech Europe	European trade association for the medical technology industry including diagnostics, medical devices and digital health. See <a href="https://www.medtecheurope.org/">https://www.medtecheurope.org/</a>
MEP	Member of the European Parliament
ML	Machine Learning
MOA	Mechanism of Action



<b>ACRONYM</b>	<b>MEANING</b>
<b>MRI</b>	Magnetic Resonance Imaging
<b>NAMs</b>	New Approach Methodologies
<b>NCA</b>	National competent authorities
<b>NGO</b>	Non-governmental organisation
<b>NGRA</b>	Next-Generation-Risk-Assessment
<b>NHP</b>	Non-human primates
<b>Non-EU IKOP</b>	Eligible costs incurred by private members, their constituent or affiliated entities, and contributing partners for implementing project activities carried out in third countries outside of the EU Member States and countries associated to Horizon Europe.
<b>OECD</b>	Organization for Economic Cooperation and Development
<b>OLAF</b>	European Anti-Fraud Office
<b>PA</b>	Payment appropriation
<b>PARC</b>	European Partnership for the Assessment of Risks from Chemicals
<b>PCR</b>	Product Category Rules
<b>PEF</b>	Product Environmental Footprint
<b>PEFCR</b>	Product Environmental Footprint Category Rules
<b>PEG</b>	Pharmaceutical Environment Group
<b>PET</b>	Positron Emission Tomography
<b>PFAS</b>	Poly- and Perfluorinated Alkyl Substances
<b>PI</b>	Principal Investigator
<b>PPP</b>	Public-private partnership
<b>PVCs</b>	Polyvinyl Chlorides
<b>R&amp;D</b>	Research and development
<b>R&amp;I</b>	Research and Innovation

ACRONYM	MEANING
RDP	European Partnership on Rare Diseases
RAE	Risk assessment exercise
RIA	Research and Innovation Actions
RNA	Ribonucleic Acid
RWD	Real-World Data
RWE	Real World Evidence
Q3	Third quarter
SAMIRA	Strategic Agenda for Medical Ionising Radiation Applications
scFvs	Single-chain variable fragments
SDG	Synthetic Data Generation
SEND	Standard for Exchange of Nonclinical Data
SIP	IHI JU Science and Innovation Panel
SMEs	Small and medium-sized enterprises
SMI	Sustainable Markets Initiative
SEDIA	Single Electronic Data Interchange Area (SEDIA), the funding & tender opportunities portal of the European Commission. See here <a href="https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/home">https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/home</a>
SEND	Standard for exchange of nonclinical Data
SiRNAs	Small interfering RNAs
SOP	Standard operating procedure
SPOC	Single Point of Contact
SRIA	Strategic Research and Innovation Agenda
SRG	IHI JU States' Representatives Group
SSbD	Safe & Sustainable by Design
TA	Temporary Agent

ACRONYM	MEANING
TRL	Technology readiness levels
UK-MHRA	UK Medicines and Healthcare products Regulatory Agency
US	United States
USA	United States of America
USP	United States Pharmacopeia
VaccinesEurope	Specialised vaccines group within the European Federation of Pharmaceutical Industries and Associations (EFPIA). See <a href="https://www.vaccineseuropa.eu/">https://www.vaccineseuropa.eu/</a>
WFI	Water for Injection
WHO	World Health Organisation

## 3 Introduction

### 3.1 Mission statement of IHI JU

The Innovative Health Initiative Joint Undertaking (IHI JU) is a partnership between the European Union and industry associations representing the sectors involved in healthcare, namely COCIR (medical imaging, radiotherapy, health ICT and electromedical industries); EFPIA, including Vaccines Europe (pharmaceutical industry and vaccine industry); EuropaBio (biotechnology industry); and MedTech Europe (medical technology industry).

IHI JU aims to pioneer a new, more integrated approach to health research, building on the experience gained from the Innovative Medicine Initiative 2 Joint Undertaking (IMI2 JU). IHI JU also builds on the learnings from the health activities in the former ECSEL JU, now Key Digital Technologies Joint Undertaking (KDT JU), such as enabling electronics components and systems, and the establishment of pilot production lines for smart medical devices and implants involving diverse MedTech actors, which are of high relevance for future activities under IHI JU.

IHI JU aims to translate health research and innovation into real benefits for patients and society, and ensure that Europe remains at the cutting edge of interdisciplinary, sustainable, patient-centric health research. Health research and care increasingly involve diverse sectors. By supporting projects that bring these sectors together, IHI JU will pave the way for a more integrated approach to health care, covering prevention, diagnosis, treatment, and disease management.

As current health challenges and threats are global, IHI JU should be open to participation by international academic, industrial and regulatory actors, in order to benefit from wider access to data and expertise, to respond to emerging health threats and to achieve the necessary societal impact, in particular improved health outcomes for Union citizens.

### 3.2 Background and link with the Strategic Research and Innovation Agenda (SRIA)

Europe has a rising burden of disease, notably non-communicable diseases, and this is linked to its ageing population. Most countries struggle with long-term expenditure and workforce planning in health care, and this problem grows as the age pyramid changes. This challenges the long-term sustainability of EU health care systems, which are under increasing fiscal and organisational pressures.

The COVID-19 health crisis has exacerbated the challenges faced by European health care systems in combatting and managing (infectious) diseases in a coordinated manner. Simultaneously, it also showed, by the delivery in record time of several COVID-19 vaccines, the critical importance of collaborative R&I to respond rapidly to emerging health threats, as well as the strategic value of public-private partnerships.

Strengthened collaboration between industry sectors, academia and public authorities will not only offer better opportunities to respond to public health needs in Europe, but also provide a strong base to launch, grow, and keep companies in Europe, and attract competitive companies to Europe.

The EU has leading health care systems and is a strong global actor in health research. However, it is still relatively weak in translating research results into tangible health solutions that are taken up by health care systems in Europe. This can partially be attributed to insufficient early consideration of the needs of society and/or patients and end-users. Thus, these actors must be involved in all stages of research, from project design through to implementation, to develop meaningful innovations.

IHI JU aims to enable the cross-sectoral integration of technologies, know-how, products, services, and workflows for people-centred health care.

IHI JU aims to lay the foundations for the development of safer and more effective health care products or solutions that respond to unmet public health needs and that can be taken up by health care systems. The goal is a more targeted intervention strategy leading to personalised treatments and improved individual health outcomes, via cost-effective and affordable health solutions.

The research supported by IHI JU should remain at pre-competitive level and does not aim to deliver products or services directly to health care systems or the market.

This partnership reflects the importance of the full spectrum of health technologies, as well as the progress in convergence of health technology areas and a significantly more prominent role for digital technologies and data analytics in health research than when IMI2 JU was established. IHI JU will thus respond to the recommendation of the IMI2 JU interim evaluation to “enable the active engagement of other industry sectors with the pharmaceutical industry”<sup>1</sup>. A key element for linking all these industry sectors is the necessity to use, and share, data involving innovative digital tools to perform people-centred translational R&I for the benefit of the European people and health systems.

The SRIA<sup>2</sup> defines the overall scope of activities of IHI JU, in line with its founding legislation<sup>3</sup>, to enable the achievement of its general objectives by 2030:

- contribute towards the creation of an EU-wide health research and innovation ecosystem that facilitates translation of scientific knowledge into innovations, notably by launching at least 30 large-scale, cross-sectoral projects, focussing on health innovations;
- foster the development of safe, effective, people-centred and cost-effective innovations that respond to strategic unmet public health needs, by exhibiting, in at least 5 examples, the feasibility of integrating health care products or services, with demonstrated suitability for uptake by health care systems. The related projects should address the prevention, diagnosis, treatment and/or management of diseases affecting the EU population, including contribution to ‘Europe’s Beating Cancer Plan’; drive cross-sectoral health innovation for a globally competitive European health industry and contribute to reaching the objectives of the new Industrial Strategy for Europe and the Pharmaceutical Strategy for Europe.

### 3.3 Strategy for the implementation of the programme

The key focus of the strategy for 2023 will be to continue to ensure the implementation of the SRIA priorities. This will be achieved through the launch of open and competitive calls for proposals. The work of the Science and Innovation Panel will be central to the development of call topics and the implementation of the scientific priorities. In addition, an essential element of implementing the priorities will be to engage and mobilise industrial partners from all the sectors covered by the programme, as well as all relevant stakeholders such as patients, health care authorities, health care professionals and providers to mention but a few. Efforts will also be committed to establishing synergies with other parts of Horizon Europe, such as missions, partnerships or specific programmes, as well as establishing links with international organisations.

<sup>1</sup> European Commission (2017), The Interim Evaluation of the Innovative Medicines Initiative 2 Joint Undertaking (2014-2016) operating under Horizon 2020. Experts Group Report. Luxembourg: Publications Office of the European Union

<sup>2</sup> [https://www.ihj.europa.eu/sites/default/files/uploads/Documents/About/IHI\\_SRIA\\_ApprovedJan22.pdf](https://www.ihj.europa.eu/sites/default/files/uploads/Documents/About/IHI_SRIA_ApprovedJan22.pdf)

<sup>3</sup> [https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.L\\_.2021.427.01.0017.01.ENG](https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.L_.2021.427.01.0017.01.ENG)

Across all of the activities planned a key element will be to adopt an assertive communication strategy to target audiences with an emphasis on the openness, transparency, relevance, and coherence of IHI JU activities with its defined objectives and those of Horizon Europe. This is particularly important to promote the new programme and attract high quality applications to IHI JU calls for proposals. A key goal of this outreach strategy will be to engage with and mobilise new players and newcomers.

An important element of the Programme Office work will be to continue to support the projects established under IMI1 and IMI2 programmes. This is important for two reasons, firstly, the monitoring and acceptance of costs associated with these projects will ensure the continued sound financial management of the programme. Secondly, it is very important to continue to disseminate and promote the results of these projects. Meetings, workshops and webinars etc will be organised to mobilise the established projects and disseminate their results to demonstrate the impact of the work supported by IHI JU and its impact on patients and wider society.

## 4 Work Programme 2023

### 4.1 Executive summary and message from the Executive Director

2023 will be the second full year of IHI JU implementation. The Programme Office, having prepared all of the structures for governance and implementation in 2022, will fine tune and solidify processes to optimise the functioning of the governing bodies of IHI JU. This will allow continued implementation of the SRIA and will result in the launch of further calls for proposals which will engage EUR 198 350 000 (Call 4 and Call 5). We will commit these funds to build new multi sectorial public private projects that take advantage of the ongoing technology convergence in the health sector, advances in digitalisation and the use of 'big' data. By doing so, we aim to accelerate the pace of innovation and allow access to the results for a large portion of the EU population, especially patients and their carers.

We will also focus on optimising the dissemination and exploitation of results coming from the large legacy of IMI projects that IHI JU is managing.

We will implement all of this taking care to abide by the principles of sound financial management which has permitted a clean opinion from the European Court of Auditors in prior years.

We will continue to proactively communicate about opportunities for funding for IHI JU ensuring the widest possible involvement from all sectors, SMEs and the widening countries. Equally assertively, we will communicate on all of the results and impacts coming from projects of IHI JU and the preceding initiatives.

IHI JU will drive new partnerships and seek synergies with those organisations with like-minded or convergent agendas. The initial contacts established in this regard with GH EDCTP3, the Cancer Mission, KDT JU, HERA and EIT Health will be further developed.

## 4.2 Operational activities of IHI JU for 2023

### 4.2.1 Objectives, indicators and risks

#### Key objectives

The key objectives for IHI JU operations in 2023 are identified by the Governing Board in the Work Programme and by the management team at operational level.

The key operational objectives for 2023 are as follows:

- execute the Strategic Research and Innovation Agenda priorities, enabling the active engagement of industry sectors covering the pharmaceutical, the biopharmaceutical, biotechnology and medical technology sectors, including companies active in the digital area, and a range of other key stakeholders involved in health care (including SMEs, academia, health care authorities, health care professionals and providers, and patient organisations), in particular through the launch of open and competitive calls for proposals;
- ensure continuity with, and manage the legacy from, the Innovative Medicines Initiative 2 Joint Undertaking;
- ensure sound budget implementation through the effective and efficient management of calls for proposals, grant award processes, close monitoring of projects and error rate;
- promote the cross sectorial partnership in health through proactive outreach strategies to attract high quality applications to IHI JU calls for proposals and engage with new players and newcomers;
- demonstrate the EU added value of IHI JU through assertive communication to target audiences with an emphasis on the openness, transparency, relevance, and coherence of IHI JU activities with its defined objectives and those of Horizon Europe;
- explore synergies with relevant programmes at Union, national, and regional level, in particular with those supporting the deployment and uptake of innovative solutions, training, education and regional development;
- improve and broaden access to project outcomes by embedding dissemination and exploitation activities in all stages of the project lifecycle.



## Indicators

IHI JU is built around the idea that cross-stakeholder and cross-sectorial collaboration will enable significant advancements and breakthrough innovations in the field of healthcare, including the pharmaceutical industry but also new sectors such as biopharmaceutical, medical technologies, and biotechnologies. Therefore, the multi-stakeholder involvement and the cross-sector alliance are fundamental aspects that will be monitored as indicators of good programme performance.

Another important aspect of IHI JU that will be tracked over its lifecycle is the ability of the projects to interact with regulators and potentially improve clinical guidelines.

Additionally, the ability of the projects to generate tools to use in clinical practice/R&D to understand health determinants and the ability to share this knowledge through publications will be observed throughout the programme. In line with the challenges of today's scientific landscape, the performance of IHI JU will be also evaluated by looking at the examples of projects that will be able to generate people-centred integrated healthcare solutions, and to produce innovations enabling the integration and management of health care data as well as the use of artificial intelligence applied to healthcare.

Ultimately, IHI JU will have to demonstrate the ability to translate knowledge into innovation, to address public health needs and to help contribute to a globally competitive EU health care industry through the novelties and inventions deriving from its funded projects.

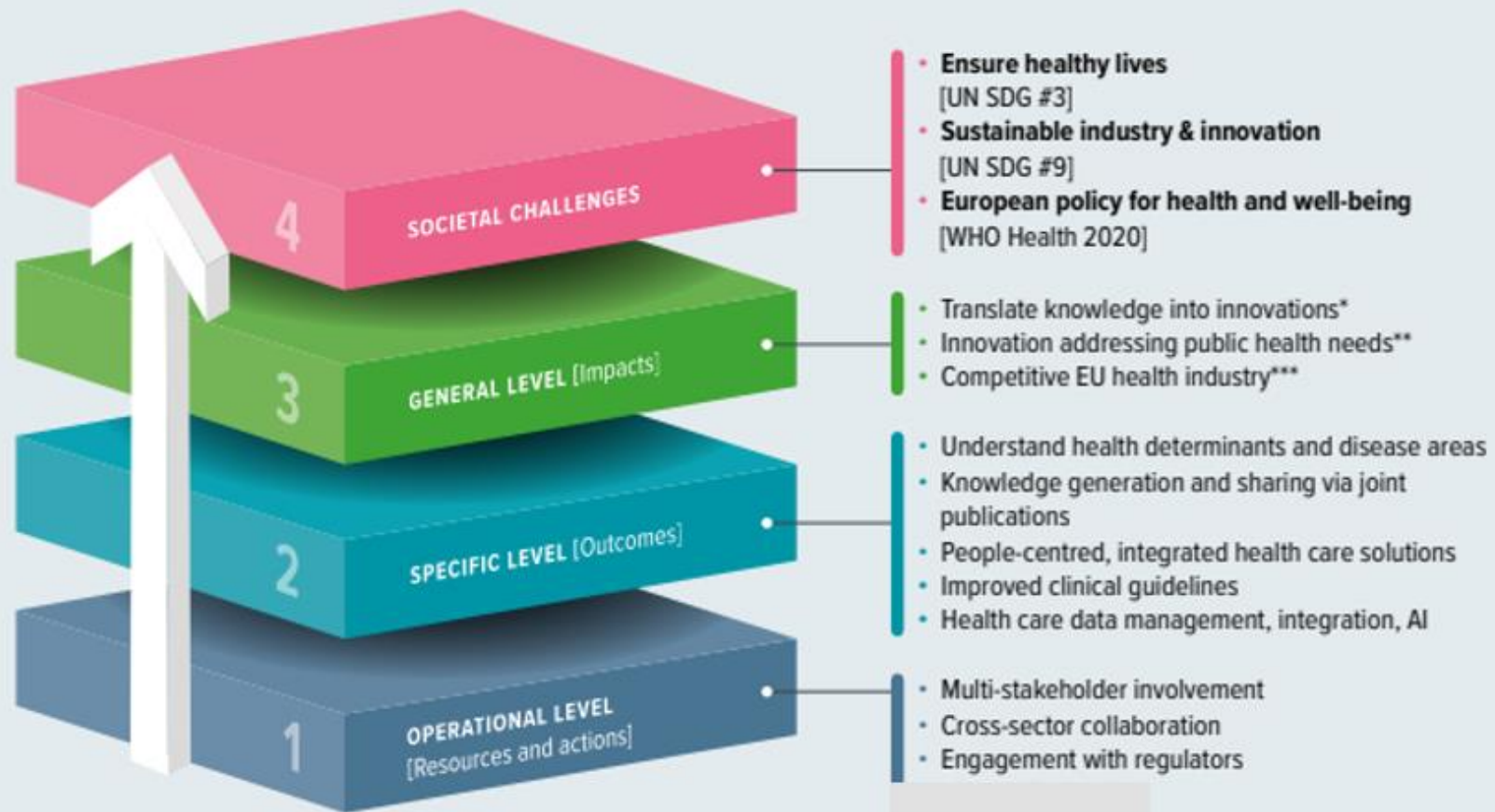
These aspects of IHI JU's nature have been translated into a monitoring framework that consists of a matrix of key performance indicators stratified in 3 levels (in line with the template provided by the EC-RTD):

- Operational objectives, also called “**resources and actions**”
- Specific objectives, also called “**outcomes**”
- General objectives, otherwise called “**impacts**”

This type of structure essentially illustrates how the resources (operational objectives) contribute to the outcomes (specific objectives) and to the impacts (general objectives) to ultimately help reach the higher-level ultimate goals:

- UN Strategic Development Goal #3 (good health and well-being)  
<https://www.un.org/sustainabledevelopment/sustainable-development-goals/>
- UN Strategic Development Goal #9 (industry, innovation, and infrastructure)  
<https://www.un.org/sustainabledevelopment/sustainable-development-goals/>
- The WHO Europe 2020 Health Priorities  
[https://www.euro.who.int/\\_data/assets/pdf\\_file/0011/199532/Health2020-Long.pdf](https://www.euro.who.int/_data/assets/pdf_file/0011/199532/Health2020-Long.pdf)

## IHI vision: contribute to societal challenges through ...



\* IHI General Objective 1:  
Contribute toward the creation of an EU-wide health research and innovation ecosystem that facilitates translation of scientific knowledge into innovations

\*\* IHI General Objective 2:  
Foster the development of safe, effective, people-centric and cost-effective innovations that respond to strategic unmet public health needs

\*\*\*IHI General Objective 3:  
Drive cross-sectoral health innovation for a globally competitive European health industry

The IHI JU specific key performance indicators (KPIs) are linked to the IHI JU vision and have been developed ensuring that there is clear alignment between the overall objectives of IHI JU and the measures used to monitor progress throughout the life of the programme. The KPIs have been elaborated and guided by the so-called RACER Principles<sup>4</sup>.

KPI name	Unit of measurement	Baseline <sup>5</sup>	Target <sup>6</sup> 2023	Target 2025	Target 2027	Ambition >2027	Status
<b>Resources (input), processes and activities</b>							
<b>1.1.</b> Involvement of multiple health care stakeholders	Share of projects involving more than two types of health care stakeholders [research higher or secondary education organisations (private or public), small & medium enterprise (SME), large company (for-profit legal entity), non-governmental organisations (NGOs), healthcare professional organisation/healthcare provider, patient / citizen organisation, regulators or regulatory body, notified body, health technology assessment body (HTA), health care payer, charity and foundation, public authority] as project participants or advisors	50%	55%	60%	65%	70%	
<b>1.2.</b> Cross-sectoriality of the partnership	Share of projects bringing together private members and/or contributing partners (or their affiliated or constituent entities) from two or more technology sectors <sup>7</sup>	25%	70%	80%	85%	90%	
<b>1.3.</b> Engagement of regulators	Number of projects interacting with regulators <sup>8</sup> to contribute to new or improved guidelines or methodologies	13	0	5	10	20	

<sup>4</sup> The RACER principles are 1- Relevant, i.e. closely linked to the objectives to be reached. They should not be overambitious and should measure the right thing (e.g. a target indicator for health care could be to reduce waiting times but without jeopardising the quality of care provided); 2- Accepted (e.g. by staff, stakeholders). The role and responsibilities for the indicator need to be well defined (e.g. if the indicator is the handling time for a grant application and the administrative process is partly controlled by Member States and partly by the EU then both sides would assume only partial responsibility). 3- Credible for non-experts, unambiguous and easy to interpret. Indicators should be simple and robust as possible. If necessary, composite indicators might need to be used instead – such as country ratings, well-being indicators, but also ratings of financial institutions and instruments. These often consist of aggregated data using predetermined fixed weight values. As they may be difficult to interpret, they should be used to assess broad context only. 4 - Easy to monitor (e.g. data collection should be possible at low cost). 5 - Robust against manipulation (e.g. administrative burden: If the target is to reduce administrative burdens to businesses, the burdens might not be reduced, but just shifted from businesses to public administration).

Source: page 250 of “*Better Regulation Guidelines*” EU Commission: [https://ec.europa.eu/info/law/law-making-process/planning-and-proposing-law/better-regulation-why-and-how/better-regulation-guidelines-and-toolbox\\_en](https://ec.europa.eu/info/law/law-making-process/planning-and-proposing-law/better-regulation-why-and-how/better-regulation-guidelines-and-toolbox_en)

<sup>5</sup> Baselines are derived (where possible) from the Innovative Medicines Initiative (IMI2) as the predecessor to IHI.

<sup>6</sup> Reporting methodology: cumulatively reporting from the beginning of IHI until 31/12/2030.

<sup>7</sup> The IHI JU private members COCIR, EFPIA, EuropaBio and MedTech Europe have members from several technology sectors. Contributing partners might also cover further technology sectors.

<sup>8</sup> In this document, the term ‘regulators’ refers to the different bodies involved in the processes regulating medical products (e.g., scientific assessment, production of scientific guidelines, scientific advice to manufacturers, granting/refusal/suspension of marketing authorisations, post-market surveillance, withdrawing/recalling of devices put on the market, authorisation and oversight of clinical trials). It includes the European Commission, National Competent Authorities (NCA), the Medical Device Coordination Group (MDCG), and the European Medicines Agency (EMA). notified bodies (NB), while designated to perform a regulatory function (verification of medical device/in-vitro diagnostics conformity), cannot be considered as regulators in the strict sense of this definition. However, the potential input and expertise of notified bodies may still be relevant for the design and implementation of the activities of the proposed initiative.

KPI Name	Unit of measurement	Baseline	Target 2023	Target 2025	Target 2027	Ambition >2027	Status
<b>Outcomes</b>							
<b>2.1. Cross-stakeholder collaboration</b>	Share of multi-stakeholders' publications identified through bibliometric data analysis [research / higher or secondary education organisations (private or public), small & medium enterprise (SME), large company (for-profit legal entity), non-governmental organisations (NGOs), healthcare professional organisation / healthcare provider, patient / citizen organisation, regulators or regulatory body, notified body, health technology assessment body (HTA), health care payer, charity and foundation, public authority]	65%	65%	66%	67%	70%	
<b>2.2. Public-private collaboration</b>	Share of publications across public and private stakeholders identified through bibliometric data analysis (academic, pharmaceutical, biopharmaceutical, medical technologies, biotechnologies)	65%	65%	66%	67%	70%	
<b>2.3. Project outputs for use in clinical practice and health research development and innovation (R&amp;D&amp;I)</b>	Number of: <ul style="list-style-type: none"> <li>new tools for studying new potential drug targets such as new pharmacological tools, therapeutic modalities, and patient-derived assays available to the scientific community;</li> <li>new tools to test diagnostically and/or therapeutically relevant hypotheses in pre-clinical models and/or clinically in uncharted areas of disease biology;</li> <li>new tools for prediction, prevention, interception, surveillance, diagnosis, treatment, and management options to prepare for major epidemic outbreaks;</li> <li>new biomarkers of disease (relevant for diagnosis, efficacy, safety, or prevention) identified and experimentally validated;</li> <li>new taxonomies of disease or new stratifications to define patient sub-populations.</li> </ul>	100	0	50	120	150	

KPI Name	Unit of measurement	Baseline	Target 2023	Target 2025	Target 2027	Ambition >2027	Status
<b>Outcomes</b>							
<b>2.4.</b> Integrated health care solutions considering end-users' needs	Number of project outputs that combine people-centred integrated solutions (pre-competitive tools, methods, solutions as well as products/services or combined products)	No baseline available	0	3	7	10	
<b>2.5.</b> Methodologies for value assessment of integrated solutions	Number of methodologies for the assessment of the added value of combinations of products/services or combined products (including development of patient reported outcomes / experience measures and statistical methods/tools), submitted to health care authorities and organisations <sup>9</sup>	No baseline available	0	2	3	5	
<b>2.6.</b> New or improved clinical guidelines	Number of projects contributing to the development of new or improved clinical guidelines	13	0	5	10	20	
<b>2.7.</b> Management of health data	Number of common standards, protocols and frameworks developed by the projects to enable better access to data, sharing and analysis of health-related data	No baseline available	0	3	7	10	
<b>2.8.</b> Demonstration of data integration	Number of pilots developed by the projects demonstrating integration of data provided by the private and public sectors	No baseline available	0	5	10	20	
<b>2.9.</b> Demonstration of AI in health care	Number of pilots developed by the projects demonstrating feasibility of use of artificial intelligence in health care	No baseline available	0	1	2	3	

<sup>9</sup> Health care authorities and organisations to which it is referred here are HTA bodies, and regulatory authorities, payers and public authorities

- HTA agencies/bodies: [http://www.adhophta.eu/toolkit/assets/tools/AdHopHTA\\_toolkit\\_tool24\\_document.pdf](http://www.adhophta.eu/toolkit/assets/tools/AdHopHTA_toolkit_tool24_document.pdf); <https://www.eunethta.eu/about-eunethta/eunethtanetwork/>
- National and regional public procurement organisations
- National payer and reimbursement organisations (incl. health insurance companies)
- National healthcare authorities: examples are: Dutch NZA; <http://www.euregha.net/> (membership list of regional and local health authorities); <https://eurohealthnet.eu/list-of-members/> (first part of the membership, not the research members)

KPI Name	Unit of measurement	Baseline	Target 2023	Target 2025	Target 2027	Ambition >2027	Status
<b>Impacts</b>							
<b>3.1.</b> Creation of sustainable resources and infrastructures that facilitate the translation of knowledge into innovations	Number of established new research networks, new clinical networks, further public-private collaborations on health R&D&I, research infrastructures, biobanks, collaborative platforms etc. (that outlive the project and are accessible to broader scientific community)	10	0	4	7	15	
<b>3.2.</b> Development of preventive or therapeutic strategies in different therapeutic areas to address unmet public health needs	Share of projects that aim to develop new or improved existing methodologies also across disciplines addressing public health needs <sup>10</sup> included in the list of the WHO Europe Health 2020 priority areas <sup>11</sup>	No baseline available	90%	90%	90%	90%	

<sup>10</sup> Definition in article 125(1) of the Council Regulation (EU) 2021/2085: “For the purpose of this Regulation, an unmet public health need shall be defined as a need currently not addressed by the health care systems for availability or accessibility reasons, for example where there is no satisfactory method of diagnosis, prevention or treatment for a given health condition or if people access to health care is limited because of cost, distance to health facilities or waiting times”.

<sup>11</sup> [https://www.euro.who.int/\\_data/assets/pdf\\_file/0011/199532/Health2020-Long.pdf](https://www.euro.who.int/_data/assets/pdf_file/0011/199532/Health2020-Long.pdf) <https://www.who.int/europe/publications/i/item/WHO-EURO-2021-1919-41670-56993>

KPI Name	Unit of measurement	Baseline	Target 2023	Target 2025	Target 2027	Ambition >2027	Status
<b>Impacts</b>							
<b>3.3.</b> Cross-sector activities established by the partnership that will help contribute to a globally competitive EU health care industry	<p>Number of activities in which cross-sector collaboration drives health innovation, such as:</p> <ul style="list-style-type: none"> <li>• Spin-off companies, entities or activities created based on outputs of the project (e.g., new commercial or non-profit entities)</li> <li>• Collaboration agreements between large companies<sup>12</sup> &amp; SMEs<sup>13</sup> established for purposes that go beyond the scope of the project during and/or after project lifetime.</li> <li>• Other activities where the joint contribution of different partners has generated cross-sectoral health innovation.</li> </ul> <p>Examples of collaboration activities across health industry sectors that contributed to the transition to a green and digital economy (as outlined in the new Industrial Strategy for Europe<sup>14</sup>)</p>	No baseline available	0	5	10	20	

<sup>12</sup> For-profit legal entities with an annual turnover of EUR 500 million or more (Article 123(5) of Council Regulation (EU) 2021/2085)

<sup>13</sup> Small and medium-sized enterprises (SMEs) are defined in the “EU recommendation 2003/361” (<https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32003H0361&from=EN>) as of page 4 and in the European Commission “User guide to SME definition” ([https://ec.europa.eu/regional\\_policy/sources/conferences/state-aid/sme/smedefinitionguide\\_en.pdf](https://ec.europa.eu/regional_policy/sources/conferences/state-aid/sme/smedefinitionguide_en.pdf)) especially in page 13

<sup>14</sup> “European industrial strategy 2019-2024” ([https://ec.europa.eu/info/strategy/priorities-2019-2024/europe-fit-digital-age/european-industrial-strategy\\_en](https://ec.europa.eu/info/strategy/priorities-2019-2024/europe-fit-digital-age/european-industrial-strategy_en)) and “Updating the 2020 New Industrial Strategy: Building a stronger Single Market for Europe’s recovery” ([https://ec.europa.eu/info/sites/default/files/communication-industrial-strategy-update-2020\\_en.pdf](https://ec.europa.eu/info/sites/default/files/communication-industrial-strategy-update-2020_en.pdf))

## Risks

Risk management is a proactive process for identifying and assessing any event that could pose a threat to the achievement of the IHI JU objectives and determining how the corresponding risks should be managed. Therefore, risks management is an integral element of the strategic planning and monitoring cycle.

Following the risk assessment exercise carried out by the Programme Office in view of this work programme, the following areas prone to critical risks might affect the achievement of the objectives planned by IHI JU in 2023. Most of these risks relate to the external environment (outside IHI JU), and to planning, processes and systems:

- The expected high degree of coverage/exposure on how IHI JU is implementing the new governance structure and generation process for ideas and call topics.
- The remaining uncertainties about the operational implementation of the new key concepts and modalities (such as the monitoring of in-kind contribution to additional activities, the management of contributions at the minimum threshold of 45 % of an indirect action's eligible costs and costs of its related additional activities throughout the project cycle), combined with the need of manual interventions in the programme management platform built and maintained by external parties.

In order to control the risks identified, the Programme Office ensures their monitoring and continuous reviewing, considering the corresponding mitigating measures identified and taking further actions where necessary to ensure controls remain effective. Relevant IHI JU financial needs and the budget for 2023 have also been appropriately estimated. The staff is regularly informed on the objectives, activities and new planning.

### 4.2.2 Scientific priorities, challenges and expected impacts

The scope of the scientific priorities 2023 will contribute to the achievement of the general and specific objectives of IHI JU as defined in the Council Regulation (EU) 2021/2085. This will be done by tackling the challenges and making progress towards the outcomes and expected impacts as described in one or more of the five SRIA<sup>15</sup> scope areas/specific objectives. IHI JU is the ideal mechanism to pioneer the integration of technologies and interventions to optimise research, health products and services, as well as healthcare delivery to ultimately move from siloed healthcare interventions to holistic disease management and patient care.

The scientific priorities reflect IHI JU's objectives which focus on the pre-competitive area, thereby creating a safe space for efficient collaboration between companies active in different health technologies. The objectives are not aimed at delivering products or services directly to healthcare systems or the market as such.

In 2023 the scientific priorities will focus on cross-sectoral approaches, methods, and tools to facilitate the creation of new products and services to prevent, intercept, diagnose, treat, and manage diseases and foster recovery more efficiently in various disease areas, focusing on unmet public health needs as defined in the Council Regulation (EU) 2021/2085<sup>16</sup>. In addition and importantly, the scientific priorities will also cover

<sup>15</sup> [https://www.ihj.europa.eu/sites/default/files/flmngnr/IHI\\_Strategic\\_Research\\_and\\_Innovation\\_Agenda\\_3.pdf](https://www.ihj.europa.eu/sites/default/files/flmngnr/IHI_Strategic_Research_and_Innovation_Agenda_3.pdf)

<sup>16</sup> an unmet public health need shall be defined as a need currently not addressed by the health care systems for availability or accessibility reasons, for example where there is no satisfactory method of diagnosis, prevention or treatment for a given health condition or if people's access to health care is limited because of cost, distance to health facilities or waiting times.



initiatives which, while not focused specifically on disease areas, have a significant potential to generate results that could have a transformational impact on innovation processes in healthcare.

To achieve these ambitious objectives, IHI JU will continue to build a pipeline of ideas from a range of sources and stakeholders in the health community, as well as from industry partners, the European Commission, and potential contributing partners.

The level of cross-sector integration to be achieved by IHI JU is uncharted territory. Thus to make sure to exploit the full potential of IHI JU, R&D, digital and medical executives from pharmaceutical and medtech companies will explore areas of common interest, the boundaries of the common pre-competitive space, and areas that would benefit most from cross-sectorial collaboration at scale to deliver significant benefit and meet important unmet public health needs. The resulting “Big Themes” will further inform the ideation process.

In addition, by 2023 IHI JU will have received the first ideas from the wider health and research community for potential IHI topics via the IHI JU dedicated portal<sup>17</sup> and more will continue to be submitted.

All ideas will be reviewed by the SIP, which comprises experts from the scientific community, various stakeholder groups, and industry sectors. The SIP will determine how well they fit IHI JU’s mission and its objectives as described in the SRIA, and if they are suitable starting points for future topics of calls for proposals to be launched in 2023 (and beyond).

The activities funded by IHI JU will be designed taking into consideration synergies with other health-oriented initiatives. These include synergising with existing and future partnerships of Cluster 1 of Horizon Europe, as well as complementing the actions of the EU4Health<sup>18</sup> programme and HERA<sup>19</sup> and upstream of the upcoming European partnership on transforming health and care systems<sup>20</sup>, wherever relevant. It is also expected that IHI JU activities will contribute to the Union priorities for health research and innovation, such as the Pharmaceutical and the Industrial Strategies for Europe<sup>21</sup>, Europe’s Beating Cancer Plan<sup>22</sup>, to digital policies such as the European Health Data Space<sup>23</sup> and Data Act<sup>24</sup> and to the European Green Deal<sup>25</sup>.

Participants in activities funded by IHI JU will have to ensure that the products and services they develop based or partly based on the results of clinical studies undertaken as part of an indirect action are affordable, available and accessible to the public at fair and reasonable conditions. For this, the general conditions relating to the IHI JU calls included in this work programme specify additional exploitation obligations applicable to specific indirect actions.<sup>26</sup>

Activities funded by IHI JU will cover the whole health innovation chain. Activities will be funded via the launch of calls for proposals and selection of projects (actions) that contribute to the scope areas of the SRIA. Due to their highly interlinked nature, it is expected that most of the activities in the scope of the

<sup>17</sup> <https://www.ihj.europa.eu/shape-our-future-research/propose-ideas>

<sup>18</sup> [https://hadea.ec.europa.eu/programmes/eu4health/about\\_en](https://hadea.ec.europa.eu/programmes/eu4health/about_en)

<sup>19</sup> [https://ec.europa.eu/health/health-emergency-preparedness-and-response-hera/overview\\_en](https://ec.europa.eu/health/health-emergency-preparedness-and-response-hera/overview_en)

<sup>20</sup> <https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/topic-details/horizon-hlth-2022-care-10-01>

<sup>21</sup> [https://ec.europa.eu/health/system/files/2021-02/pharma-strategy\\_report\\_en\\_0.pdf](https://ec.europa.eu/health/system/files/2021-02/pharma-strategy_report_en_0.pdf) and [https://ec.europa.eu/info/strategy/priorities-2019-2024/europe-fit-digital-age/european-industrial-strategy\\_en](https://ec.europa.eu/info/strategy/priorities-2019-2024/europe-fit-digital-age/european-industrial-strategy_en)

<sup>22</sup> [https://ec.europa.eu/health/system/files/2022-02/eu\\_cancer-plan\\_en\\_0.pdf](https://ec.europa.eu/health/system/files/2022-02/eu_cancer-plan_en_0.pdf)

<sup>23</sup> [https://ec.europa.eu/health/ehealth-digital-health-and-care/european-health-data-space\\_en](https://ec.europa.eu/health/ehealth-digital-health-and-care/european-health-data-space_en)

<sup>24</sup> <https://digital-strategy.ec.europa.eu/en/policies/data-act>

<sup>25</sup> [https://ec.europa.eu/info/strategy/priorities-2019-2024/european-green-deal\\_en](https://ec.europa.eu/info/strategy/priorities-2019-2024/european-green-deal_en)

<sup>26</sup> In accordance with Article 125(3) of the Council Regulation (EU) 2021/2085

priorities will address more than one of the areas (corresponding to the IHI JU specific objectives), albeit with a main focus on one of them.

Specific Objective 1 (SO1) addresses the challenge of unravelling causal factors of disease that are still poorly understood, such as the interplay between genetic and environmental factors, for example the impact of climate change on health. By elucidating the mechanisms of diseases and factors contributing to health status, better targets and approaches can be developed for new and more precise personalised health innovations in prevention, diagnosis, and therapy, as well as for facilitating good health while aging. Activities in scope of the scientific priorities of 2023 are expected to contribute to this objective in several ways: 1) by paying attention to the important aspect of disease prevention; 2) by including standardisation activities to facilitate the development of new health technologies and to assess the efficacy of targeted treatments; 3) by fostering as outcomes of topics novel tools or hypotheses for new treatments tested preclinically and/or in early-stage clinical or in silico trials.

Specific Objective 2 (SO2) addresses one or more of the barriers for the development of new types of products or services in the health domain that integrate diverse components (such as diagnostics, medicinal products, medical devices, wearables, treatment monitoring, digital solutions), also including the challenge of enabling the green transition across all aspects of healthcare. To fully exploit the potential of various technologies and approaches, existing silos must be broken down across discovery science and translational research as well as between different academic research disciplines and industry sectors. New and harmonised approaches to data generation must be pursued and it would be important to exploit the significant potential of digital R&D for transformative breakthroughs in healthcare. Regulatory challenges related to products that combine different technologies and services must be addressed by offering a neutral platform for all interested stakeholders to exchange experiences and views on issues such as the harmonisation of approaches to evidence generation across sectors. The expected impact for both patients and healthcare would be the enabling of faster development of people-centred, safe, effective, cost-effective, and affordable health solutions along the health care pathway with a reduced environmental footprint, and fostering hospital efficiencies and decreased staff burden.

To contribute to the achievement of the above impacts, IHI JU will launch three topics: **“Patient-centric blood sample collection to enable decentralised clinical trials and improve access to healthcare”**, **“Improved prediction, detection and treatment approaches for comprehensive stroke management”** and **“Development and proof of principle of new clinical applications of theranostic solutions”**.

A priority of IHI JU in 2023 will be to launch initiatives to foster innovative robust solutions that improve the translation from animal to human in the evaluation of new health technologies, and have the potential to enhance the development and manufacturing/production of new, efficient, and safe health technologies, while at the same time contributing to the aims of Directive 2010/63/EU<sup>27</sup> on the protection of animals used for scientific purposes and the principle of the 3Rs (replace, reduce and refine the use of animals). This priority will contribute to SO2 by improving the sustainability and quality of biomedical research and development (R&D), including manufacturing, in areas of unmet medical need.

In this context the IHI JU will launch two topics. The first one **“Accelerating the implementation of New Approach Methodologies and other innovative non-animal approaches for the development, testing and production of health technologies”** will address importantly the delivery of improved tools and methods building among others on recent improved biological knowledge, technological/manufacturing advances, computer simulations and innovative methods (such as organoids, complex 3D cell models and microphysiological systems among others) that are relevant to human health and biology and provide the opportunity to minimise/replace the need for animal experiments.

<sup>27</sup> <https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:276:0033:0079:en:PDF>

In addition to respond to the special focus of Directive 2010/63/EU on the need to replace the use of non-human primates in research. IHI JU will launch the topic “**Expanding translational knowledge in minipigs: a path to reduce and replace non-human primates in non-clinical safety assessment**” as meaningful contribution to the demonstration of the latest *in vivo* models as alternative to non-human primates in the later-stage evaluation of medical technologies, medical devices, and pharmaceuticals, while exploiting the latest *in vivo* technologies to boost animal welfare and improving understanding of the impact of animal welfare on scientific outcomes.

The European Green Deal aims to make the European Union climate neutral by 2050. To fulfil this ambitious plan, contributions will be needed from across the spectrum of the healthcare sector, from healthcare systems delivering care to patients, to the full healthcare value chain producing medical products and services, extending to early stage innovation across multiple technologies. Stakeholders from across the healthcare ecosystem must be engaged, including regulatory, standards, policy and technology leaders.

IHI will include as a priority area for 2023 a meaningful contribution to the development of a greener and more sustainable healthcare sector via two topics “**Safe & Sustainable by Design (SSbD) packaging and single use device solutions for healthcare products**” and “**Sustainable circular development and manufacturing of healthcare products and their quantitative environmental impact assessment**”.

Outputs from this priority area will ensure that the quality, safety and efficacy of medical products and services and the performance of healthcare systems are safeguarded while significantly improving their environmental footprint and sustainability. Activities from this priority area will contribute to the achievement of SO2 by supporting commercial sustainability transition and reducing the overall environmental impact of healthcare.

The great majority of activities in scope of the scientific priorities of 2023 are expected to contribute to Specific Objective 3 (SO3), which addresses the patient-centricity of innovations and the challenge of effectively engaging with all relevant health care actors (patients and civil society, health care professionals, health care providers, regulators, health technology assessment bodies and payers) for the design and development of new and/or integrated health solutions. As stated in the IHI JU SRIA: “*Patients and end-users need to be involved in all stages of research, from project design through to implementation, to develop meaningful innovations*”.

Specific Objective 4 (SO4) addresses the issue that currently, data in many countries are hard to gather and demonstrate limited interoperability. Even when available, data and databases may exhibit variable quality, lack of standardisation and poor interconnectivity. Europe also still lacks a sufficiently skilled workforce to handle, analyse and interpret the data. The Union offers a strengthened framework on data protection, but uncertainties remain, like on the secondary use of health data, which creates an additional layer of complexity. Furthermore, security, explainability for users, and ethical considerations should be ensured when developing new data analytics tools, including the use of artificial intelligence. In 2023, to contribute specifically to SO4 IHI JU will launch the topic “**Maximising the potential of synthetic data generation in healthcare applications**”.

In addition, it is expected that most of the activities generated from the 2023 priorities will contribute to the achievement of the impacts of this objective, e.g. by contributing to the European Health Data Space that was put forward as the legislative proposal from the Commission<sup>28</sup>.

In 2023, to contribute to the objective SO5 of enabling the development of new and improved methodologies and models for a comprehensive assessment of the added value of innovative and integrated healthcare solutions, IHI JU will launch two topics to address the way clinical studies, including clinical trials for

<sup>28</sup> [https://health.ec.europa.eu/publications/proposal-regulation-european-health-data-space\\_en](https://health.ec.europa.eu/publications/proposal-regulation-european-health-data-space_en)

medicinal products, clinical investigations for medical devices, and performance studies for *in vitro* diagnostics, are conducted in Europe. The first topic **“Inclusive clinical studies for equitable access to clinical research in Europe”** will notably aim to facilitate and increase patient recruitment and retention, with a particular focus on under-represented and underserved patient populations. The second topic **“Establishing novel approaches to improve clinical trials for rare and ultra-rare diseases”** will consider ways for enhancing patient access to clinical trials and trial preparedness of investigational sites for these important group of diseases. As expected impacts of the topics, through increased access and inclusiveness of diverse patient populations in clinical studies, more patients would benefit from improved innovative health technologies that meet the specific needs and profiles of all patient populations; patients’ trust in the evidence will be enhanced; and health equity advanced. The topics will also contribute to the ACT EU (Accelerate Clinical Trials in EU)<sup>29</sup> objectives to proactively deliver inclusive patient-oriented medicines development and delivery across populations.

Impacts achieved in 2023 will be monitored using the predefined key performance indicators, as well as via bibliographic analysis to capture projects’ scientific outputs in terms of publications and collaborations.

<sup>29</sup> <https://www.ema.europa.eu/en/news/accelerating-clinical-trials-eu-act-eu-better-clinical-trials-address-patients-needs>

## 4.2.3 Calls for proposals

### a. General presentation of the 2023 calls for proposals

During 2023, IHI JU will launch single and two-stage open and competitive calls for proposals.

The topic ideas and indicative budgets are drawn up from a range of sources, including industry partners, potential contributing partners, and other stakeholders in the health community and in consultation with the SIP and the SRG. The Programme Office leads the drafting of the topic texts and the Work Programme will be updated accordingly.

#### For IHI JU call 4:

The submission deadline for short proposals (SPs) will be 8 November 2023, and the deadline for full proposals (FPs) will be 23 April 2024.

Scientific evaluation of the SPs under the two-stage call will be completed by 2023. Grant Agreement Preparation (GAP) will be completed within 3 months from the notification to applicants of the evaluation results of the full proposal, and maximum eight months from the final date of submission of the FPs, in line with the applicable time to grant (TTG).

#### For IHI JU call 5:

The submission deadline for full proposals (FPs) will be 16 January 2024.

Scientific evaluation of the single-stage call will take place in Q1 2024. GAP will be completed within 3 months from the notification to applicants of the evaluation results of the full proposal, and maximum eight months from the final date of submission of the FPs, in line with the applicable time to grant (TTG).

### b. Conditions of the calls and call management rules

For call management, IHI JU will utilise the EC IT infrastructure available under Funding & Tender opportunities - Single Electronic Data Interchange Area (SEDIA).

The General Annexes of the Horizon Europe Work Programme 2023-2024 shall apply *mutatis mutandis* to the calls for proposals covered by this Work Programme. In accordance with Article 5(2)(a) of the Council Regulation (EU) 2021/2085, in duly justified cases, derogations related to the specificities for IHI JU may be introduced in the relevant Work Programme. Where necessary, this will be done when the topic texts are identified in this Work Programme.

To maximise the efficiency of the calls management, IHI JU will continuously explore and implement simplifications and improve its processes while maintaining the highest standards of the evaluation process, in line with the applicable Horizon Europe rules.

All proposals must conform to the conditions set out in Regulation (EU) 2021/695 of the European Parliament and of the Council of 28 April 2021 establishing Horizon Europe – the Framework Programme for Research and Innovation, laying down its rules for participation and dissemination.

Any specificity for IHI JU is highlighted in the below sections.

## GENERAL CONDITIONS RELATING TO THE IHI JU CALLS

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### **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**

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.

## **STANDARD ADMISSIBILITY CONDITIONS, PAGES LIMITS AND SUPPORTING DOCUMENTS**

General Annex A ('Admissibility') to the Horizon Europe Work Programme 2023-2024 shall apply *mutatis mutandis* for the calls for proposals covered by this Work Programme.

In addition, page limits will apply to proposals as follows:

- for a single-stage call, the limit for RIA full proposals is 50 pages;
- at stage 1 of a two-stage call, the limit for RIA short proposals is 20 pages;
- at stage 2 of a two-stage call, the limit for RIA full proposals is 50 pages.

## **STANDARD ELIGIBILITY CONDITIONS**

General Annex B to the Horizon Europe Work Programme 2023-2024 shall apply *mutatis mutandis* for the calls for proposals covered by this Work Programme unless otherwise provided in this Work Programme.

Per the above and by way of derogation from General Annex B of the Horizon Europe Work Programme 2023-2024:

According to Article 119 of the Council Regulation (EU) 2021/2085, for indirect actions selected under calls for proposals covered by this Work Programme:

- applicant consortia must ensure that at least 45% of the action's eligible costs and costs for additional activities related to the action are provided by contributions (IKOP, FC, IKAA) from private members which are members of IHI JU, their constituent or affiliated entities, and contributing partners;
- While the constituent or affiliated entities of the members other than the union of IHI JU can contribute any of those contribution types, contributing partners can only contribute IKOP and FC, not IKAA;

- further to the above, the applicant consortium must submit a self-declaration that the required percentage of 45% contributions will be provided;
- the eligibility condition above and self-declaration requirement do not apply to the first stage of a two-stage application;
- at project level, the maximum amount of non-EU IKOP is set to:
  - one hundred percent (100%) for IHI JU Call 4
  - Thirty percent (30%) for IHI JU Call 5<sup>30</sup>

This is justified as a means to ensure the achievement of project objectives based on Article 119(5) of Council Regulation (EU) 2021/2085, and to ensure full openness to non-EU IKOP in these calls<sup>31</sup>.

## ENTITIES ELIGIBLE FOR FUNDING

In relation to the single-stage calls for proposals covered by this Work Programme, the relevant provisions of the General Annex B to the Horizon Europe Work Programme 2023-2024 shall apply *mutatis mutandis*.

By way of derogation, in relation to the two-stage calls for proposals covered by this Work Programme, the following provisions shall apply:

- Legal entities identified in the topic text of the call for proposals shall not be eligible for funding from IHI JU. Nevertheless:
  - These entities will be entitled to provide contributions as IHI JU members other than Union or contributing partners.
  - Legal entities participating in indirect actions selected under this type of calls for proposals shall not be eligible for funding where:
    - (a) they are for-profit legal entities with an annual turnover of EUR 500 million or more;
    - (b) they are under the direct or indirect control of a legal entity described in point (a), or under the same direct or indirect control as a legal entity described in point (a);
    - (c) they are directly or indirectly controlling a legal entity referred to in point (a).

In line with Article 5(2)(a) (additional conditions in duly justified cases) and Article 119(3) (private contributions to amount of at least 45 % of an indirect action's eligible costs and costs of its related additional activities) of the Council Regulation (EU) 2021/2085, under two-stage submission procedures, the following additional condition applies:

- The applicants which are IHI JU members other than the Union, or their constituent entities and affiliated entities, and contributing partners and that are pre-identified in the topics – under the section 'Industry consortium' – of a call for proposals shall not apply at the first stage of the call. The applicant consortium selected at the first stage shall, in preparation for the proposal submission at the second stage, merge with the pre-identified industry consortium.

<sup>30</sup> Even if this threshold of 30% is not intended as an eligibility condition *per se*, proposals recommended for funding that will feature a non-EU IKOP amount higher than the 30% of IKOP, will be requested to remove the exceeding part. If this case, this non-EU IKOP reduction exercise will need to comply with eligibility criteria whereby at least 45% of the action's eligible costs and costs for additional activities related to the action are provided by contributions (IKOP, FC, IKAA) from private members which are members of IHI JU, their constituent or affiliated entities, and contributing partners.

<sup>31</sup> It has to be noted that, pursuant Article 119(4) of Council Regulation (EU) 2021/2085, at the level of the IHI JU programme, non-EU IKOP must not exceed 20% of in-kind contributions to operational costs provided by private members which are IHI JU members, their constituent or affiliated entities, and contributing partners. Furthermore, at the level of the IHI JU programme, IKAA shall not constitute more than 40% of in-kind contributions provided by private members which are IHI JU members.



In addition, in line with Articles 11 and 119(1) and (3) of the Council Regulation (EU) 2021/2085, legal entities providing in kind contributions as constituent entities or affiliated entities of IHI JU private members or as contributing partners that are:

- Not eligible for funding in two-stage calls for proposals; or
- Not established in a country generally eligible for funding in accordance with Part B of the General Annexes to the Horizon Europe Work Programme 2023 – 2024,

May exceptionally sign the grant agreement.

This is subject to the following conditions:

- Their participation is considered essential for implementing the action by the granting authority; and
- They participate without requesting any funding.

The essentiality of non-EU legal entities for implementing the action shall be ascertained by the granting authority.

### **LIST OF COUNTRIES AND APPLICABLE RULES FOR FUNDING**

With reference to Article 23 of the Council Regulation (EU) 2021/2085, the eligibility of participants in a proposal submitted to a call for proposals for any of the topics in this Work Programme will take into account any application of Art 22(5) of the Horizon Europe Regulation triggered for topics from other Horizon Europe Work Programmes for proposals with similar scope.

### **TYPES OF ACTION: SPECIFIC PROVISIONS AND FUNDING RATES**

General Annex B ('Eligibility') to the Horizon Europe Work Programme 2023-2024 shall apply *mutatis mutandis* for the calls for proposals covered by this Work Programme.

### **TECHNOLOGY READINESS LEVELS (TRL)<sup>32</sup>**

TRL definitions included in General Annex B ('Eligibility') to Horizon Europe Work Programme 2023-2024 shall apply *mutatis mutandis* for the calls for proposals covered by this Work programme.

### **EVALUATION RULES**

General Annex D ('Award Criteria') to the Horizon Europe Work Programme 2023-2024 shall apply *mutatis mutandis* for the calls for proposals covered by this Work Programme with the following additions: The relevant calls for proposals launched under this Work Programme shall specify whether the call for proposals is a single-stage or two-stage call, and the predefined submission deadline.

Award criteria and scores:

Experts will evaluate the proposals on the basis of criteria of 'Excellence', 'Impact' and 'Quality and efficiency of the implementation' according to the type of action, as follows:

For all evaluated proposals, each criterion will be scored out of 5. Half marks may be given.

For the evaluation of proposals under both single-stage and two-stage submission procedures:

- the threshold for individual criteria will be 3;
- the overall threshold, applying to the sum of the three individual scores, will be 10;

<sup>32</sup> The TRL is not utilised for IHI calls 4 and 5, however, it might be used in future IHI JU calls



- proposals that pass individual thresholds and the overall threshold will be considered for funding, within the limits of the available budget. Proposals that do not pass these thresholds will be rejected.

Under the single-stage evaluation process, evaluated proposals will be ranked in one single list. The highest ranked proposals, within the framework of the available budget, will be invited to prepare a Grant Agreement.

Under the two-stage evaluation procedure, and on the basis of the outcome of the first stage evaluation, the applicant consortium of the highest ranked short proposal (first stage) for each topic will be invited to discuss with the relevant industry consortium the feasibility of jointly developing a full proposal (second stage).

If the first-ranked consortium and industry consortium decide that the preparation of a joint full proposal is not feasible, they must formally notify IHI JU within 30 days from the invitation to submit the stage 2 proposal. This notification must be accompanied by a joint report clearly stating the reasons why a stage 2 proposal is considered not feasible. In the absence of a joint notification within the deadline, it is deemed that the first ranked applicant consortium and the industry consortium are going to submit the joint stage 2 proposal. Accordingly, the second and third-ranked short proposals will be formally rejected.

If the preliminary discussions with the higher ranked proposal and the industry consortium fail, the applicant consortia of the second and third-ranked short proposals (stage 1) for each topic may be invited by IHI JU, in priority order, for preliminary discussions with the industry consortium. The decision to invite lower-ranked consortia to enter into discussions with the industry consortium will take into account the content of the report from the joint report from the first-ranked consortium and industry consortium.

Under the two-stage evaluation procedure, contacts or discussions about a given topic between potential applicant consortia (or any of their members) and any member of the relevant industry consortium are prohibited throughout the procedure until the results of the first stage evaluation are communicated to the applicants.

As part of the panel deliberations, IHI JU may organise hearings with the applicants to:

- clarify the proposals and help the panel establish their final assessment and scores, and/or
- improve the experts' understanding of the information presented

In cases clearly identified in the relevant call for proposals where a given topic is composed of two or more sub-topics, one short proposal per sub-topic will be invited.

The IHI JU evaluation procedure is confidential.

The members of the applicant consortia shall avoid taking any actions that could jeopardise confidentiality.

Following each evaluation stage, applicants will receive an ESR evaluation summary report) regarding their proposal.

## **INDICATIVE TIMETABLE FOR EVALUATION AND GRANT AGREEMENT PREPARATION**

Information on the outcome of the evaluation (single-stage, or first stage of a two-stage):

- Single-stage: Maximum 5 months from the submission deadline at the single-stage.
- Two-stage: Maximum 5 months from the submission deadline at the first stage.

Information on the outcome of the evaluation (second stage of a two stage):

- Maximum 5 months from the submission deadline at the second stage.

Indicative date for the signing of grant agreement:

- Single-stage: Maximum 8 months from the submission deadline.
- Two-stage: Maximum 8 months from the submission deadline at the second stage.

General Annex G ('Legal and Financial setup of the Grant Agreements') to the Horizon Europe Work Programme 2023-2024 shall apply *mutatis mutandis* for the calls for proposals covered by this Work Programme.

## **BUDGET FLEXIBILITY**

General Annex F to the Horizon Europe Work Programme 2023-2024 shall apply *mutatis mutandis* to the calls for proposals covered by this Work Programme.

## **SUBMISSION TOOL**

Proposals in response to a topic of an IHI JU call for proposals must be submitted online, before the call deadline, by the coordinator via the Submission Service section of the relevant topic page available under Funding & Tender opportunities - Single Electronic Data Interchange Area (SEDIA). No other means of submission will be accepted.

## **PROPOSALS INCLUDING CLINICAL STUDIES<sup>33</sup>**

Under the single-stage submission procedures and for stage 2 of the two-stage submission procedures: Applicants envisaging including clinical studies must provide details of their clinical studies in the dedicated annex using the template provided in the submission system<sup>34</sup>.

## **SPECIFIC CONDITIONS ON AVAILABILITY, ACCESSIBILITY AND AFFORDABILITY (3A)**

When the specific topic condition so requires, the following conditions shall apply:

- The participants must, during the lifetime of the project and for a period of four years after project end, use their best efforts to ensure that those products or services that are developed by any of the participants and are totally or partly based on the results of clinical studies performed as part of the activities of the selected project, will be broadly<sup>35</sup> available and accessible, at fair and reasonable conditions.
- In particular, and always to the extent permitted by applicable competition law:
  - a) At the proposal stage<sup>36</sup>, and as part of the Plan for the Dissemination, Exploitation, and Communication Activities ('PDECA') which forms part of the proposal, the applicant consortium must identify potential and expected project results that may be subject to the 3A conditions and broadly outline their strategy to achieve the above objectives.<sup>37</sup>
  - b) At the project interim review stage, if relevant<sup>38</sup>, the PDECA should be updated with a revised 3A strategy. This update should be based on the progress of the clinical studies conducted or to be conducted as part of the project and include any pertinent action to be implemented both during the project and over the four years after project end.

<sup>33</sup> Clinical study covers clinical studies/trials/investigations/cohorts and means, for the purpose of this document, any systematic prospective or retrospective collection and analysis of health data obtained from individual patients or healthy persons in order to address scientific questions related to the understanding, prevention, diagnosis, monitoring or treatment of a disease, mental illness, or physical condition. It includes but it is not limited to clinical studies as defined by Regulation 536/2014 (on medicinal products), clinical investigation and clinical evaluation as defined by Regulation 2017/745 (on medical devices), performance study and performance evaluation as defined by Regulation 2017/746 (on in vitro diagnostic medical devices).

<sup>34</sup> Template for providing essential information in proposals involving clinical studies - [https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/temp-form/af/information-on-clinical-studies\\_he\\_en.docx](https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/temp-form/af/information-on-clinical-studies_he_en.docx)

<sup>35</sup> This covers EU Member States and countries that are associated to Horizon Europe at the time of call opening.

<sup>36</sup> As mentioned, for those 3A specific projects, the 3A content in the PDECA will be checked during the evaluation stage.

Omission/inadequate treatment of 3A would be identified as a shortcoming. The content however, once considered adequate, will not be utilised for positive scoring and will not contribute towards any evaluation criteria.

<sup>37</sup> Suggested components would be 1) Identification of planned clinical studies that might generate results for which the provisions are relevant; 2) Confirmation that the consortium members are aware of the provisions and will consider them accordingly. 3) Tentatively identifying markets/areas where the product/service could be made affordable, accessible, available. These points could be checked at the evaluation stage.

<sup>38</sup> As discussed, this interim point allows a realistic appraisal of the 3A possibilities during the project lifetime, particularly as to the viability of specific expected 3A results.

- c) At the end of the project, the PDECA should be updated, to provide the expected planning for further product development and (if already scheduled) product launch, within the timeframe of four years after the project end and in order to meet those objectives laid out under point 1 above.<sup>39</sup>
- d) Within 12 months from the project end date, and on a yearly basis thereafter for a period of 3 years (totalling four years from project end), a confidential report<sup>40</sup> must be submitted to IHI JU by the owner of the project result describing the status of the development of the product and of any other exploitation actions, planned or undertaken, concerning the products/services.

## JU RIGHT TO OBJECT TO TRANSFER/EXCLUSIVE LICENSING

According to the Horizon Europe rules, and in order to protect Union interests, the right for IHI JU to object to transfers of ownership of results or to grants of an exclusive licence regarding results should apply to participants. Therefore, the provisions set out in General Annex G to the Horizon Europe Work Programme 2023-2024 on the right to object apply generally. It should be noted that in accordance with the Council Regulation (EU) 2021/2085 and the Horizon Europe model Grant Agreement, the right to object applies also to participants that have not received funding from IHI JU and for the periods set therein. In choosing whether to exercise the right to object, IHI JU will, on a case-by-case basis, make a reasoned decision in compliance with the legal basis.

### c. Country specific eligibility rules

Following the Horizon Europe Programme Guide, participation in IHI JU indirect actions will be open but eligibility for funding will be however limited to legal entities established in an EU Member State, Associated Country or Low and Middle Income Countries (please consult the list in the Horizon Europe Programme Guide<sup>41</sup>).

Given the invasion of Ukraine by Russia and the involvement of Belarus, legal entities established in Russia, Belarus or in any occupied territory of Ukraine are not eligible to participate in any capacity. Exceptions may be granted on a case-by-case basis for justified reasons, such as for humanitarian purposes, civil society support or people-to-people contacts.

## 4.2.4 Calls for tenders and other actions

In 2022 the Programme Office prepared the tender documents of the new multiannual framework contract to source the relevant bibliometric data and analysis of IMI1 JU, IMI2 JU and IHI JU publications as from 2024. The call for tender will be launched in the beginning of 2023.

<sup>39</sup> Per the Model Grant Agreement ('MGA') Article 16, the beneficiaries must complete the Results Ownership List ('ROL') which identifies each result generated in the project and the owner thereof. The ROL should inform on the relevant results for which owners implement the 3A strategy in the PDECA for the four years following the project.

<sup>40</sup> Cognizant of IP sensitivities, confidential info, and commercial realities, the IHI JU suggests that the confidential report PDECA could, if needed, be composed of two parts:

1. **A high-level abstract**, to be made publicly available (not containing confidential information), comprising:
  - a) Broad summary of the result's development to this point, including a detailed description of the result and the potential product or service that could incorporate or partly incorporate the result;
  - b) Broad description of expected downstream actions (including product and service applications);
  - c) broad assessment of expected impact of the above downstream actions towards ensuring Affordability, Availability, and Accessibility.
2. **A Confidential Annex** in which:
  - a) The owning beneficiary explains if the result is a product or service (or is expected to become one within 4 years) or not, and if yes, further confirms:
    - i. The planned measures to be taken to effect the 3A obligations;
    - ii. That the owning beneficiary will undertake all necessary actions to adhere to the 3A provisions to the best of its capacity;
    - iii. That the owing beneficiary will keep the IHI JU updated on a yearly basis on the progress.

<sup>41</sup> [https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/programme-guide\\_horizon\\_en.pdf](https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/programme-guide_horizon_en.pdf)



#### 4.2.5 Follow-up activities linked to past calls: monitoring, evaluation and impact assessment

IMI calls	Total	Ongoing at 01.01.2023	Of which	
	Projects		Total reports	Project ending in 2023
IMI1 call 1	15			
IMI1 call 2	8			
IMI1 call 3	7			
IMI1 call 4	7			
IMI1 call 5	1			
IMI1 call 6	2	1	1	1
IMI1 call 7	2			
IMI1 call 8	4			
IMI1 call 9	4	1	1	1
IMI1 call 10	1			
IMI1 call 11	8	1	1	1
<b>Total</b>	<b>59</b>	<b>3</b>	<b>3</b>	<b>2</b>
<b>IMI1</b>				
IMI2 call 1	1	1	1	1
IMI2 call 2	8	0	0	0
IMI2 call 3	5	0	0	0
IMI2 call 4	1	0	0	0
IMI2 call 5	6	1	1	1
IMI2 call 6	4	1	1	1
IMI2 call 7	7	4	4	3
IMI2 call 8	4	3	3	2
IMI2 call 9	6	3	3	3
IMI2 call 10	8	6	6	4
IMI2 call 11	3	0	0	0
IMI2 call 12	7	6	6	3
IMI2 call 13	13	9	9	1

IMI calls	Total	Ongoing at 01.01.2023	Of which	
	Projects		Total reports	Project ending in 2023
IMI2 call 14	4	3	3	0
IMI2 call 15	7	7	6	1
IMI2 call 16	5	4	5	1
IMI2 call 17	3	3	3	0
IMI2 call 18	6	6	6	0
IMI2 call 19	2	2	2	1
IMI2 call 20	6	6	6	0
IMI2 call 21	8	4	4	1
IMI2 call 22	3	3	3	1
IMI2 call 23	6	6	6	0
<b>Total</b>	<b>123</b>	<b>78</b>	<b>78</b>	<b>24</b>
<b>IMI2</b>				
IHI call 1	-	-	-	-
IHI call 2	-	-	-	-
IHI call 3	-	-	-	-
<b>Total</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>
<b>IHI *</b>				
<b>Totals IMI+ IMI2 +IHI</b>	<b>182</b>	<b>81</b>	<b>81</b>	<b>26</b>

\* Numbers on projects/reports will be further defined after the conclusion of the respective IHI JU calls

## **Monitoring and analysis of project results**

81 project periodic reports will be submitted in 2023 (see column in the table above 'Total reports'). These reports will be used to track progress against their stated objectives and deliverables as laid out in the relevant description of the action.

This reporting will also allow an assessment of project achievements and the impact of results. In addition to the usual ex-ante controls, a combination of internal management information systems, external databases, independent evaluations and, if necessary, commissioned studies and surveys will be used to measure the progress and identify significant achievements of IMI projects.

In 2023, the analysis of the IMI project scientific outputs in terms of publications and collaboration among IMI researchers will be continued. Where feasible, monitoring and analysis approaches will be refined in line with observations from the European Court of Auditors (ECA) to ensure the highest possible standards.

## **Impact assessment of the IMI projects**

An important part of evaluating the performance of IMI2 JU consists in assessing the impact of the IMI projects. As set out in the Strategic Research Agenda for IMI2 JU, the Programme Office remains focused on the needs of patients and society, and on delivering tools and resources to speed up the development of urgently-needed treatments.

In 2022 the Programme Office supported the impact assessment activities under the specific contract "Evaluation Study of the European Framework Programmes for Research and Innovation for a Resilient Europe–RTD/2021/SC/021" under the inter-institutional Multiple Framework Contract N° 2018/RTD/A2/OP/PP-07001-2018 "Studying, assessing, and evaluating research and innovation programmes and policies (SARI)". The assessment was led by a pool of consultants and involved desk research as well as interviews with relevant stakeholders. The outcome of this effort was the case study "The Innovative Medicine Initiative – An analysis of the contribution to health emergency preparedness" which evaluates the input of the Innovative Medicines Initiative (IMI) to health emergency preparedness using the examples of selected projects (ZAPI, EHDEN, EBOVAC 1, EBOVAC 2, EBOVAC 3 and EBODAC). The case study will be published on IHI web site as soon as available in 2023. The aim of the first phase of the Evaluation Study was and is to support the ex-post evaluation of Horizon 2020. This will include the Final Evaluation of IMI2, which will be carried out by the European Commission in 2023.

## 4.2.6 Cooperation, synergies and cross-cutting themes and activities

The Council Regulation (EU) 2021/2085 states that IHI JU should seek and build close collaborations and synergies with other relevant initiatives at Union, national and regional level, in particular, with other European partnerships, to achieve greater scientific, socioeconomic and environmental impact and ensure uptake of results. Therefore, in 2023 it is planned that IHI JU will continue to explore possible synergies with other health-oriented initiatives, with the Cancer Mission, the partnerships created in Cluster 1 of Horizon Europe (notably GH EDCTP3 JU) and EIT Health, complementing the actions of the EU4Health<sup>42</sup> programme, HERA<sup>43</sup> and Coalition for Epidemic Preparedness Innovations (CEPI)<sup>44</sup>, wherever relevant. It is also expected that IHI JU activities will complement those of the Digital Europe programme<sup>45</sup> that will deploy digital capacities and infrastructure related to the health area.

IHI JU will seek the advice of the GB, SIP and SRG in order to identify the most relevant programmes and initiatives.

In addition to attempting to establish institutional collaborations, IHI JU will continue to engage with its key stakeholders such as patients, regulators and SMEs.

### Patients

The IHI JU's goal is to translate health research and innovation into tangible benefits for patients and society by enabling the faster development of people-centred, safe, effective, cost-effective and affordable health solutions that respond to unmet health needs. To achieve this, it is essential to involve all stakeholders including patients in the co-design, co-development and co-implementation of those innovative solutions. IHI JU's aim is to champion a patient-centric approach and especially encourage all funded projects to work in partnership with patients wherever possible.

Patients play an important role when designing and implementing the SRIA, alongside researchers from the public and private sectors including the European life science industry, academia, and regulators. Therefore, IHI JU will strive to embed the patient perspective at all levels, from agenda setting for research in medical innovation and proposal evaluation processes, to project planning, implementation and close out. Therefore, the systematic involvement of patients in IHI JU's projects and activities will be further supported, facilitated, and strengthened.

Specifically, IHI JU plans to: launch a new call for expressions of interest and create the IHI patient pool to reflect all the health areas covered by the IHI JU objectives; ensure that patient input is considered at the idea generation and topic writing stage; communicate on patient engagement needs and opportunities at call launch; facilitate patient engagement in consortia; identify the most effective channels of communicating information on calls to patients and other relevant organisations; share best practices of patient engagement in IHI JU projects; continue to produce materials for the promotion of patient engagement in IHI JU.

### Small and medium-sized enterprises

Small and medium-sized enterprises (SMEs) are important IHI JU stakeholders as they can help bring the latest health innovations to the market, leading to tangible benefits for patients and society. An objective of IHI JU is to enhance the research and innovation capabilities and performance of SMEs by promoting their involvement in IHI JU funded projects. To facilitate this objective, IHI JU will emphasise the importance of SME involvement during IHI JU info days, consortium-building brokerage meetings, topic webinars and other relevant events.

<sup>42</sup> [https://hadea.ec.europa.eu/programmes/eu4health/about\\_en](https://hadea.ec.europa.eu/programmes/eu4health/about_en)

<sup>43</sup> [https://ec.europa.eu/health/health-emergency-preparedness-and-response-hera/overview\\_en](https://ec.europa.eu/health/health-emergency-preparedness-and-response-hera/overview_en)

<sup>44</sup> <https://cepi.net/>

<sup>45</sup> [https://ec.europa.eu/info/funding-tenders/find-funding/eu-funding-programmes/digital-europe-programme\\_en](https://ec.europa.eu/info/funding-tenders/find-funding/eu-funding-programmes/digital-europe-programme_en)



## Regulatory bodies

The regulatory environment is key to ensuring that safe and effective health innovations are developed to address public health needs. To ensure that the science generated by IMI projects is translated into people-centred healthcare solutions, IHI JU will continue engaging with all relevant regulatory authorities. Notably in addition to continued successful collaboration with the European Medicines Agency (EMA), IHI JU will pursue its efforts to engage more broadly with the national competent authorities (NCA) and the Medical Device Coordination Group (MDCG) to reflect the cross-sectoral nature of the partnership.

IHI JU will seek to increase the awareness of applicants and projects' consortia about regulatory needs to be considered when relevant. It will also continue to provide support to consortia through guidance and information sessions to encourage early interactions with regulators whenever relevant to ensure greater impact of projects by translating research outcomes into regulatory practice.

The regulators' perspective will be embedded in the scientific priorities and calls for proposals, most notably through the representation of regulators in the SIP, as well as consideration of the list of regulatory science research needs established by EMA<sup>46</sup>.

Using feedback and advice from the members of the SIP and the SRG, IHI JU will lead efforts to further reach out to regulators to promote the programme, encourage their participation in the programme notably by taking part in IHI projects and foster cooperation wherever possible.

IHI JU will also strengthen engagement with other international agencies. and will seek to enhance collaboration with health technology assessment (HTA) bodies. For instance in addition to have the HTA's perspective embedded in the scientific priorities and calls for proposals, most notably through the representation of HTA bodies in the SIP, IHI JU will encourage consortia to engage with HTA bodies when relevant in order to better understand the evidence requirements for reimbursement decision-making.

<sup>46</sup> [https://www.ema.europa.eu/en/documents/other/regulatory-science-research-needs\\_en.pdf](https://www.ema.europa.eu/en/documents/other/regulatory-science-research-needs_en.pdf)

## 4.3 Support to operations of IHI JU in 2023

### 4.3.1 Communication, dissemination and exploitation

#### **Dissemination and information about projects results**

Although the responsibility for maximising the impact of their own research and innovation lies primarily with the project consortia, promoting the successes of projects is a core element of both the IHI JU communications and dissemination strategies.

The Programme Office identifies results and successes in a variety of ways, including through formal routes (project periodic reports, interim reviews) and informal routes (direct contacts with project participants, monitoring of project websites and social media, etc.). IHI JU will continue to support and supplement the dissemination of projects' public deliverables via a variety of channels.

In addition, IHI JU will continue to explore how to make better use of EU-specific dissemination tools and channels for the promotion of IMI projects and their results by actively participating in the European Commission's Dissemination and Exploitation Network (D&E Net) and intensively promoting the Innovation Radar, the Horizon Results Portal and the Horizon Results Booster among both IHI staff and IMI/IHI projects.

In 2023, IHI JU expects to receive approximately 29 final project reports. The exact number remains to be determined as the COVID-19 pandemic continues to affect the activities of projects and this may result in further no cost extension requests.

For most of the projects ending late 2022 and in 2023, close-out meetings will be organised around the time of submission of the final report. IHI JU will prepare specific communication materials for each project based on information provided in the final report and close out meeting. When necessary, the Programme Office may organise cross-project meetings, or meetings in thematic areas to facilitate the identification of significant impacts and learnings from the projects and ensure that this information is disseminated via the channels previously described.

Lastly, IHI JU will continue to fulfil its role/obligation to look after policy conformity, effectiveness and efficiency of the dissemination and exploitation at the level of each project in the portfolio.

#### **Communication**

##### *Unfolding IHI's new communication strategy*

The 2023 IHI JU communication work plan will be the first plan developed under the new IHI communication strategy.

In 2023 the first IHI projects will hit the ground running while a large number of ongoing IMI projects will yield new results. One of the communications team's main objectives will be to report on how both newly launched and ongoing projects will or have met the challenges they were set to address by: writing news articles, organising impact-focused events, and acting as sounding board for the communications activities of the projects themselves, building a continuum between the JU's communication and dissemination activities.

The communications team will join forces with the operations team in supporting the call for proposals cycle from ideation to project award, targeting our current stakeholders and opening our reach to the new sectors that have been brought on board. Targeted thematic workshops, IHI JU info days, brokerage events and call specific webinars, as well as external events will remain a crucial instrument to address this objective.

Since IHI will still be a very young programme in 2023, the communication team's third strategic objective will be to establish the IHI brand and raise stakeholders' awareness regarding the partnership's new research focus, new structures and new processes, in close collaboration with IHI partners and governance structures.

In order to amplify the reach of new calls for proposals, project success stories and results, IHI JU will keep working in close collaboration with the communication units of the founding partners and our governance bodies, with special emphasis on the SRG.

At the same time, the communications team will remain alert to issues that could damage IHI JU's reputation and respond accordingly by providing timely feedback on stakeholders' views and reactions.

### **Communication channels**

IHI JU will continue to develop content for the following channels with the aim of providing all interested stakeholders with access to relevant and specific information on the work of IHI JU and its projects:

- events;
- website;
- newsletter;
- social media (LinkedIn, Twitter);
- videos;
- multipliers (e.g. European Commission & industry partners, SIP, SRG, National Contact Points, relevant scientific associations, patient organisations, healthcare professional associations, etc.);
- media (general and specialist, mainly in Europe but also elsewhere);
- direct mailings;
- publications;
- direct contacts with opinion leaders.

### 4.3.2 Procurement and contracts

In order to reach its objectives and adequately support its operations and infrastructures, IHI JU will allocate funds to procure the necessary services and supplies.

To make tender and contract management as effective and efficient as possible, IHI JU resorts extensively to multi-annual framework contracts and EU inter-institutional tenders. In 2023, IHI JU intends to implement one such framework contract by concluding a specific contract for infrastructure as a service (IaaS) and IT development and support of SOFIA, the intranet, collaborative platforms and other IHI JU specific applications.

In 2023 IHI JU will continue the roll out of the public procurement corporate e-procurement tool to simplify, harmonise, modernise and digitise the procurement processes.

Most essential framework contracts are already in place and will be renewed beyond 2023. Additionally, IHI will create synergies with other JUs by launching inter-JU joint procurement e.g., ICT services, catering services and event logistics under the back-office arrangements.

### 4.3.3 Other support operations

#### a. Relevant functions and administrative synergies within back office arrangements<sup>47</sup>

The JUs have a well-established experience of close collaboration in several areas, including HR, IT, procurement, data protection etc. A lot of information and best practices sharing is taking place on a regular basis among the peers. E.g., the Executive Directors, Heads of Administration, HR officers, legal officers etc. meet regularly to discuss and share experiences. As several JUs are also located in the same premises, the collaboration is concrete serving the business needs e.g., in joint business continuity planning, managing the joint office building and sharing common infrastructure and meeting rooms. In 2023 IHI JU will also continue to provide office space for GH EDCTP3 JU's use. This will bring important cost-benefits to the Programme Office and is enabled by the new hybrid working mode implemented in accordance with the EC guidelines.

In alignment with the Council Regulation (EU) 2021/2085 a number of areas will be implemented within the back office arrangements (BOA). In 2022 the BOA implementation were launched by the JUs in accounting, ICT, procurement and HR services. In 2023 the experience from the implementation from the first set of service areas will be used to explore further collaboration within the BOA in the additional areas like anti-fraud measures, legal and corporate services. This will further enhance the already close collaboration of JUs in order to gain additional cost-efficiencies.

#### b. IT operations

The IHI JU information technologies (IT) team's strategic objective is to deliver value to the organisation and to be a key enabler of new organisational initiatives with the goal of supporting and shaping the present and future of the Programme Office.

IHI JU is part of common governance of IT operations and infrastructure, together with five JUs located in the same premises. This provides efficiency, economy of scale and gains in the operation of the organisation.

<sup>47</sup> Article 13 of the Council Regulation (EU) 2021/2085

Another very important key success factor is cooperation, shared services and knowledge sharing within ICTAC (Information and Communication Technologies Advisory Committee, part of the European Union Agencies Network) and with EC services.

To achieve the afore-mentioned goals, the IT team will focus its 2023 activities on the following areas:

*1. Stable, secure and agile IT infrastructure and office automation, more and more focused on the modern (anywhere, anytime) way of working*

The Programme Office will continue with adoption of software-as-a-service (SaaS) solutions both from the market and the European Commission.

Microsoft 365 (SaaS) will eventually become the main office automation and core IT infrastructure tool. After careful evaluation, most of the obsolete infrastructure-as-a-service (IaaS) components will be retired.

*2. Business operations information systems*

The main business operations (management of the evaluation of proposals and grants) will continue to be based on the EC eGrants tools. The IT team will monitor the satisfactory functioning for all end-users, in close liaison with the European Commission services, including Single Point of Contact (SPOC) functions.

SOFIA, the IHI JU grant management IT system, will be maintained as:

- main tool for the ongoing IMI1 JU projects
- complementary tool for information missing in eGrants IMI2 and IHI JU specificities - e.g. annual reporting of in-kind contributions, overview of project outputs for JU-specific KPIs (including completely new module for IHI JU) etc.

The Programme Office will also continue the further development of the IHI JU data warehouse and Qlik sense analytical platform with a particular focus on the integration of IHI JU data and data quality. The IT team will support existing tools and the migration to new European Commission tools.

*3. Collaboration, communication and administration management information systems*

The IHInet (intranet) and collaborative platforms, providing support to the governance bodies, will continue their evolution on M365 SharePoint technology. They have already proved their effectiveness as the main internal communication tool supporting business activities.

*4. IT Procurement and transition to the FWCs*

In 2023 the main IT operations will be onboarded to new FWCs as follows:

IT managed services: current inter-JUs FWC awarded to RealDolmen in 2018 will expire in 2022. The services will be handed over to the winner of the open call for tenders, which will be concluded in 2022.

Infrastructure as a service (IaaS): after the expiration of the European Food Safety Authority (EFSA) FWC “Broker model for the provision of cloud services” in 2023, IHI JU we will move the remaining part of IaaS from the Cancom data centre to the EC DIGIT CLOUD II FWC provider.

IT development and support of SOFIA, intranet, collaborative platforms and other IHI JU specific applications, currently carried out by Intrasoft via DIGIT-XM FWC (expiring in March 2023) will be procured via a new FWC as well.

### *5. New Regulation on Information Security*

The adoption of the new Regulation on Information Security, expected in 2023, will enforce the establishment of an internal cybersecurity risk management, governance and control framework that ensures an effective and prudent management of all cybersecurity risks.

IHI JU will evaluate the requirements in the final text of the regulation and will find the most effective way to create this framework.

#### **c. Record management, data protection and access to documents**

Document management at IHI JU is governed by several regulations. On the one hand, several regulations define the necessary registration and retention, while on the other hand the data protection regulation and the information security policy define access restrictions and deposition of documents.

Therefore IHI JU will continue its efforts undertaken in the wake of the entry into effect of the vademecum on record management adopted in 2021 (ED DEC No19/2021<sup>48</sup>), establishing a new records management policy for IHI JU based on the European Commission decision C(2020)4482<sup>49</sup>.

The Record Management Working Group<sup>50</sup> established in IHI JU will continue to take the necessary steps to ensure that all records, data, information, IT systems, transmission (handling) and storage are secure and suitable for both electronic and paper media, are used by IHI JU and fulfil the requirements set in applicable regulations and decisions.

To keep awareness among staff at a high level, IHI JU will continue with procedural guidance and trainings on these matters.

#### **Record management**

Record management covers all information, both electronic and physical records, necessary to ensure evidence of IHI JU's activities ensuring an appropriate level of accountability, transparency, and retention of IHI JU's legacy. Effective record management helps to meet IHI JU's transparency obligations, in particular by facilitating public access to documents and implementing the principle of accountability of public actions.

#### **Data protection**

The data protection rules are enshrined in the General Data Protection Regulation ("GDPR") for public organisations and businesses. For IHI JU, the data protection rules are laid down in Regulation (EU) 2018/1725 on the protection of natural persons regarding the processing of personal data by the Union institutions.

<sup>48</sup> ED Decision 19/2021 Ares(2021)5474488

<sup>49</sup> Commission Decision on records management and archives C(2020)4482.

<sup>50</sup> The composition of the group: Head of Administration and Finance, Document Management Officer (DMO), Data Protection Officer (DPO), IT Manager with the Internal Control and Risk Manager as an observer (non-statutory).

IHI JU is liaising with the relevant services of the European Data Protection Supervisor and contributing to the activities of the inter-institutional data protection networks and working groups to raise awareness among the staff and stakeholders.

#### **Access to information**

IHI JU will continue to address requests for access to documents according to Regulation (EC) No 1049/2001, in a spirit of openness and transparency, in order to bring its activities and outputs closer to the public and to keep a high-level of public confidence in IHI JU by giving the opportunity to the public to monitor its work.

#### **d. Accounting**

2023 will be the first year with the new accounting services and new Accounting Officer within the back office arrangements. The performance of the new accounting services will be monitored carefully in order to ensure business continuity and sound implementation of accounting tasks.

#### **e. Feedback to policy**

European partnerships are a key element of the policy approach of Horizon Europe.

The SRIA of IHI JU has been designed to deliver on Union priorities targeted by Horizon Europe and ensure a clear impact for the Union and its people, which can be achieved more effectively in partnership rather than by the Union alone. More specifically, IHI JU's projects aim to contribute to EU policies, most notably Horizon Europe (of which IHI JU is a part), as well as Europe's Beating Cancer Plan, the new Industrial Strategy for Europe, the Pharmaceutical Strategy for Europe and the European Health Data Space. In addition, IHI JU aims to contribute to the United Nations Sustainable Development Goal (SDG) 3 on ensuring healthy lives and promoting well-being for all at all ages.

The SRIA identifies the other candidate European partnerships of potential relevance, notably with the Mission Cancer, the partnerships in Cluster 1 of Horizon Europe and EIT Health, complementing the actions of the EU4Health<sup>51</sup> programme and HERA<sup>52</sup> wherever relevant. It is also expected that IHI JU activities will contribute to and complement those of the Digital Europe programme<sup>53</sup> that will deploy digital capacities and infrastructure related to the health area, and the European Green Deal<sup>54</sup> by contributing to the development of a greener and more sustainable healthcare sector.

IHI JU will begin to seek opportunities to synergise with other Union, national or regional health-oriented programmes, to involve representatives of other European partnerships and initiatives during the process of idea generation and topic drafting, and to identify the areas in which complementary or joint activities would address the challenges more effectively and efficiently.

The SIP will support IHI JU in advising on the creation of synergies. The SRG will support IHI JU by reporting on the status of national or regional policy, programmes and activities of relevance.

Lastly, IHI JU will encourage the exploitation of research and innovation results and actively disseminate and exploit results, in particular for leveraging private investments and for policy development.

<sup>51</sup> [https://hadea.ec.europa.eu/programmes/eu4health/about\\_en](https://hadea.ec.europa.eu/programmes/eu4health/about_en)

<sup>52</sup> [https://ec.europa.eu/health/health-emergency-preparedness-and-response-hera/overview\\_en](https://ec.europa.eu/health/health-emergency-preparedness-and-response-hera/overview_en)

<sup>53</sup> [https://ec.europa.eu/info/funding-tenders/find-funding/eu-funding-programmes/digital-europe-programme\\_en](https://ec.europa.eu/info/funding-tenders/find-funding/eu-funding-programmes/digital-europe-programme_en)

<sup>54</sup> [https://ec.europa.eu/info/strategy/priorities-2019-2024/european-green-deal\\_en](https://ec.europa.eu/info/strategy/priorities-2019-2024/european-green-deal_en)

## 4.3.4 Human resources

### a. HR management

In 2023, the total number of IHI JU staff will be 54 (of which 39 temporary agents and 15 contract agents). Due to the reduction in the staff numbers in the Staff Establishment Plan (SEP), in 2023 IHI will no longer employ Seconded National Experts (SNE). In September 2022, Dr Hugh Laverty, IHI Head of Scientific Operations was appointed by the IHI Governing Board as IHI Executive Director *ad interim*, while the selection procedure of the new Executive Director has been ongoing.

In 2023, the Programme Office will start its second year of activity, which should lead to a decrease in staff turnover in comparison to the previous transition years. Nevertheless, the overall reduction in the number of human resources combined with the necessity to manage (i) a large and complex legacy from IMI1 JU and IMI2 JU projects and (ii) new IHI projects will result in a significant impact on the management of the Programme Office's human resources. This will unavoidably lead to an increased pressure on staff. Therefore, the management team of IHI JU will need to continue exploring measures to minimise potential impacts on well-being of its staff and to ensure business continuity.

#### 1. Selection and recruitment

In 2023, the HR priorities will remain: (i) the successful and timely management of the selection procedures to guarantee that the best talents, with the necessary set of competences and skills will be recruited; and (ii) the efficient on-boarding of statutory staff, trainees and interims. To this end, the HR team will set up measures to attract the best candidates and will ensure alignment throughout the organisation establishing a strong link between HR processes and business results, connecting the Programme Office overall strategic goals with staff performance management. The new e-selection tool SYSTAL implemented in 2022 will be fully operational in 2023 and will contribute to the achievement of the above-mentioned objectives.

Gender balance and equality will remain important elements in IHI JU selection and recruitment procedures (today the ratio is 33% male and 66% female with an equal distribution in the IHI JU management team). IHI JU will also foster its traineeship programme to provide young university graduates with the opportunity to gain hands-on professional experience in scientific fields related to IHI JU and to develop and strengthen their skills and competences. To guarantee business continuity, some interims might also be recruited to cope with peaks of work and absences during the year. Finally, further development and improvement of recruitment practices and employer branding may be envisaged.

#### 2. Career development

To ensure that IHI JU existing talents are retained, the HR team will further explore internal mobility opportunities, staff engagement actions, career coaching, and other career development activities (e.g. job shadowing, staff exchanges, learning opportunities, etc.). Particular attention will continue to be given to the performance management cycle (appraisal and reclassification exercises). To optimise the daily management of the HR activities, and to streamline these two exercises, in 2023, the HR team will aim to implement the SYSPER II module Evaluation and Promotion, as well as organise tailor-made training courses for managers and staff.

The human resources team will keep overseeing duties and responsibilities assigned to staff in order to achieve the fulfilment of IHI JU's objectives and tasks.

#### 3. Learning & Development

To help the development and the personal and professional growth of IHI JU staff and to keep staff knowledge up-to-date, the human resources team will further develop the learning and development framework, paying particular attention to the training needs of its staff and the Programme Office.

The HR team will also continue advising management on means and actions to enhance operational efficiency and effectiveness. Tailor-made training courses and coaching programmes for managers will be organised to support and keep them abreast in their day-to-day management of staff and operational activities, and particular attention will be given to performance management.



The Programme Office is committed to preserve a physically and psychologically healthy work environment where work is meaningful, and people have the conditions to contribute to their best. To this end, the Programme Office will: (i) keep paying particular attention to the well-being of its staff, by developing tailor-made well-being activities to increase wellness in the workplace (e.g. well-being lunchtime sessions, workshops, etc); (ii) develop teambuilding activities to strengthen collaboration among staff members, to enhance the team spirit and culture, and to help staff get acquainted with the hybrid working; (iii) remain vigilant and reiterate its strong commitment to a zero tolerance towards psychological and sexual harassment and disrespectful work environments.

#### **4. Legal matters**

IHI JU will continue working closely with DG HR and the Standing Working Party (group following the Staff Regulation and its implementing rules) to ensure the adoption of the implementing rules and to strengthen its legal framework also adopting internal guidelines. The COVID-19 outbreak showed that new ways of working are possible and revision of some existing rules will be needed to adapt to the “new norm”.

In addition to the above, the human resources team will deal with core functions such as: day-to-day management of administrative workflows and processes, salary, compensation and benefits, performance management, career development, reclassification, learning and development, safety and wellbeing at work; employees' motivation and communication.

#### **b. Strategy for achieving efficiency gains and synergies**

Under the IHI JU 2023 Staff Establishment Plan there is a decrease of 3.6% of the human resources, from a total of 56 staff members in 2021 to 54 staff members in 2023. In addition, no new resources were provided to IHI JU while setting up the new programme requiring to manage three complex programmes in parallel (IMI1 JU, IMI2 JU and IHI JU). Thus, in 2023 the Programme Office will have to pay even more attention to the efficiency and cost-effective management of its resources due to the limited allocation of human resources.

In 2023, the JUs will continue sharing the human resources IT tools (e.g. the e-recruitment tool SYSTAL, SYSPER, etc) and, where necessary, common calls for tender, selection procedures, training courses for JU staff and managers as well as a common approach to the implementing rules of the EU staff regulations. The JUs also share an inter-JU network of confidential counsellors; this network will be reinforced in 2022 with the publication of a new call and appointment of additional confidential counsellors. Their assignment will start in 2023.

**c. Staff Establishment Plan**

Function group and grade	2021				2022		2023	
	Authorised budget		Actually filled as of 31/12		Authorised budget		Authorised budget	
	Permanent posts	Temporary posts	Permanent posts	Temporary posts	Permanent posts	Temporary posts	Permanent posts	Temporary posts
AD 16								
AD 15								
AD 14		1		1		1		1
AD 13								
AD 12		2		1		2		2
AD 11		2		2		2		2
AD 10		1		2		1		1
AD 9		7		5		7		7
AD 8		6		4		6		6
AD 7		2		4		3		4
AD 6		11		6		10		9
AD 5		1		6		2		3
<b>TOTAL AD</b>		<b>33</b>		<b>31</b>		<b>34</b>		<b>35</b>
AST 11								
AST10								
AST 9								
AST 8		1		1		1		1
AST 7								
AST 6								
AST 5								
AST 4		4		3		4		3

Function group and grade	2021				2022		2023	
	Authorised budget		Actually filled as of 31/12		Authorised budget		Authorised budget	
	Permanent posts	Temporary posts	Permanent posts	Temporary posts	Permanent posts	Temporary posts	Permanent posts	Temporary posts
AST 3				1				
AST 2		1						
AST 1								
<b>TOTAL AST</b>		<b>6</b>		<b>5</b>		<b>5</b>		<b>4</b>
AST/SC 6								
AST/SC 5								
AST/SC 4								
AST/SC 3								
AST/SC 2								
AST/SC 1								
<b>TOTAL AST/SC</b>								
<b>TOTAL AD+AS T+ AST/SC</b>								
<b>GRAND TOTAL</b>	<b>39</b>		<b>36</b>		<b>39</b>		<b>39</b>	

<b>Contract Agents</b>	<b>FTE corresponding to the authorised budget 2021</b>	<b>Executed FTE as of 31/12/2021</b>	<b>Headcount as of 31/12/2021</b>	<b>FTE corresponding to the authorised budget 2022</b>	<b>FTE corresponding to the authorised budget 2023</b>
Function Group IV	3	3	3	4	4
Function Group III	11	9	9	11	11
Function Group II	1	1	1		
Function Group I					
<b>TOTAL</b>	<b>15</b>	<b>12</b>	<b>12</b>	<b>15</b>	<b>15</b>

<b>Seconded National Experts</b>	<b>FTE corresponding to the authorised budget 2021</b>	<b>Executed FTE as of 31/12/2021</b>	<b>Headcount as of 31/12/2021</b>	<b>FTE corresponding to the authorised budget 2022</b>	<b>FTE corresponding to the authorised budget 2023</b>
<b>TOTAL</b>	<b>2</b>	<b>1</b>	<b>2</b>	<b>1</b>	<b>0</b>

<b>Recruitment forecasts 2023 following retirement/mobility or new requested posts</b>					
<b>Job title in the JU</b>	<b>Type of contract (Official, CA, TA)</b>		<b>TA/Official</b>		<b>CA</b>
			<b>Function group/grade of recruitment internal (Brackets) and external (single grade) foreseen for publication</b>		<b>Recruitment Function Group (I, II, III and IV)</b>
	<b>Due to foreseen retirement/mobility</b>	<b>New post requested due to additional tasks</b>	<b>Internal (brackets)</b>	<b>External (brackets)</b>	
	0	0			

## 4.4 Governance activities in 2023

### Planned activities

- Support the Governing Board (GB), the Science and Innovation Panel (SIP), the States' Representatives Group (SRG) and provide all necessary information for the performance of their respective tasks.
- Align planning activities (strategy, annual Work Programme and related budget) and the associated monitoring and reporting activities.
- Improve responsibilities and accountability.
- Enhance communication and transparency.

#### 4.4.1 Governing Board

The GB gathers representatives of IHI JU members. It is the main decision-making body, and as such has the responsibility for ensuring that IHI JU achieves its objectives and overseeing the operations of IHI JU and the implementation of its activities.

Two meetings are planned for 2023. The chairperson may be invited to attend the SRG meetings as an observer.

#### 4.4.2 States' Representatives Group

The SRG acts as an advisory body. It shall be consulted and, in particular, it shall review information and provide opinions on the following matters: Work Programme (and subsequent amendment(s)), the progress of IHI JU and achievement of its targets.

The SRG shall report to the GB, in particular on the status of relevant national or regional research and innovation programmes and identification of potential areas of cooperation.

Two meetings of the SRG are planned for 2023. The chairperson and the vice-chairperson shall participate in the GB meetings as observers and in the SIP meetings as permanent panellists.

#### 4.4.3 Science and Innovation Panel

The SIP is the scientific advisory body. It provides the GB with science-based advice on a range of matters, in particular on the annual scientific priorities, the draft call topics, the planning of additional activities and synergies with other Horizon Europe activities, including other European partnerships, as well as other EU and national programmes. The permanent panellists include representatives of the European Commission, industry partners and the SRG as well as representatives from the scientific community and the wider healthcare community appointed by the GB for a period of three (3) years following an open selection process (call for expressions of interest launched in January 2022).

Two meetings are planned for 2023. The chairperson may be invited to participate in the GB meetings as an observer whenever issues falling within the scope of the SIP tasks are discussed.

## 4.5 Strategy and plans for the organisational management and the internal control system in 2023

### 4.5.1 Internal Control Framework

The priority objective of 2023 will be to implement and maintain an effective internal control system so that reasonable assurance can be drawn that: (1) resources assigned to the activities are used according to the principles of sound financial management; (2) risk of errors in operations is minimised; and (3) the control procedures put in place give the necessary assurance concerning the legality and regularity of the underlying transactions.

This is achieved by IHI JU via a combination of systems, procedures, and supervision, notably including ex-ante and ex-post controls of transactions and the monitoring of financial performance.

The implementation of recommendations from audits by the European Court of Auditors and the Commission's Internal Audit Service also play a key role in this area.

Due consideration will be given to:

- optimising and updating internal procedures and processes in order to ensure efficiency, effectiveness and better synergies;
- risk management process integrated in the annual planning cycle by performing risk assessment exercise and following up risk mitigation action plans;
- incorporating to a broad extent the horizontal guidance and controls to ensure compliance and a harmonised approach across the implementation of the programme and fair and equal treatment towards beneficiaries, and to gather reasonable assurance.

### 4.5.2 Ex-ante and ex-post controls

#### Ex-ante controls

Ex-ante controls are rigorously implemented by IHI JU for each transaction (commitments and payments). Standard ex-ante control measures are in place for FP7, Horizon 2020 and for Horizon Europe programmes. They are tailored to the different forms of costs and combine trust-based baseline checks and risk-based targeted controls. Together, ex-ante and ex-post controls (see following section) provide the Authorising Officers with the necessary elements of assurance on the research and innovation budget under their responsibility. To that purpose, IHI JU will continue to work in 2023 with all R&I family services and the European Court of Auditors to conclude and start implementing the control strategy for the Horizon Europe programme (including ex-ante and ex-post controls and anti-fraud).

Specific attention will be paid to:

- raising beneficiaries' awareness of the financial and administrative aspects of the H2020 and Horizon Europe rules and how to avoid errors in cost reporting;
- validation of financial and technical reports;
- ex-ante controls for interim and final payments;
- following up recovery orders where needed.

## **Ex-post controls**

### For IMI1 JU projects running under the Seventh Framework Programme

The Programme Office will carry on with the implementation of its ex-post audit strategy as a means to ensure the legality and regularity of operational expenditure. This strategy complements ex-ante controls embedded in IHI JU's management processes and includes the rejection of any costs found to be in breach with the requirements of IMI JU Grant Agreement. Representative ex-post audits of participants will be launched on new cost claims accepted by the Programme Office since the last audited period to reach the audit coverage ratio set in its ex-post audit strategy. If necessary, risk based ex-post audits will be launched according to the Programme Office risk-based audit strategy. Rejection of systematic errors identified in ex-post audits will continue to be extended to unaudited financial statements ('Form C') of the audited participants.

Ex-post audits of accepted declarations of in-kind contributions by EFPIA companies will not be carried out in 2023 as the work plan on ex-post audits of EFPIA companies under IMI JU has reached its end in 2021 and the majority of the EFPIA companies' in-kind contributions have been covered by ex-post audits. Controls of in-kind contributions by EFPIA companies will also be based on the review of audit certificates provided by independent auditors for the final reporting period. Risk-based ex-post audits of accepted declarations of in-kind contributions may nevertheless be initiated should a specific need arise.

### For IMI2 JU projects running under the H2020 Framework Programme

Ex-post controls of grants are aligned with the harmonised strategy adopted for the entire H2020 Programme. The Commission Common Audit Service (CAS) will carry out the H2020 ex-post audits in accordance with the common H2020 audit strategy. The Programme Office contributes to the implementation of the H2020 audit strategy in close cooperation with the CAS and ensures that its ex-post audit strategy is complied with, including its audit coverage ratio. If necessary, risk based ex-post audits will be launched according to the Programme Office risk based audit strategy. The harmonised legal framework will enable the Programme Office to draw an additional element of assurance from the extension of systematic errors identified in ex-post audits to unaudited financial statements of common audited beneficiaries across H2020.

In line with Article 4.4 of the applicable Regulation (Council Regulation (EU) No 557/2014), controls of in-kind contributions by EFPIA companies will be based on the review of audit certificates provided annually by independent auditors and their validation by the Authorising Officer. In case of remaining uncertainties, ex-post audits of accepted declarations of in-kind contributions may be performed.

### For IHI JU projects running under the Horizon Europe Framework Programme

Article 31 "Ex-post audits" of the Council Regulation (EU) 2021/2085 stipulates that audits of expenditure on indirect actions shall be carried out in accordance with Article 53 "Audits" of the Horizon Europe Regulation (Regulation (EU) 2021/695 of the European Parliament and of the Council), in particular in line with the audit strategy referred to in Article 53(2) of that Regulation (EU) 2021/695. The Programme Office contributes to the implementation of the Horizon Europe audit strategy in close cooperation with the Commission Common Audit Service and ensures that its ex-post audit strategy is complied with, including its audit coverage ratio. In line with Article 53(2) of Regulation 2021/695, the representative ex-post audits shall be complemented by risk based ex-post audits according to the Programme Office risk-based audit strategy. The harmonised legal framework will enable the Programme Office to draw an additional element of assurance from the extension of systematic errors identified in ex-post audits to unaudited financial statements of common audited beneficiaries across Horizon Europe.

In line with Article 11.2 of the Council Regulation (EU) 2021/2085, controls of in-kind contributions to additional activities by members other than the Union will be based on the review of audit certificates provided annually by independent auditors and their validation by the Authorising Officer.

### 4.5.3 Audits

#### Internal and external audits

IHI JU audit arrangements are set up in accordance with Article 28 and 54 of the IHI JU Financial Rules. The audits provide reasonable assurance about the state of effectiveness of risk management, control and governance processes and serve as a building block for the annual Declaration of Assurance of the Executive Director.

The Audit Manager will coordinate audits carried out by IHI JU's internal and external auditors, will follow up and assess the implementation of the Internal Audit Service (IAS) of the European Commission and the European Court of Auditors (ECA) recommendations with the objective to confirm their effective implementation.

Internal audits are carried out by the IAS in liaison with the Audit Manager.

In 2023 IAS will commence implementation of the Strategic Internal Audit Plan (2023-2025)<sup>55</sup> and launch an audit engagement on the topic of Governance and relations with stakeholders

In 2023, the focus will be put on:

- coordinating and supporting IAS's audit work and ensuring an adequate level of assurance from internal audit.

External audits are carried out by the ECA. The ECA will audit and issue opinions on the legality and regularity of the underlying transactions, revenue, and reliability of accounts. In accordance with the IHI JU Financial Rules, IHI JU's 2022/2023 annual accounts will be audited by a selected external audit company that IHI JU contracts. The ECA will draw up its annual audit opinion on the basis of their work and issue a special annual report on joint undertakings. In view of the overall corporate objective of receiving an unqualified ('clean') ECA audit opinion and positive statement of assurance, the key activities will focus on:

- liaising and supporting ECA auditors throughout the audits of 2022 and 2023 accounts and following up on preliminary findings and recommendations;
- liaising with an independent external auditor and coordinating with the ECA throughout the audits of the accounts for the financial years 2022 and 2023.

<sup>55</sup> Ares(2023)638585 of 27/01/2023



#### 4.5.4 Anti-fraud

The objective of 2023 will be to carry on with the implementation of the IHI JU anti-fraud strategy and the new action plan adopted in 2022.

IHI JU implements the common Research Anti-Fraud Strategy. In March 2019, CIC adopted the revised Research Family Anti-Fraud Strategy (RAFS 2019) and the associated action plan (replacing RAFS 2015 and its action plan). The implementation of the action plan, which deals with the fraud risks related to the implementation of the research and innovation programmes concerning grant management, is monitored through regular meetings of the Fraud and Irregularities Committee (FAIR), in which IHI JU takes part.

IHI JU will continue to apply harmonised preventive measures for fraud detection, e.g. via the enhanced monitoring tool available as a feature in Sygma-Compass workflow.

The IHI JU anti-fraud strategy also covers areas that are not related to grant management, i.e. fraud risks related to procurement, expert management, internal misconduct, etc.

IHI JU will continue to collaborate closely with the services of the European Anti-Fraud Office (OLAF) and build relations with EPPO and will actively participate in the FAIR committee and other anti fraud activities elated forums and trainings.

## 5 Amended Budget 2023

The budget for the financial year 2023 is revised based on information available. The following elements are reflected in this amended 2023 budget: Outline the budget of Call 4 and Call 5 under Horizon Europe, on the specific budget lines, the budget for Call 4 being EUR 83.3 million and the budget for Call 5 being EUR 115 million. Carry overs of unused commitment appropriations from 2022 to 2023, of EUR 1.6 million. Out of it, the amount of EUR 1.5 million is made available for Calls to be launched in 2023 and EUR 0.1 million is made available for potential positive ex-post audit implementation of FP7 and H2020 closed projects and potential late payment interest of the FP7 and H2020 payments. Revision of the operational payment appropriations per programme, in view of upcoming pre-financings to be paid for the first projects under Horizon Europe. As such, the payment appropriations for IMI2 JU are reduced by EUR 4 million, while the payment appropriations for IHI JU are increased by EUR 4 million. The total payment appropriations remain unchanged (EUR 210 mil). Regarding the administrative budget, the total amount for 2023 remain unchanged, at the level of EUR 9,500,000 in commitment appropriations. The amount is divided equally (50%-50%) between the EC and industry partners (EFPIA, EuropaBio, COCIR and MedTech). The total EC contribution to the administrative budget is EUR 4,750,000 and the total industry contribution to the administrative budget is equal, of EUR 4,750,000. EU and industry contributions are stemming from IMI2 JU and IHI JU budgets.

EC and EFPIA contribute to the IMI2 JU budget. EFPIA contribution to the IMI2 JU budget for 2023 is EUR 3,325,000, equal to the EC contribution to the IMI2 JU budget.

EC and the industry partners (EFPIA, EuropaBio, COCIR and MedTech) contribute to IHI JU budget. The industry contribution to IHI JU budget for 2023 is EUR 1,425,000, equal to the EC contribution to the IHI JU budget.

The table below shows how the industry contribution is divided between the IMI2 and IHI programmes and the percentages per funding source.

<b>Industry contribution to the total administrative budget for 2023 (EUR)</b>	<b>4,750,000</b>	<b>%</b>
<b>IHI JU</b>	1,425,000	30%
<b>IMI2</b>	3,325,000	70%

An overview of the 2023 revenue per chapter is set out below.

**IHI JU - STATEMENT OF REVENUE (EUR)**

Chap ter/ Line	Heading Revenue	Budget 2023.1		Budget 2023 Amendment 1		Amended Budget 2023.1		Comments
		Commitment Appropriation (CA)	Payment Appropriation (PA)	Commitment Appropriation (CA)		Commitment Appropriation (CA)	Payment Appropriation (PA)	
<b>10</b>	<b>European Commission contribution</b>							
<b>1000</b>	European Commission contribution (including EFTA contribution) for current year out of IMI2 budget	3,325,000	137,325,000		-4,000,000	3,325,000	133,325,000	Commitment appropriations include EUR 3,325,000 for administrative costs. Payment appropriations include EUR 3,325,000 for administrative costs and EUR 130,000,000 for operational costs.
<b>1002</b>	European Commission contribution (including EFTA contribution) for current year out of IHI JU budget	207,205,000	77,425,000		4,000,000	207,205,000	81,425,000	Commitment appropriations include EUR 1,425,000 for administrative costs and EUR 205,780,000 for operational costs. Payment appropriations include EUR 1,425,000 for administrative costs and EUR 80,000,000 for operational costs.
<b>1001</b>	European Commission - appropriations carried over from previous years			1,602,600		1,602,600	-	
<b>10</b>	<b>European Commission contribution - total</b>	<b>210,530,000</b>	<b>214,750,000</b>	<b>1,602,600</b>		<b>212,132,600</b>	<b>214,750,000</b> <small>56</small>	
<b>20</b>	<b>JU members other than the Union contribution</b>							
<b>2000</b>	EFPIA contribution for current year out of IMI2 budget	3,325,000	3,325,000			3,325,000	3,325,000	EFPIA contribution to IHI administrative costs

<sup>56</sup> The total EC payment appropriations remain unchanged. With the budget amendment 1, the EC payment appropriations have been reflected on separate budget lines, on IMI2 related programmes (FP7 and H2020), respectively Horizon Europe related programme.

IHI JU - STATEMENT OF REVENUE (EUR)

	Heading Revenue	Budget 2023.1		Budget 2023 Amendment 1		Amended Budget 2023.1		Comments
2002	EFPIA contribution for current year out of IHI budget	697,500	697,500			697,500	697,500	EFPIA contribution to IHI administrative costs
2001	EFPIA - appropriations carried over from previous years							
	<b>EFPIA contribution - total</b>	<b>4,022,500</b>	<b>4,022,500</b>	-		<b>4,022,500</b>	<b>4,022,500</b>	
2010	EuropaBio contribution for IHI current year	15,000	15,000			15,000	15,000	EuropaBio contribution to IHI administrative costs
2011	EuropaBio - appropriations carried over from previous years							
	<b>EuropaBio contribution - total</b>	<b>15,000</b>	<b>15,000</b>	-		<b>15,000</b>	<b>15,000</b>	
2020	COCIR contribution for IHI current year	356,250	356,250			356,250	356,250	COCIR contribution to IHI administrative costs
2021	COCIR - appropriations carried over from previous years							
	<b>COCIR contribution - total</b>	<b>356,250</b>	<b>356,250</b>	-		<b>356,250</b>	<b>356,250</b>	
2030	MedTech Europe contribution for IHI current year	356,250	356,250			356,250	356,250	MedTech contribution to IHI administrative costs
2031	MedTech Europe - appropriations carried over from previous years							
	<b>MedTech Europe contribution - total</b>	<b>356,250</b>	<b>356,250</b>	-		<b>356,250</b>	<b>356,250</b>	

**IHI JU - STATEMENT OF REVENUE (EUR)**

	Heading Revenue	Budget 2023.1		Budget 2023 Amendment 1		Amended Budget 2023.1		Comments
20	JU members other than the Union contribution - total	4,750,000	4,750,000	-		4,750,000	4,750,000	
	<b>Total revenue</b>	<b>215,280,000</b>	<b>219,500,000</b>	<b>1,602,600</b>		<b>216,882,600</b>	<b>219,500,000</b>	

An overview of the 2023 expenditure per chapters is set out below.

STATEMENT OF EXPENDITURE (EUR)								
	Heading Title 1	Budget 2023.1		Budget 2023 Amendment 1		Amended Budget 2023.1		Comments
Title Chapter		Commitment Appropriation (CA)	Payment Appropriation (PA)	Commitment Appropriation (CA)	Payment Appropriation (PA)	Commitment Appropriation (CA)	Payment Appropriation (PA)	
<b>1</b>	<b>Staff expenditure</b>							
11	Staff in active employment	5,922,000	5,922,000			5,922,000	5,922,000	Salaries and allowances of current staff (TAs and CAs), SNE, promotion and indexation
12	Staff recruitments - miscellaneous expenditure	5,000	5,000			5,000	5,000	Miscellaneous expenditure on staff recruitment: publication of vacancy calls, medical visits to take up duties, services provided by the European Personnel Selection Office (EPSO)
13	Missions and duty travels	144,000	144,000			144,000	144,000	Missions expenditure
14	Socio-medical structure	232,000	232,000			232,000	232,000	Other staff costs: EU school, medical check-up, trainings
15	External staff services	175,000	175,000			175,000	175,000	Interim staff expenses
17	Representation	10,000	10,000			10,000	10,000	Representation expenses
<b>Total Title 1 (Staff expenditure)</b>		<b>6,488,000</b>	<b>6,488,000</b>	<b>0</b>	<b>0</b>	<b>6,488,000</b>	<b>6,488,000</b>	
	Heading Title 2	Budget 2023.1		Budget 2023 Amendment 1		Amended Budget 2023.1		Comments
Title Chapter		Commitment Appropriation (CA)	Payment Appropriation (PA)	Commitment Appropriation (CA)	Payment Appropriation (PA)	Commitment Appropriation (CA)	Payment Appropriation (PA)	
<b>2</b>	<b>Infrastructure expenditure</b>							
20	Office building and associated costs	698,000	698,000			698,000	698,000	Building related expenditure: rent, works, charges, maintenance, repairs, security and surveillance

STATEMENT OF EXPENDITURE (EUR)								
	Heading Title 1	Budget 2023.1		Budget 2023 Amendment 1		Amended Budget 2023.1		Comments
21	Information technology purchases	1,090,000	1,090,000			1,090,000	1,090,000	IT purchases, software licences, software development
22	Office equipment (movable property and associated costs)	5,000	5,000			5,000	5,000	Purchases and rental of office equipment, maintenance and repair
23	Current administrative expenditure	124,000	124,000			124,000	124,000	Office supply, newspaper subscriptions, translation services, bank charges and miscellaneous office expenditure
24	Telecommunication and postal expenses	40,000	40,000			40,000	40,000	Data communication such as telephone, video and audio conferences and postal services
25	Expenditure on formal meetings	80,000	80,000			80,000	80,000	Official meetings such as States Representative Group, Science and Innovation Panel, Governing Board and working groups created by the Governing Board
26	Administrative expenditure in connection with operational activities	250,000	250,000			250,000	250,000	Administrative expenditure in connection with research activities and objectives of IHI (workshops, meetings and events targeting IHI projects)
27	External communication, information and publicity	300,000	300,000			300,000	300,000	External communication and events such as Info Days, stakeholder forums
28	Service contracts	425,000	425,000			425,000	425,000	Ex-post audits, studies, audits, accounting services
29	Expert contracts and cost of evaluations	-	-			0	0	Costs linked to evaluations, expert contracts
<b>Total Title 2 (Infrastructure expenditure)</b>		<b>3,012,000</b>	<b>3,012,000</b>	<b>0</b>	<b>0</b>	<b>3,012,000</b>	<b>3,012,000</b>	

STATEMENT OF EXPENDITURE (EUR)								
	Heading Title 1	Budget 2023.1		Budget 2023 Amendment 1		Amended Budget 2023.1		Comments
<b>Total Title 1 + 2 (administrative expenditure)</b>		<b>9,500,000</b>	<b>9,500,000</b>	<b>0</b>	<b>0</b>	<b>9,500,000</b>	<b>9,500,000</b>	
	Heading Title 3	Budget 2023.1		Budget 2023 Amendment 1		Amended Budget 2023.1		Comments
Title Cha pter	Operational expenditure	Commitment Appropriation (CA)	Payment Appropriation (PA)	Commitment Appropriation (CA)	Payment Appropriation (PA)	Commitment Appropriation (CA)	Payment Appropriation (PA)	
30	Implementing the research agenda of IMI2 JU		134,000,000		-4,000,000		130,000,000	Payments: FP7, H2020
31	Implementing the research agenda of IHI JU	205,180,000	75,400,000		4,000,000	205,180,000	79,400,000	Commitments: Calls Horizon Europe Payments: Horizon Europe
39	Evaluation experts	600,000	600,000			600,000	600,000	Costs linked to evaluations experts contracts
30	Appropriations carried over from 2022			1,602,600		1,602,600	0	Appropriations carried over from 2022
<b>Total Title 3 (Operational expenditure)</b>		<b>205,780,000</b>	<b>210,000,000</b>	<b>1,602,600</b>	<b>0</b>	<b>207,382,600</b>	<b>210,000,000</b>	
<b>Total expenditure</b>		<b>215,280,000</b>	<b>219,500,000</b>	<b>1,602,600</b>	<b>0</b>	<b>216,882,600</b>	<b>219,500,000</b>	

## Operational budget

The operational budget for the financial year 2023 is based on the currently available information. With 2023 budget amendment 1, the unused administrative and operational commitment appropriations from 2022 are carried over to operational commitment appropriations in 2023, for a total amount of EUR 1.6 million.

It has been outlined the budget for IHI JU Call 4 (EUR 83.3 million) and IHI JU Call 5 (EUR 115 million) on the respective budget lines.

In view of pre-financings to be paid for projects under Horizon Europe, the operational payment appropriations are revised. Thus, the payment appropriations for IMI2 JU are reduced by EUR 4 million and the payment appropriations for IHI JU are increased by EUR 4 million. The total operational payment appropriations remain unchanged, of EUR 210 million.

A table overview of the operational budget for 2023 is set out below.



Operational budget financial year 2023								
	Heading Title 3	Budget 2023.1		Budget 2023 Amendment 1		Amended Budget 2023.1		Comments
Chapter		Commitment Appropriation (CA)	Payment Appropriation (PA)	Commitment Appropriation (CA)	Payment Appropriation (PA)	Commitment Appropriation (CA)	Payment Appropriation (PA)	
3	<b>Operational expenditure</b>							
30	Implementing the research agenda of IMI1 and IMI2 JU		134,000,000		-4,000,000	-	130,000,000	Payment appropriations: payments FP7, H2020.
31	Implementing the research agenda of IHI JU	205,180,000	75,400,000		4,000,000	205,180,000	79,400,000	Commitment appropriations: Calls Horizon Europe. Payment appropriations: payments Horizon Europe.
39	Evaluation experts	600,000	600,000			600,000	600,000	Costs linked to evaluations, experts contracts.
30	Appropriations carried over from 2022			1,602,600		1,602,600		Appropriations carried over from 2022
	<b>Total Title 3 (Operational expenditure)</b>	<b>205,780,000</b>	<b>210,000,000</b>	<b>1,602,600</b>	<b>0</b>	<b>207,382,600</b>	<b>210,000,000</b>	

A breakdown of the appropriations carried over to operational budget is set out below.

Description	Commitment Appropriation (CA)	Payment Appropriation (PA)
50% unused administrative costs 2022 to be carried over to operational budget 2023 for new Calls under Horizon Europe	825,232	
unused operational commitment appropriations 2022 to be carried over to 2023 on FP7 and H2020 budget lines, stemming from recoveries from beneficiaries. Reserve funds for potential positive ex-post audit implementation of FP7 and H2020 closed projects and potential late payment interests.	150,000	
unused Horizon Europe commitment appropriations 2022 to be carried over to 2023 on Horizon Europe new Calls' budget lines	627,368	
<b>TOTAL</b>	<b>1,602,600</b>	<b>0</b>

## Administrative budget

The administrative budget for the financial year 2023 is based on the currently available information. Regarding the administrative budget, the total amount for 2023 remain unchanged, at the level of EUR 9,500,000 in commitment appropriations.

For commitment appropriations, a comparison table of the financial years 2022 and 2023 budget is set out below.

	Heading	Financial year 2022	Financial year 2023	Evolution	Comments
Title Chapter		Budget EUR	Budget EUR		
<b>1</b>	<b>Staff expenditure</b>				
<b>11</b>	Staff in active employment	6,032,000	5,922,000	-2%	reduction of costs by 1 SNE; it includes 2% promotions and indexations as well as prices indexation of services provided by PMO and OIB
<b>12</b>	Staff recruitments - miscellaneous expenditure	5,000	5,000	0%	
<b>13</b>	Missions and duty travels	80,000	144,000	80%	increase due to expected higher number of missions during 2023. 2022 was budgeted in the context of effects of COVID-19.
<b>14</b>	Socio-medical structure	212,000	232,000	9%	increase of EU school, transport and trainings due to prices indexation
<b>15</b>	External staff services	125,000	175,000	40%	increase due to operational needs
<b>17</b>	Representation	10,000	10,000	0%	
<b>Total Title 1 (Staff expenditure)</b>		<b>6,464,000</b>	<b>6,488,000</b>	<b>0%</b>	
	Heading	Financial year 2022	Financial year 2023	Evolution	Comments
Title Chapter		Budget EUR	Budget EUR		
<b>2</b>	<b>Infrastructure expenditure</b>				
<b>20</b>	Office building and associated costs	660,000	698,000	6%	increase due to price indexation
<b>21</b>	Information technology purchases	1,009,000	1,090,000	8%	increase due to price indexation
<b>22</b>	Office equipment (movable property and associated costs)	5,000	5,000	0%	

	Heading	Financial year 2022	Financial year 2023	Evolution	Comments
Title Chapter		Budget EUR	Budget EUR		
23	Current administrative expenditure	124,000	124,000	0%	
24	Telecommunication and postal expenses	38,000	40,000	5%	increase due to price indexation
25	Expenditure on formal meetings	70,000	80,000	14%	increase due to expected higher number of meetings during 2023.
26	Administrative expenditure in connection with operational activities	200,000	250,000	25%	increase due to expected higher number of meetings during 2023.
27	External communication, information and publicity	300,000	300,000	0%	
28	Service contracts	410,000	425,000	4%	increase due to price indexation
<b>Total Title 2 (Infrastructure expenditure)</b>		<b>2,816,000</b>	<b>3,012,000</b>	<b>7%</b>	
<b>Total Title 1+2 (Administrative expenditure)</b>		<b>9,280,000</b>	<b>9,500,000</b>	<b>2%</b>	

## Overview of the budget per budget line

An overview of the 2023 Budget per budget line is set out in the table below.

Budget line Chapter	Description	Commitment Appropriations (CA)	Payment Appropriations (PA)
1100	Staff in active employment and costs linked to employees	3,620,000	3,620,000
1101	Family Allowances	370,000	370,000
1102	Transfer and expatriation allowances	500,000	500,000
1110	Contract Agents	930,000	930,000
1111	Seconded National Experts	-	0
1130	Insurance against sickness	122,000	122,000
1131	Insurance against accidents and occupational diseases	15,000	15,000
1132	Unemployment insurance for temporary staff	48,000	48,000
1133	Pension		
1140	Birth and death allowances	1,000	1,000
1141	Annual travel costs from the place of employment to the place of origins	60,000	60,000
1144	Fixed local travel allowances		
1149	Other allowances		
1172	Cost of organising traineeships within IMI2 JU	10,000	10,000
1175	Translation and typing services		
1177	Other services rendered	110,000	110,000
1178	Paymaster Office (PMO) fees	70,000	70,000
1180	Sundry recruitment expenses	5,000	5,000
1181	Travelling expenses (including taking up duty)	1,000	1,000
1182	Installation allowance	30,000	30,000
1183	Moving expenses	10,000	10,000
1184	Temporary daily allowance	15,000	15,000
1190	Weightings (correction coefficient)	5,000	5,000

Budget line Chapter	Description	Commitment Appropriations (CA)	Payment Appropriations (PA)
1191	Salaries adaptation		
<b>11</b>	<b>Staff in active employment</b>	<b>5,922,000</b>	<b>5,922,000</b>
1200	Miscellaneous expenditure on staff recruitment	5,000	5,000
<b>12</b>	<b>Staff recruitments - miscellaneous expenditure</b>	<b>5,000</b>	<b>5,000</b>
1300	Mission expenses	144,000	144,000
<b>13</b>	<b>Missions and duty travels</b>	<b>144,000</b>	<b>144,000</b>
1401	EU school costs	120,000	120,000
1410	Other trainings	50,000	50,000
1430	Medical service	20,000	20,000
1440	Trainings covered by the EC service level agreement	30,000	30,000
1490	Other interventions	12,000	12,000
<b>14</b>	<b>Socio-medical structure</b>	<b>232,000</b>	<b>232,000</b>
1500	External staff expenditure	175,000	175,000
<b>15</b>	<b>External staff services</b>	<b>175,000</b>	<b>175,000</b>
1700	Representation expenses	10,000	10,000
<b>17</b>	<b>Representation</b>	<b>10,000</b>	<b>10,000</b>
<b>Total Title 1 (Staff expenditure)</b>		<b>6,488,000</b>	<b>6,488,000</b>

Budget line Chapter	Description	Commitment Appropriations (CA)	Payment Appropriations (PA)
2000	Rentals office building	480,000	480,000
2001	Guarantees		
2002	Contributions		
2010	Insurance		
2020	Charges (water, gas, electricity, works)	208,000	208,000
2030	Cleaning and maintenance		

Budget line Chapter	Description	Commitment Appropriations (CA)	Payment Appropriations (PA)
2040	Furnishing of premises	10,000	10,000
2050	Security and surveillance		
2090	Other expenditure on buildings		
<b>20</b>	<b>Office building and associated costs</b>	<b>698,000</b>	<b>698,000</b>
2101	Hardware, infrastructure and related services	325,000	325,000
2102	Software development, licenses and related services	765,000	765,000
2103	Other expenses maintenance and repair		
<b>21</b>	<b>Information technology purchases</b>	<b>1,090,000</b>	<b>1,090,000</b>
2200	Purchase office equipment	0	0
2201	Rentals office equipment	0	0
2202	Maintenance utilisation and repair	5,000	5,000
2203	Other office equipment		
<b>22</b>	<b>Office equipment (movable property and associated costs)</b>	<b>5,000</b>	<b>5,000</b>
2300	Stationery and office supply	50,000	50,000
2320	Bank charges		
2321	Exchange rate losses		
2329	Other financial charges		
2330	Legal expenses	15,000	15,000
2350	Other operating expenditure	3,000	3,000
2351	Petty expenses		
2360	Library stocks purchase of books and subscriptions	51,000	51,000
2370	Translation, interpretation	5,000	5,000
<b>23</b>	<b>Current administrative expenditure</b>	<b>124,000</b>	<b>124,000</b>
2400	Correspondence and communication expenses	40,000	40,000
<b>24</b>	<b>Telecommunication and postal expenses</b>	<b>40,000</b>	<b>40,000</b>

Budget line Chapter	Description	Commitment Appropriations (CA)	Payment Appropriations (PA)
2500	Formal meetings	80,000	80,000
<b>25</b>	<b>Expenditure on formal meetings</b>	<b>80,000</b>	<b>80,000</b>
2600	Administrative costs in connection with operational activities	30,000	30,000
2601	Events targeting IMI projects		
2602	Workshops	220,000	220,000
2603	Knowledge Management		
<b>26</b>	<b>Administrative costs in connection with operational activities</b>	<b>250,000</b>	<b>250,000</b>
2700	External communication	60,000	60,000
2701	Events external communication	200,000	200,000
2702	Material	40,000	40,000
<b>27</b>	<b>External communication, information and publicity</b>	<b>300,000</b>	<b>300,000</b>
2800	Ex-post Audits	200,000	200,000
2801	Studies, consultancy	100,000	100,000
2802	Audit services	55,000	55,000
2803	Accounting services	70,000	70,000
<b>28</b>	<b>Service contracts</b>	<b>425,000</b>	<b>425,000</b>
2900	Evaluation Experts meetings		
2901	Evaluation Facilities		
2902	Evaluations Exploring New Scientific Opportunities (ENSO)		
<b>29</b>	<b>Expert contracts and cost of evaluations</b>	<b>0</b>	<b>0</b>
<b>Total Title 2 (Infrastructure expenditure)</b>		<b>3,012,000</b>	<b>3,012,000</b>

Budget line Chapter	Description	Commitment Appropriations (CA)	Payment Appropriations (PA)	Budget 2023 Amendment 1 Payment Appropriations (PA)	Amended Budget 2023.1 Payment Appropriations (PA)
3000	Implementing the research agenda of IMI1 JU		14,000,000	-6,500,000	7,500,000
3001	IMI1 JU Call 1				
3002	IMI1 JU Call 2				
3003	IMI1 JU Call 3				
3004	IMI1 JU Call 4				
3005	IMI1 JU Call 5				
3006	IMI1 JU Call 6				
3007	IMI1 JU Call 7				
3008	IMI1 JU Call 8				
3009	IMI1 JU Call 9				
3010	IMI1 JU Call 10				
3011	IMI1 JU Call 11				
3012	Exploring New Scientific Opportunities (ENSO) 2012				
3013	Exploring New Scientific Opportunities (ENSO) 2013				
3020	Implementing the research agenda of IMI2 JU		120,000,000	2,500,000	122,500,000
3021	IMI2 JU Call 1				
3022	IMI2 JU Call 2				
3023	IMI2 JU Call 3				
3024	IMI2 JU Call 4				
3025	IMI2 JU Call 5				
3026	IMI2 JU Call 6				
3027	IMI2 JU Call 7				
3028	IMI2 JU Call 8				
3029	IMI2 JU Call 9				
3030	IMI2 JU Call 10				



Budget line Chapter	Description	Commitment Appropriations (CA)	Payment Appropriations (PA)	Budget 2023 Amendment 1 Payment Appropriations (PA)	Amended Budget 2023.1 Payment Appropriations (PA)
3031	IMI2 JU Call 11				
3032	IMI2 JU Call 12				
3033	IMI2 JU Call 13				
3034	IMI2 JU Call 14				
3035	IMI2 JU Call 15				
3036	IMI2 JU Call 16				
3037	IMI2 JU Call 17				
3038	IMI2 JU Call 18				
3039	IMI2 JU Call 19				
3040	IMI2 JU Call 20				
3041	IMI2 JU Call 21				
3042	IMI2 JU Call 22				
3043	IMI2 JU Call 23				
3100	Implementing the research agenda of IHI JU	8,282,600	75,400,000	4,000,000	79,400,000
3101	IHI JU Call 1				
3102	IHI JU Call 2				
3103	IHI JU Call 3				
3104	IHI JU Call 4	81,897,400			
3105	IHI JU Call 5	115,000,000			
3900	Evaluations experts	600,000	600,000	0	600,000
3999	Recovery Ex-post audit				
<b>30-C1</b>	<b>Implementing the research agenda of IHI JU</b>	<b>205,780,000</b>	<b>210,000,000</b>	<b>0</b>	<b>210,000,000</b>

<b>C2</b>	<b>C2 Appropriations reactivated</b>	<b>C2 - Commitment Appropriations (CA)</b>	<b>C2 - Payment Appropriations (PA)</b>
3000	Implementing the research agenda of IMI2 JU (FP7)	100,000	
3020	Implementing the research agenda of IMI2 JU (H2020)	50,000	
3104	IHI JU Call 4	1,452,600	
<b>30-C2</b>	<b>Implementing the research agenda of IHI JU</b>	<b>1,602,600</b>	<b>0</b>
<b>Total Title 3 (Operational expenditure)</b>		<b>207,382,600</b>	<b>210,000,000</b>
<b>Total expenditure</b>		<b>216,882,600</b>	<b>219,500,000</b>

## 6 Annexes

### 6.1 IKAA Plan for 2023

The IKAA Plan shall contain additional activities expected to be carried out by IHI JU private members, their constituent or affiliated entities. It shall be composed of two types of additional activities:

- Project-specific additional activities contribute towards the achievement of objectives of the IHI JU funded projects, or the dissemination, sustainability, or exploitation of IHI JU project results.
- Programme-specific additional activities contribute to the uptake of results from funded projects (by IHI JU or its preceding initiatives, i.e. IMI1 JU or IMI2 JU) or have a significant added value for the Union.

Project-specific additional activities related to grants signed of call 1 amount EUR 15,023,959 and are reflected in the IKAA Plan available on the IHI JU website [here](#).

Project-specific additional activities related to projects selected under the IHI JU call 2 and 3 amount respectively EUR 1,127,000.00 for call 2 and EUR 5,589,966 for IHI JU call 3. The concerned additional activities shall be formally included in the IKAA Plan during 2023 after the respective grant agreements are signed and subject to a separate GB decision before publication on the IHI JU website.

There will be no project-specific additional activities for 2023 related to projects to be selected under the IHI JU call 4 as the full proposals submission stage is expected in 2024.

Programme-specific additional activities expected to be carried out in 2023 by IHI JU private members, their constituent and affiliated entities are identified in the IKAA Plan below.

OVERVIEW ESTIMATED IKAA FOR YEAR 2023					
Additional Activities type	Description of the Additional Activities	Link to JU objectives [1]	Link to JU project/ topic (if applicable)	Estimated <u>annual</u> value (in EUR)	Estimated <u>total</u> value (in EUR)
<b>Support to additional R&amp;I</b>					
Support to public-private partnership cooperation	<b>Facilitating data sharing in precompetitive projects:</b> User-friendly online IMI/IHI Data Sharing Playbook to facilitate data sharing including solutions, good practice, workflows, and document templates, etc. (consultancy support, time, workshops)	General objective c	IMI2 projects with data-sharing dimension, including but not limited to ND4BB projects	10,000	100,000
Support to public-private partnership cooperation	<b>Science and technology watch and building cross sector understanding and integration</b> to increase the impact of projects and enable deployment of results: desk research, workshops	Specific objective b	n.a	10,000	25,000
Complementary research and innovation activities with a clear link to the Strategic Research and Innovation Agenda but not funded by Horizon Europe	<b>Complementary research activities focused on the uptake of results from the IMI CARE project:</b> One of the goals of the CARE project is the development of therapeutics to address the current and/or future coronavirus outbreaks. To identify potential antiviral drugs, more than 800,000 compounds in various assays were screened. These screening efforts resulted in numerous hits and hit series that are being evaluated under the umbrella of the CARE project. One chemical series is further being developed internally.	General objectives a and b	IMI2 CARE	2,707,150	5,000,000

<sup>57</sup> The IKAA Plan 2023 includes only potential programme-specific additional activities expected to be carried out by IHI JU private members, their constituent and affiliated entities in 2023. It does not include project-specific additional activities. The IKAA Plan including project-specific additional activities for the grants signed of Call 1 is available at [here](#). The IKAA Plan (project and programme levels) may be subject to modification following a separate GB decision in 2023. The updated IKAA Plan will be available on the IHI JU website [here](#).

OVERVIEW ESTIMATED IKA FOR YEAR 2023					
Additional Activities type	Description of the Additional Activities	Link to JU objectives [1]	Link to JU project/ topic (if applicable)	Estimated <u>annual</u> value (in EUR)	Estimated <u>total</u> value (in EUR)
	These additional activities complement the other activities, e.g. the development of mAbs, performed under the IMI CARE project to accelerate the development of a potential COVID-19 treatment, contributing to the world's response to the current COVID-19 outbreak, and ensure we are better prepared for further coronavirus outbreaks in the future.				
Complementary research and innovation activities with a clear link to the Strategic Research and Innovation Agenda but not funded by Horizon Europe	<p><b>Complementary activities focused on the uptake of results from the IMI EBOVAC Programme:</b></p> <p>In support of the Janssen Ebola vaccine licenses (Ervebo and Mveabea licenses) Janssen is continuing the research and development efforts. These activities add on to the work performed on the IMI Ebovac1-2-3 projects to ensure the future manufacturing of Ebola vaccine supplies can be maintained. This also includes EMA post marketing commitments, lifecycle management activities, and process development optimizations</p>	General objectives a and b	IMI2 EBOVAC3	967,748	3,000,000
Complementary research and innovation activities with a clear link to the Strategic Research and Innovation Agenda but not funded by Horizon Europe	<p><b>Complementary research activities focused on the uptake of results from the IMI ESCULAB project:</b></p> <p>The IMI ESCULAB envisages the screening of a shared compound collection on a set of novel targets owned by the various consortium members. Each consortium member screens a number of unique targets during the project and (if successful) identifies a number of active hit compounds / lead series of compounds, suitable for further development.</p>	General objectives a and b	IMI2 ESCULAB	440,000	880,000

OVERVIEW ESTIMATED IKA FOR YEAR 2023					
Additional Activities type	Description of the Additional Activities	Link to JU objectives [1]	Link to JU project/ topic (if applicable)	Estimated <u>annual</u> value (in EUR)	Estimated <u>total</u> value (in EUR)
	Such further development activities are no longer part of the project, and occur outside or after the project. Further chemistry investigation into the lead series, synthesizing additional compound analogues to improve the activity, SAR and profile of the compound, to come to an Optimized Lead or even NME candidate, and the biological and in-vitro ADME-TOX evaluation of these additional or improved compound analogues, including secondary and tertiary in-vitro or in-vivo activity evaluation on the disease target.				
Complementary research and innovation activities with a clear link to the Strategic Research and Innovation Agenda but not funded by Horizon Europe	<b>Research and innovation activities supportive of PPP projects in EU.</b> Optimization of clinical trial design and recruitment. Developing and implementing strategies to maximize patient engagement and incorporation of patient preferences in trial design and data sharing.	General objective a	IMI2 Trials@Home, FACILITATE, EHDEN, H2O, SISAQOL and other IMI2 projects	458,000	458,000
Complementary research and innovation activities with a clear link to the Strategic Research and Innovation Agenda but not funded by Horizon Europe	<b>Uptake of results of IMI2 project RESCEU:</b> Support to the sustainability of the biobank of the IMI2 RESCEU project (Respiratory syncytial virus consortium in Europe)  <i>Additional activity planned by two private members.</i>	Specific objectives a and b	IMI2 RESCEU	36,666	36,666

OVERVIEW ESTIMATED IKAA FOR YEAR 2023					
Additional Activities type	Description of the Additional Activities	Link to JU objectives [1]	Link to JU project/ topic (if applicable)	Estimated <u>annual</u> value (in EUR)	Estimated <u>total</u> value (in EUR)
Complementary research and innovation activities with a clear link to the Strategic Research and Innovation Agenda but not funded by Horizon Europe	<p><b>Uptake of results of IMI2 project PharmaLedger</b> by supporting the PharmaLedger Association (PLA), which is a global not-for-profit association founded as a result of the IMI2 project PharmaLedger. The association provides an open-source platform as framework to help support collaborative innovation in a healthcare Digital Trust Ecosystem, putting patients first and creating added value for all ecosystem members.</p> <p><i>Additional activity planned by four private members.</i></p>	Specific objectives a and b	IMI2 Pharmaledger	751,000	1,751,000
Complementary research and innovation activities with a clear link to the Strategic Research and Innovation Agenda but not funded by Horizon Europe	<p><b>Uptake of results of IMI2 project GetReal</b> by supporting the GetReal Institute, a non-profit entity built on the success of two IMI projects (Get Real and The GetReal Initiative) and which facilitates the adoption and implementation of real-world evidence in health care decision-making in Europe by e.g.; organizing meetings; clarifying scientific and operational uncertainties in real-world evidence approaches and methods; emphasizing best practices; developing translational means to implement best practices; designing and executing educational activities; and conducting scientific research projects.</p> <p><i>Additional activity planned by four private members.</i></p>	Specific objectives a and b	IMI2 GetReal Initiative	166,000	254,000

OVERVIEW ESTIMATED IKAA FOR YEAR 2023					
Additional Activities type	Description of the Additional Activities	Link to JU objectives [1]	Link to JU project/ topic (if applicable)	Estimated <u>annual</u> value (in EUR)	Estimated <u>total</u> value (in EUR)
Complementary research and innovation activities with a clear link to the Strategic Research and Innovation Agenda but not funded by Horizon Europe	<p><b>Additional Analyses to research influenza vaccine effectiveness maintaining and using the IMI2 project DRIVE Database:</b></p> <p>Support to the sustainability and accessibility of the DRIVE Database, publication and website of the IMI2 DRIVE project (Development of Robust and Innovative Vaccine Effectiveness).</p> <p>The DRIVE Database consists of the data collected across all Study Sites contributing to the Test Negative Design DRIVE studies, and through the four influenza seasons (2018 -2022). During DRIVE a framework was defined to support the open access of these data for secondary use as described on the DRIVE website: <a href="https://www.drive-eu.org/index.php/governance/open-data/">https://www.drive-eu.org/index.php/governance/open-data/</a>. This allows post-DRIVE research and recognition through transparent data model access.</p>	Specific objective b	IMI2 DRIVE	10,000	10,000
Complementary research and innovation activities with a clear link to the Strategic Research and Innovation Agenda but not funded by Horizon Europe	<p><b>Maintain and improve existing drug safety database from eTransafe project</b> (publicly available database supported with compound data) to improve predictability of safety issues of new lead structures in drug development</p>	Specific objective b	IMI2 eTRANSAFE	40,000	80,000



OVERVIEW ESTIMATED IKAA FOR YEAR 2023					
Additional Activities type	Description of the Additional Activities	Link to JU objectives [1]	Link to JU project/ topic (if applicable)	Estimated <u>annual</u> value (in EUR)	Estimated <u>total</u> value (in EUR)
Complementary research and innovation activities with a clear link to the Strategic Research and Innovation Agenda but not funded by Horizon Europe	<p><b>EMA Scientific Advice for the Virtual Control Group concept of IMI2 project eTRANSAFE</b> with intended broader use / implementation</p> <p>Shared historical animal control group data could be used to construct virtual control groups (VCGs) for toxicity studies. The use of VCGs has the potential of a 25% reduction in animal use by replacing control group animals with existing randomized data. EMA scientific advice is requested for this concept (a side product of eTRANSAFE).</p>	Specific objective e	IMI2 eTRANSAFE	3,000	3,000
Complementary research and innovation activities with a clear link to the Strategic Research and Innovation Agenda but not funded by Horizon Europe	<p><b>Uptake of MELLODDY results.</b> Publication of tools for broader use is intended.</p> <p>Collaboratively trained MELLODDY polypharmacology models (predicting pharmacological and toxicological activities of small molecules), will be implemented in internal decision-making processes defining which candidate drug molecules will be synthesized and tested in in vitro assays.</p> <p>Uptake involves benchmarking with internal data that are produced post MELLODDY model training, identification of predictive model endpoints, structuring of data outputs by target classes and assay types, implementation into internal drug discovery applications, documentation, and publication of tools and results for broader use.</p>	Specific objective b	IMI2 MELLODDY	80,000	80,000

OVERVIEW ESTIMATED IKAA FOR YEAR 2023					
Additional Activities type	Description of the Additional Activities	Link to JU objectives [1]	Link to JU project/ topic (if applicable)	Estimated annual value (in EUR)	Estimated total value (in EUR)
<b>Creating new business opportunities</b>					
Matchmaking between different start-ups, SMEs, participating companies, stakeholders	<b>Sustainability and deployment of project assets:</b> Activities to guide project teams in sustaining their project assets by enabling resource effective (re)use of project outcomes, on a consortium level or within the company (e.g. continued database access, FAIRIFICATION of data, further EFPIA-wide sustainability arrangements, bridging between existing knowledge networks in the field of asset deployment, ...)	General objective a, specific objectives b and d	Entire IMI2 portfolio and upcoming IHI portfolio	610,918	6,109,180
<b>Supporting ecosystem development</b>					
Activities to develop the ecosystem at EU/national/regional or international level that will enable or accelerate the development of the solutions from the partnership	Europe-wide industrial engagement with stakeholders in rare diseases and ATMPs, with a focus on regulatory frameworks and active participation of SMEs within the project objectives linked to accelerated development of ATMPs.	General objectives a and c	n.a	30,000	120,000
<b>Communication, dissemination, awareness raising, citizen engagement</b>					
Knowledge building in the specific area and/or among stakeholders community	<b>Analysis of IMI projects regulatory science impact,</b> including mapping of IMI projects against EMA regulatory science research needs.	Specific objective b	Relevant IMI projects need to be mapped	30,000	40,000

OVERVIEW ESTIMATED IKAA FOR YEAR 2023					
Additional Activities type	Description of the Additional Activities	Link to JU objectives [1]	Link to JU project/ topic (if applicable)	Estimated <u>annual</u> value (in EUR)	Estimated <u>total</u> value (in EUR)
Organisation of conferences and webinars on specific topics, networking events	<b>Workshop with stakeholders to explore facilitate deployment and upscaling of results</b> such as digital technologies and dissemination activities to put the IMI Scaling Up Field Manual into practice.	General objective b, specific objectives b and e	n.a	5,000	10,000
Investment in societal uptake and citizen engagement	<b>Mapping and analysis of impact projects</b> related to modernisation and patient centricity of clinical trials and to optimisation of health outcomes + communication/dissemination activities.	Specific objectives b, d and e	IMI clinical trials projects	160,000	170,000
<b>TOTAL ALL PLANNED IKAA</b>				6,515,482	18,126,846

[1] IHI JU's general and specific objectives are defined in Articles 115 of the Council Regulation (EU) 2021/2085

## 6.2 IHI JU call 4

### Topic 1: Expanding translational knowledge in minipigs: a path to reduce and replace non-human primates in non-clinical safety assessment

#### Expected impacts to be achieved by this topic

EU legislation<sup>58</sup> makes it a legal obligation to replace, reduce and refine the use of animals in research (the '3Rs' principle), including a specific focus on restricting the use of the non-human primates (NHPs) unless scientifically justified. The development of *in vitro* models for human safety assessment is still challenging due to complex biological responses in various organ systems following drug treatment. Therefore, laboratory animals will still be requested in the safety testing of new therapeutics and innovative medical technologies until non-animal approaches have reached the necessary level of maturity and validation to ensure that only safe treatments reach patients, and that patients get timely access to the most innovative therapeutics.

A substantial amount of work has already been conducted to increase the scientific knowledge and understanding of the role of minipigs in toxicity testing<sup>59</sup> and the pig is often used e.g., in the toxicological evaluation of small molecules. Replacing NHPs with minipigs in the safety testing of new therapeutic modalities has been, however, more difficult, due to the lack of translational knowledge, but will be an important ethical step towards minimising the use of NHPs. New drug modalities are often designed to engage human targets with high specificity, which is the rationale for selecting NHPs in the safety testing of this kind of drug candidates. By expanding the translational knowledge in minipigs versus NHPs and humans, the scientific justification for selecting pigs as an alternative to NHPs can be improved.

The project funded under this topic adheres to the principles of the 3Rs by: i) closing the current translational knowledge gaps regarding minipigs versus NHPs and humans, offering the opportunity to replace NHPs with pigs, improve the reproducibility of pig studies, and advance the underlying knowledge of biological processes to facilitate the development of non-animal alternatives (reduce, refine and replace); ii) creating scientific and technological opportunities in animal housing facilities to collect, digitalise and generate more reproducible data in freely moving, undisturbed animals with the potential to reduce the total number of animals, and improve animal welfare and data quality (reduce, refine).

Closing the translational knowledge gap regarding minipigs versus NHPs and humans will enable the development of new, refined, and digital research tools, which will contribute to:

- reducing and replacing the overall number of NHPs in research without compromising human safety.
- improving disease understanding that will open up new research pathways, and enhanced use of non-invasive digital technologies that can improve animal welfare (refinement), and furthermore, are potentially applicable to humans.
- improving the sustainability and quality of biomedical research and development (R&D) in areas of unmet medical need by ensuring access to well-characterised minipig models in R&D of new therapeutics and innovative medical technologies.

<sup>58</sup> DIRECTIVE 2010/63/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 22 September 2010 on the protection of animals used for scientific purposes; <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32010L0063>

<sup>59</sup> The RETHINK project on minipigs in the toxicity testing of new medicines and chemicals: Conclusions and recommendations. <https://doi.org/10.1016/j.vascn.2010.05.008>

- optimising knowledge sharing between academia, regulators, and the health care industry to accelerate the generation of knowledge and medical innovation.
- fostering the development and validation of non-animal models and approaches by implementing translational data obtained in the future project, which could pave the way to such models. Data generation will be based on early discussions with regulatory authorities and academic partners, thereby ensuring the contribution to the development and validation of non-animal approaches.

### Expected outcomes

- Obtain and share biological knowledge of minipigs, thereby facilitating the development of innovative solutions by improving the translational understanding between minipigs *versus* NHPs and humans, including further understanding of the minipig immune system, with the overall aim to replace, reduce and refine the use of animals in non-clinical safety assessment.
- A regulatory pathway for nonclinical safety assessment of biologicals and other new therapeutic modalities in minipigs with the potential to impact regulatory strategies.
- Publicly available databases and software for physiological, genomic, transcriptomic, metabolomic, proteomic and epigenetic minipig data to understand underlying mechanisms of disease/toxicities and find new mode of actions for pharmaceutical interventions.
- Characterised and validated genetically modified minipig models:
  - genetically modified minipig models based on the CRISPR/Cas9 gene-editing technology.
  - minipigs with 'humanised' immune system components and effectors for testing biologicals.
  - small-sized micropig for efficacy/safety assessment to facilitate compound availability in pharmaceutical R&D.
- Assessment of the utility of the minipig as a relevant toxicology species for immuno-safety testing using therapeutics which have been tested preclinically and clinically. Assisting and synergising the already existing translational and regulatory efforts related to immunological safety evaluation. Developing validated antibodies and *in vitro* immunoassays to characterise the immune system and assess the immuno-safety of therapeutics in minipigs.
- Minipig-specific technology for automated study data: validated medical devices, biosensors, algorithms, software, and digital animal housing. Machine learning and artificial intelligence (AI)-based tools to monitor abnormalities in behaviour and physiological systems in undisturbed animals.

To ensure long-term sustainability, all the interdisciplinary science-based knowledge obtained and generated in the project arising from this topic will be shared, integrated, digitalised, and published in peer-reviewed journals, encouraging industry and academia to develop innovative medical science solutions and technologies, such as scientifically and ethically sound animal models, assays, biomarkers, monitoring devices, biosensors for normal physiological behaviour, and algorithms. Based on the close collaboration with regulatory bodies, the knowledge generated in the project is further expected to impact regulatory guideline strategies. All outputs will require long-term sustainability and maintenance to fulfil the scope of the project.

## Scope

### **Challenges**

- Increasing need to find alternatives to testing in NHPs in line with EU legislation.
- Almost no precedence in minipig use for safety testing of biologicals and new therapeutic modalities [e.g., oligonucleotides, small interfering RNAs (SiRNAs), crystallisable fragments (Fcs), antigen-binding fragments (Fabs), single-chain variable fragments (scFvs), monoclonal antibodies (mAbs), vaccines, gene-editing and cell-based therapies].
- Lack of scientific knowledge to scientifically justify a de-selection of NHPs in the non-clinical safety assessment of new therapeutics. Lack of public minipig reference 'omics' with good quality annotation: Full genome sequencing, in parallel with baseline transcriptomics, proteomics, metabolomics and epigenetic information.
- Lack of 'humanised' and genetically modified models available for efficacy/safety testing, including genetically modified smaller micropigs to address cases of limited substance supply.
- Significant knowledge gap on the minipig immune system and reduced number of laboratory tools and reagents when compared to other toxicology species (rodent and non-rodent).
- Lack of widespread use of biosensors, medical devices, 'intelligent' animal housing for automated data collection and analysis in minipig studies.

### **Objectives**

The overall objective of this topic is to characterise the minipig for use in R&D of new therapeutics and innovative medical technologies. The knowledge generated in this proposal may facilitate innovative health solutions and improve disease understanding and human predictions. The goal is to advance biomedical R&D by generating background scientific data to evaluate if the minipigs could be a viable and feasible alternative to NHPs in key therapeutic areas, with a special focus on translatability from minipigs to humans.

### **Key activities**

- Compile and publish existing historical safety data in minipig biomedical R&D and discuss data with regulators.
- Evaluate the translatability of minipigs in human risk assessment following treatment with biologicals and new therapeutic modalities, and discuss future perspectives of the minipigs with regulatory agencies, e.g., by requesting regulatory interactions with European Medicines Agency (EMA) such as scientific advice and/or novel methodology qualification advice to understand possible regulatory hurdles in using minipigs for safety assessment.
- Minipigs multi-omics and imaging: Generate omics reference data (genomics, transcriptomics, proteomics, metabolomics, and epigenetic information) to enable translational research in minipigs. To further characterise the minipig, imaging technologies such as magnetic resonance imaging (MRI), computed tomography (CT) scans and positron emission tomography (PET) scans are also of interest.
- Genetically modified pig models including the micro-pig: Characterise and validate humanised and genetically modified minipig models, including the micropig to generate translatable animal models in non-clinical safety assessment.

- iPig: Digital technologies, clinical data collection and AI: Create, validate, qualify, and benchmark digital solutions that can objectively measure clinically relevant and functional biomarkers in minipigs for use in preclinical toxicity studies in line with the regulatory agencies' requirements.
- Minipig immune system: validate reagents, assays, and biomarkers for immunological investigations: Conduct investigative studies in minipigs to support their translational significance in immuno-safety assessments and validate reagents/assays.
- Project management: Compile, digitalise, and publish existing and newly-produced data.

### Why the expected outcomes can only be achieved by an IHI project

Generating and compiling comprehensive and complex biomedical datasets within various therapy areas, some of which will be for AI purposes, requires the involvement of multidisciplinary skills across several industry sectors (pharmaceuticals, medical technologies, biotech, vaccines, etc.) including small and medium-sized Enterprises. Previous examples of precompetitive public-private projects (SAFE-T and eTRANSAFE) within the Innovative Medicines Initiative (IMI) and private multi-company initiatives (such as BioCelerate) demonstrated the value of a neutral broker to facilitate precompetitive sharing of proprietary information. Expanding such collaborations beyond one sector to integrate tools, data and know-how from the technology and biotechnology sectors, and joining forces with academic partners from various sectors in unprecedented collaborations, requires exploring new precompetitive grounds and calls for this neutral brokerage to continue.

The involvement of regulatory authorities at all stages of the project generated by this topic is essential considering its objective to develop alternatives that can be used to generate data for regulatory purposes. Close collaboration will contribute to accelerating the development of new knowledge; align validation processes with regulatory requirements; and ultimately, lead to the implementation of new solutions in regulatory practice and their deployment in research practice.

### Pre-identified industry consortium and contributing partner(s)

The pre-identified industry consortium that will contribute to this cross-sectoral IHI proposal is composed of the following industry partners:

Pharmaceutical/biotech/vaccine companies:

- Bayer
- Boehringer Ingelheim
- Bristol Myers Squibb
- Lundbeck
- Merck KGaA
- Novo Nordisk (Lead)
- Novartis
- Pfizer
- Roche
- Sanofi

Other companies:

- LabCorp
- Charles River

In addition, the following contributing partners will participate to the IHI project:

- VeriSim Life
- JDRF

In the spirit of partnership, and to reflect how IHI two-stage call topics are built upon identified scientific priorities agreed together with a number of proposing industrial beneficiaries, it is envisaged that IHI proposals and projects may allocate a leading role within the consortium to an industrial beneficiary. Within an applicant consortium discussing the full proposal to be submitted for the second stage, it is expected that one of the industrial beneficiaries may become the coordinator or the project leader. Therefore, to facilitate the formation of the final consortium, all beneficiaries are encouraged to discuss the weighting of responsibilities and priorities with regards to such leadership roles. Until such roles are formalised by execution of the Grant Agreement, one of the proposing industrial leaders shall facilitate as project leader an efficient drafting and negotiation of project content and required agreements.

### Indicative budget

The maximum financial contribution from IHI is up to EUR 8 500 000.

The indicative in-kind contribution from industry partners is in total EUR 8 910 000.

The indicative in-kind and financial contribution from IHI JU contributing partners is EUR 492 000.

Due to the global nature of the participating industry partners, it is anticipated that some elements of the contributions will be in-kind contributions to operational activities from those countries that are not part of the EU nor associated to the Horizon Europe programme.

The indicative in-kind contribution from industry partners may include in-kind contributions to additional activities.

### Indicative duration of the action

The indicative duration of the action is 60 months.

This duration is indicative only. At the second stage, the consortium selected at the first stage and the pre-identified industry consortium and contributing partners may jointly agree on a different duration when submitting the full proposal.

Phase 1: Evaluation of existing minipig data, develop databases, develop bio sensors and algorithms. Data will be published in peer reviewed journals. Knowledge gaps will be identified, and the development of minipig models will be initiated. Molecule selection and investigations for Phase 2 will be planned and slots for the studies will be booked.

Phase 2: Adolescent and adult male and female minipigs will be treated with modalities e.g., oligos, siRNAs, Fcs, Fabs, scFvs, mAbs, vaccines, gene-editing, or cell-based therapies, as an alternative to the current precedence of safety testing in NHPs.

Phase 3: Biomaterial from the minipig studies in Phase 2 will be distributed to various work package members (iPig, multi-omics, immuno-safety) for further evaluation. Mechanisms and translational aspects will be explored.



Phase 4: Database scrutinisation, compile, discuss and distribute new knowledge, publication in peer reviewed journals, propose regulatory recommendations, and promote digital solutions.

## Contribution of the pre-identified industry consortium and contributing partners

The pre-identified industry consortium and contributing partners expect to contribute to the IHI proposal by providing the following expertise and assets:

- Experimental settings: Pharmaceutical drug candidates, drug products, animals including genetically modified animals, animal units, experimental equipment, laboratories.
- Data: access to standard toxicology and clinical safety endpoints, historical data, gene expression, immunosafety biomarkers and assays.
- Expertise: nonclinical expertise, data science, regulatory expertise, immunosafety, 'omics' evaluation, disease models, devices.
- Technology: Standard for Exchange of Nonclinical (SEND) databases and SEND visualisation systems, implants, device software.

The allocation of the EUR 200 000 financial contribution will be decided by the full consortium at the second stage when preparing the full proposal.

## Applicant consortium

### **Public partners:**

- Database constructors: merging large databases from different sectors (various public and industry partners) containing complex biological datasets e.g., genomic, transcriptomic, metabolomic, proteomic and epigenetic data.
- Suppliers of genetically modified minipigs and tissue samples.
- Partners experienced with, and suppliers of, MRI, CT and PET scanning in pigs.
- Academic partners developing and validating biomarkers to ensure human translatability.
- Inventors of technologies for automated digital data collection in patients and pigs: validated medical devices and biosensors to measure normal physiological behaviour.
- Inventors of validated algorithmic tools for machine learning and artificial intelligence for automated digital animal housing and prediction of toxicities in minipig vs. human.
- Inventors of validated antibodies and *in vitro* immunoassays to characterise the immune system and assess immuno-safety of therapeutics in minipigs.
- Project administration with experience in public-private partnerships.

**Regulatory authorities:** Advisors.

## Dissemination and exploitation obligations

The specific obligations described in the Conditions of the calls and call management rules under 'Specific conditions on availability, accessibility and affordability' do not apply.

## Topic 2: Patient-centric blood sample collection to enable decentralised clinical trials and improve access to healthcare

### Expected impacts to be achieved by this topic

Collecting venous blood samples for diagnostic purposes has been the cornerstone for informing patient care and a key element of clinical trials. Ordering a blood draw has become almost a reflex for clinicians and drug developers, however venipuncture is still the traditional way to collect blood. Venipuncture can be painful and requires individuals to see their healthcare provider or visit a clinic. This results in a burden on patients, doctors, healthcare systems, payers, and the pharmaceutical industry. A particularly high burden may be imposed on vulnerable populations such as children and elderly individuals, as it may lead to increased exposure to disease during a pandemic, or to anaemia (e.g. in oncology). Furthermore, the current procedure is too inflexible to allow for ongoing monitoring for treatment, progression, or intervention in decentralised clinical trials and clinical practice [1]. There is a great need for the acceptance and implementation of patient-centric (as opposed to clinic-centric) sampling approaches.

The generation of an infrastructure and logistics for at-home collection of small-volume (less than 500 µl) blood samples ('microsampling') as an alternative to venipuncture for routine central lab analysis will contribute to the following impacts:

- It will deliver a much-improved experience to our patients by decreasing the burden on patients (in particular vulnerable populations) and optimising patient care in Europe.
- It will improve decentralised clinical trials, trials at home, and inclusion trials.
- It will facilitate monitoring for prevention, treatment, and surveillance.

### Expected outcomes

The results of the project generated by this topic will enable innovations in healthcare delivery and research by generating the infrastructure and logistics for blood collection at home, that is simple, minimally invasive, less painful, convenient, and feasible.

Importantly, the project will also provide new insights and enrich information related to the research questions by creating an unprecedented data set that will enable multiple secondary research options for years to come. Notably:

- It will create insights into the public acceptability for microsampling home: are patients comfortable with a new kind of medical technology? What training is necessary?
- Are we able to advance the transition of care from the hospital to the home? Does the care quality improve?
- How do we utilise the higher frequency of data, including its integration with electronic medical records and using advanced analytics methodology?
- Do doctors' practices and decisions change with the increased frequency of biomarker data, and does it lead to better outcomes for the patient?

While integrating existing components for microsample collection and central lab analysis, quality standards for the new infrastructure and logistics will be rigorously and transparently validated and established in Europe and harmonised with parallel ongoing efforts in the USA. The harmonisation will critically enhance the implementation of microsampling in global clinical trials of new therapeutics. The validation and establishment of microsampling at home by patients and/or their caregivers will be undertaken in ways that

are acceptable for patients and their caregivers, health care professionals, regulatory agencies, policy makers, Health Technology Assessment (HTA) experts, payers, and advocacy groups.

## Scope

The overall aim of the project generated from this topic is to create and validate the infrastructure and logistics for blood collection by the patient and/or caregiver at home as a healthcare tool and an alternative to the current gold standard venous blood for routine clinical assays. This project will employ only commercially available CE-marked microsampling devices, according to their intended use.

The development of new devices for blood sampling or of new clinical assays / analytes is not the focus of this project, and no new clinical assays will be evaluated. Similarly, given their current maturity, home sample analysis is out of scope.

Training materials, customised for patients and caregivers as well as for medical personnel will be developed, ensuring the acceptability of the new approach to these groups. Interactions with regulatory authorities, the European Medicines Agency (EMA), local European agencies as well as regulatory agencies from non-EU European countries and the US Food and Drug Administration (FDA) will be sought to advance the regulatory acceptability of the logistics model and harmonisation across the EU, other non-EU European countries and the US. Further, key stakeholders (e.g. policy makers, HTA experts, payers, patient advocacy groups) will be encouraged to implement the infrastructure and logistics throughout Europe. Lastly, the best ways to integrate, transmit, and analyse (including AI) the data generated will be explored. Results will be shared broadly through peer-reviewed publications or other mechanisms.

To be noted – home blood microsampling has been used in geographically restricted pilot projects [2]. With the project generated from this topic, it is expected to generalise them, and leverage the learnings from the pilot projects, to enable broad adoption. Importantly, it is known that patients greatly appreciated this experience compared to the traditional blood sampling methods currently in use.

Applicants should in their proposal address the following:

### **Demonstration of concordance between patient-centric microsampling techniques and venipuncture**

This requires delivery of a framework across Europe for establishing concordance between capillary blood as collected by microsampling devices outside of traditional collection setting by the patient and/or caregiver, versus the gold standard venous blood, for routine clinical assays.

- To generate an umbrella / master protocol that is acceptable for regulatory authorities in EU and non EU-European countries, and can be easily adopted for future applications (e.g. in additional patient populations, countries, by any vendor or organisation). To assure patient-centricity, feedback on the umbrella protocol by patient representatives and caregivers will be sought.

The umbrella / master protocol should include:

- sites in at least 3 EU Member States,
- and may include additional sites in (with at least one in Eastern Europe<sup>60</sup>):
  - third countries associated to Horizon Europe

<sup>60</sup> Armenia, Azerbaijan, Belarus, Georgia, the Republic of Moldova and Ukraine are European countries but not part of the EU ([https://www.eeas.europa.eu/eeas/eastern-europe\\_en](https://www.eeas.europa.eu/eeas/eastern-europe_en)).

Due to the ongoing conflict in Ukraine, the participation of legal entities from Russia or Belarus in Horizon Europe and IHI JU projects is prohibited. [https://research-and-innovation.ec.europa.eu/strategy/strategy-2020-2024/europe-world/international-cooperation/russia\\_en#:~:text=Russian%20researchers%20and%20organisations%20are,various%20EU%20and%20Russian%20funding](https://research-and-innovation.ec.europa.eu/strategy/strategy-2020-2024/europe-world/international-cooperation/russia_en#:~:text=Russian%20researchers%20and%20organisations%20are,various%20EU%20and%20Russian%20funding)

- third countries not associated to Horizon Europe
- **at least** two different types (e.g., finger stick, upper arm capillary) of commercially available CE-marked microsampling devices; for clarity, at least one device should perform liquid blood sampling, the additional devices may collect dried blood;
- routine clinical assays: i.e. blood chemistry, liver and lipid panels;
- collection of at least 50% of microsamples by the patient and/or the caretaker; the other 50% may be taken by hospital or nursing personnel (including remote nurses, e.g., in general practices, or traveling nurses);
- collection of at least 50% of microsamples at home; the project may include collections in other locations (e.g. hospitals, general practitioners, specialists' offices) for concordance testing and establishing microsampling of capillary blood versus venous blood for routine assays.
- To design, adapt, and translate patient-facing materials, obtain ethics board approvals, obtain competent/regulatory authority approvals, recruit healthy human volunteers and expand to a patient population which should be agreed upon in a project committee, collect biological samples and conduct bioanalysis according to the study protocol.
- To investigate potential errors related to the mishandling of samples and design ways to mitigate them, as well as the potentially harmful downstream effects for the individual.
- To conduct concordance analyses according to existing regulatory guidance for routine clinical assays [3], and define sample quality criteria (if applicable).

#### **Validation of the logistics of sample collection and shipping, standardising central lab analysis.**

This requires identification of an optimum workflow for device ordering, fulfilment, shipping, at-home collection and return to central labs and a seamless integration of microsampling into current central lab processes, accessioning, analysis and reporting.

- To select at least two different types of CE-marked microsampling devices and identify and audit device vendors with ordering (portal) and fulfilment capabilities; to work with device vendors on ordering devices.
- To define appropriate shippers/processing/temperature based on the devices and assay requirements, and confirm requisition requirements.
- To identify strategic partners in terms of logistical expertise, e.g. global couriers.
- To identify countries to test devices in and confirm regulatory requirements for self-collections or collections by caretaker and shipping of devices.
- To define the support need for the use of devices and training participants on devices; to identify telehealth partners e.g. for identification verification.
- To identify the best ways to integrate the new data with existing electronic medical records and medical decision frameworks.
- To investigate the 'green dimension' of logistics: microsampling has the potential to reduce the green footprint of office visits and transportation required (fuel, costs, carbon emissions).
- To confirm the accessioning process needed, reporting requirements, and data management model.
- If possible, to assess the cost savings obtained with microsampling methods as compared to gathering blood in the hospital.

## **Education and medical & patient acceptability**

- To deliver training materials for patients, caregivers and clinical trial sites, taking into account the variety of patients' and caregivers' ages, abilities, etc., and ensuring smooth behind-the-scenes shipment logistics and support.
- To develop guidelines for compiling training materials to meet expectations from different training recipients, such as clinical sites, patients, caregivers, telehealth and home health providers, leveraging previous feedback collected from users (patients, caregivers, principal investigators (PIs) and medical personnel), including to develop training by telehealth.
- To develop a plan to collect patient, caregiver and medical personnel (site staff, PIs, trial coordinator) experience and feedback:
  - to develop a well-designed questionnaire that will be used either electronically or in paper format, develop tool(s) to collect feedback and store the information, pilot the use, refine the questionnaire and data base as needed;
  - to implement the questionnaire to collect feedback from different groups (patients and caregivers, medical personnel, regulators, device manufactures);
  - to maintain a database of information collected and perform data analysis to obtain patient acceptability scores;
  - to get insights into research questions related to the implementation of microsampling which are described in 'Expected outcomes' (see above).
- To publish survey results to validate the training and feedback with other patient advocacy groups.

## **Regulatory acceptability and implementation in clinical practice in the EU, other non-EU European countries and the US**

- To prepare an overview of the regulatory landscape of microsampling at home per country in the EU, third countries associated to Horizon Europe, and other European countries, and to conduct an in-depth exploration in those countries that might be suitable for the microsampling logistics modelling.
- To establish an early and continuous dialogue with the European Medicine Agency (EMA) Innovation Task Force, in addition to local regulatory agencies of the EU, and relevant authorities of other non-EU European countries and the FDA:
  - to assess acceptability with regulators and seek prospective input on the umbrella / master protocol, choice of countries and approach to validating the logistics;
  - to discuss the best strategy/timing for qualification and/or integration of project outputs into regulatory practices, prepare relevant documents (e.g. briefing books, guidance document) to share project results, request scientific and qualification advice, and seek a harmonisation with the regulatory agencies from other non-EU European countries and the FDA, which is key to global clinical trials of new therapeutics.
- To interact with policy makers, HTA experts, payers, and advocacy groups to facilitate the implementation of project results in clinical practice throughout the EU, and other non-EU European countries and the US.

## Why the expected outcomes can only be achieved by an IHI project

A joint concerted initiative is required to create a practical implementation path in Europe for patient-centric blood samples in decentralised clinical trials, trials at home, and inclusion trials.

It is essential that industry partners from different sectors, e.g. the pharmaceutical industry, medical device manufactures, *in vitro* diagnostic companies, exchange knowledge and experience and contribute complementary infrastructures. Moreover, collaboration is required with clinical centres that are experienced in conducting decentralised trials, and with academia and SMEs that are experienced in methods and devices for microsampling and data collection and analysis. The engagement of patients, caregivers, and health care professionals is required to ensure the incorporation of the user experience into the novel infrastructure and logistics for patient-centric blood microsample collection at home. Lastly, the involvement of regulators, policy makers, payers, and HTA experts will facilitate the acceptance of the microsampling logistics model.

It is crucially important to develop a harmonised approach that is both acceptable and accessible to all stakeholders in the healthcare systems to ensure implementation across Europe, and this can be best assured under a public-private partnership.

## Pre-identified industry consortium and contributing partners

The pre-identified industry consortium that will contribute to this cross-sectoral IHI project is composed of the following pharmaceutical and medical technology industry partners:

- Astra Zeneca
- Bayer
- Becton Dickinson
- Eli Lilly (Lead)
- Gilead
- GlaxoSmithKline
- Labcorp
- MSD
- Novartis
- Pfizer
- Q2labs solutions
- Roche
- Servier
- Janssen

In addition, the following contributing partners will participate to the IHI project:

- JLL
- Miebach Consulting

In the spirit of partnership, and to reflect how IHI Two-Stage call topics are built upon identified scientific priorities agreed together with a number of proposing industrial beneficiaries, it is envisaged that IHI proposals and projects may allocate a leading role within the consortium to an industrial beneficiary. Within an applicant consortium discussing the full proposal to be submitted for Second Stage, it is expected that one of the industrial beneficiaries may become the coordinator or the project leader. Therefore, to facilitate

the formation of the final consortium, all beneficiaries are encouraged to discuss the weighting of responsibilities and priorities with regard to such leadership roles. Until such roles are formalised by execution of the Grant Agreement, one of the proposing industrial leaders shall facilitate as project leader an efficient drafting and negotiation of project content and required agreements.

### **Indicative budget**

The maximum financial contribution from IHI is up to EUR 4 500 000.

The indicative in-kind and financial contribution from industry partners is EUR 3 574 000.

The indicative in-kind contribution from IHI JU contributing partners is EUR 300 000.

Due to the global nature of the participating industry partners, it is anticipated that some elements of the contributions will be in kind contributions to operational activities from those countries that are neither part of the EU nor associated to the Horizon Europe programme.

The indicative in-kind contribution from industry partners may include in-kind contributions to additional activities.

### **Indicative duration of the action**

The indicative duration of the action is 42 months.

This duration is indicative only. At Second Stage, the consortium selected at First Stage and the predefined industry consortium and contributing partners may jointly agree on a different duration when submitting the full proposal.

### **Contribution of the pre-identified industry consortium and contributing partners**

The industry consortium and contributing partners expect to contribute to the IHI project by providing the following expertise and assets:

#### **Grant administration:**

- To provide legal support for project related tasks.

#### **Clinical trial and medical expertise:**

- To design the protocol of the umbrella / master study.

#### **Technologies:**

- Analytical techniques and sample analysis.
- Microsampling techniques and provision of 1 device for the collection of capillary blood of the finger stick; for clarity, at least one device should perform liquid blood sampling, the additional devices may collect dried blood.
- Relevant samples might be provided.

#### **Logistics:**

- To identify and audit device vendors, logistics and telehealth partners.
- To define acceptable sample quality, collection compliance tests, and shipment requirements ensuring appropriate sample bioanalysis given collection (including at-home collection) and shipment.

- To confirm accessioning processes needed, reporting requirements, and the data management model.

#### **Training materials:**

- Expertise in defining needed support for use of devices, providing guidance in feedback collection and guiding principles for developing training materials for patients, caregivers and healthcare professionals.
- To facilitate user group, technical and compliance Key Opinion Leader (KOL) panel discussions.

#### **Integration of requirements of regulatory authorities, HTA, payers, policy makers, and advocacy groups:**

- To prepare an overview of the regulatory landscape of microsampling at home in Europe.
- To interact with regulatory authorities, HTA, payers, policy makers and advocacy groups to facilitate acceptability of the microsampling logistics modelling and its implementation throughout the EU and harmonization with efforts in other non EU-European countries and the USA.

Furthermore, the industry consortium will help with data flow, data management, operational support for clinical sites, project management, data and knowledge management, and the communication and dissemination of results. It will also provide contributions to joint meetings and steering committees, networking, exploitation and sustainability.

### **Applicant consortium**

The First Stage applicant consortium is expected, in the submitted short proposal, to address the scope and deliver on the expected outcomes of the topic, taking into account the expected contribution from the pre-identified industry consortium and contributing partners.

The applicant consortium is expected to address all the research objectives and make key contributions to the defined deliverables in synergy with the industry consortium. The focus of this project is not on development of novel devices or assays, but on integration of existing innovative technologies to establish the infrastructure and logistics for patient-centric blood microsample collection at home in Europe.

Applicant consortia should bring together partners with relevant expertise such as patients and patient representatives, patient-centric organisations, healthcare professionals, clinical trial centres with experience in decentralised trials, research organisations, and health technology developers. SMEs are encouraged to join the consortium, in particular those with expertise in various methods and devices that enable microsampling. Moreover, the participation is encouraged of SMEs which have expertise in interaction with patient groups, collecting user experience data and prioritising patient care needs, and the development of training materials for patients, caregivers and healthcare professionals. For facilitating acceptability and implementation of the microsampling logistics model across Europe, input from other relevant stakeholders, in particular regulatory agencies, payers, HTA bodies and advocacy groups would be necessary.

Applicants should clearly outline their approach for data capture, storage and sharing within the consortium as well as sharing results through peer-reviewed publications or other mechanisms. They must ensure that the relevant results and data repositories will be sustainable after the end of the project and made public.

This will require mobilising the following expertise and/or resources:

#### **Grant administration:**

- To provide financial administration, submission of deliverables, periodic reports etc.



**Project management:**

- To coordinate internal communication and meetings, general oversight and management of communication, exploitation and dissemination activities, risk management.
- To provide and maintain an IT infrastructure, to develop and implement an efficient data governance and management strategy of the joint consortium according to adequate standards and deliver the “Data Management Plan”.
- To coordinate networking, joint activities and synergies with other European initiatives, or other relevant groups (e.g. patient-centric organisations, advocacy groups).
- To develop a strategy for the exploitation and sustainability of project results and outcomes and deliver the “Exploitation and Sustainability Plan”.

**Umbrella / master study:**

- To obtain the necessary authority approvals, develop participant / patient facing materials, provide recruitment of participants / patients and conduct the umbrella / master study including the collection of biological samples.

**Technologies:**

- To analyse samples according to the protocol.
- To perform statistical evaluations of concordance according to existing regulatory guidance for routine clinical assays.
- To provide microsampling techniques and at least 1 device for the collection of capillary blood of the upper arm.

**Logistics:**

- To develop logistical capability around implementing new technologies for microsampling, work with device vendors on ordering devices, develop protocols for the testing of microsampling devices, act as investigative sites to test devices including Institutional Review Boards (IRB), consents etc., and train participants on devices.

**Training materials:**

- To engage and activate patients, caregivers, clinicians, and hospitals and obtain feedback on the support needed, develop questionnaires to collect their experience, perform data analysis, assess acceptability and concerns, and develop and refine training materials for different recipients.

**Interactions with regulatory authorities, HTA bodies, payers, policy makers, and advocacy groups:**

- To contribute to the regulatory landscape for microsampling at home in the EU and in other non-EU European countries.
- In conjunction with industry, to discuss with regulatory authorities, HTA bodies, payers, policy makers, and advocacy groups the acceptability and implementation of the microsampling logistics modelling in the EU and harmonisation with efforts in other non-EU European countries and the US.
- To prepare relevant documents of the approach and the results being generated by the project (e.g. briefing books, EMA guidance document).

At Second Stage, the consortium selected at First Stage and the predefined industry consortium and contributing partners will form the full consortium. The full consortium will develop in partnership the full proposal, including the overall structure of the work plan and the work packages, based upon the selected short proposal at First Stage.

### **Dissemination and exploitation obligations**

The specific obligations described in the Conditions of the calls and calls management rules under “Specific conditions on availability, accessibility and affordability” do not apply.

### **References**

- 1) Fantana AL, Cella GM, Benson CT, Kvedar JC, The Future of Drug Trials Is Better Data and Continuous Monitoring, Harvard Business Review, 2019 <https://hbr.org/2019/05/the-future-of-drug-trials-is-better-data-and-continuous-monitoring>
- 2) Wickremsinhe ER, Fantana AL, et al. Standard Venipuncture Versus a Capillary Blood Collection Device for the Prospective Determination of Abnormal Liver Chemistry. JALM 2022 (accepted for publication).
- 3) CLSI. Measurement Procedure Comparison and Bias Estimation Using Patient Samples. CLSI guideline EP09c, Wayne, PA: Clinical and Laboratory Standards Institute; 2018.

## Topic 3: Inclusive clinical studies for equitable access to clinical research in Europe

### Expected impacts to be achieved by this topic

The following impacts are expected:

- Awareness and understanding of what diversity, under-represented and underserved communities look like in geographies across Europe, including barriers and gaps to recruitment and retention in different types of clinical research, such as clinical studies<sup>61</sup> on medical products, clinical investigations for medical devices, and performance studies in *in vitro* diagnostics (IVDs), cohorts, and registries.
- Enhanced representativeness of underserved populations in clinical studies across Europe, through the building of a patient-centric, sustainable infrastructure that improves the recruitment and retention of these patients.
- Increased study data reliability and genetic diversity by including different demographic groups, thereby enhancing patient trust in the evidence generated. More patients benefit from increased access to improved innovative health technologies including medicinal products and medical devices that meet the specific needs and profiles of all patient populations.
- Promoting the implementation of new tools, solutions, approaches, or process models that will reduce the burden of clinical studies and facilitate and increase diverse patient populations' access to clinical studies.
- Contribution to the Accelerating Clinical Trials in the EU<sup>62</sup> (ACT-EU) objectives to proactively deliver inclusive patient-oriented medicines development and delivery across populations.

### Expected outcomes

The research and innovation (R&I) action (project) to be supported under this topic should aim to deliver results that contribute to all of the following expected outcomes.

- Researchers, including industry stakeholders, clinical investigators and healthcare providers, strengthen the understanding, through use cases, of the impact of study design/protocols and study conduct on patient recruitment/retention that will help future clinical studies. These stakeholders will also benefit from gaining clarity on what clinical study diversity means in Europe, especially considering the emerging guidance from the US Food and Drug Administration (FDA) on clinical trial diversity in the US.
- Patients will benefit from a sustainable, easy-to-use digital platform, built with input from patients and/or patient support organisations, enabling more underserved patients to identify clinical studies that they are eligible for. Investigators/sites would be able to locate patients for ongoing clinical studies. This will benefit both recruitment and retention of underserved patients as it will act as a match-making portal that

<sup>61</sup> Clinical study EC definition as per Horizon Europe information on clinical studies template: Clinical study covers clinical studies/trials/investigations/cohorts and means, any systematic prospective or retrospective collection and analysis of health data obtained from individual patients or healthy persons in order to address scientific questions related to the understanding, prevention, diagnosis, monitoring or treatment of a disease, mental illness, or physical condition. It includes but it is not limited to clinical studies as defined by Regulation 536/2014 (on medicinal products), clinical investigation and clinical evaluation as defined by Regulation 2017/745 (on medical devices), performance study and performance evaluation as defined by Regulation 2017/746 (on *in vitro* diagnostic medical devices).

<sup>62</sup> [https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/accelerating-clinical-trials-eu-act-eu-delivering-eu-clinical-trials-transformation-initiative\\_en.pdf](https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/accelerating-clinical-trials-eu-act-eu-delivering-eu-clinical-trials-transformation-initiative_en.pdf)

will be accessible to all sponsors (including academics/investigator-initiated trials, industry, etc.), and provide patient support to enable patients to allay their concerns in a timely manner, increasing their knowledge/education and building trust toward clinical research

- Researchers, including industry stakeholders, sponsors, clinical investigators, clinical research organisations, healthcare providers and patients/caregivers benefit from a toolbox of new approaches, tools, solutions and best practice approaches to facilitate and increase patient recruitment and retention, to better design and conduct clinical studies including adaptive designs, registry studies and decentralised studies with a particular focus on under-represented and underserved patient populations in Europe. Taking account of regulatory requirements, this will lead to more effective clinical studies with an increased recruitment/retention of diverse patient populations that is supported by a community-informed approach.
- Increasing population representativeness also better reflects real-world patients and helps the generalisability of the study findings, leading to better innovations. This is a positive outcome for all patients (not just underserved patients). Targeted under-represented and underserved patient populations have increased trust in clinical studies, which helps to overcome recruitment, participation, and retention challenges through educational programmes, public outreach, and community outreach/engagement.
- Clinical investigators, clinical sites and existing clinical networks benefit from cultural competency and educational training to better engage with diverse populations. New investigators from underserved communities will benefit from inclusion in clinical studies.
- The pool of clinical sites with access to diverse clinical research staff that can facilitate the education, recruitment, and retention of diverse populations in clinical studies is broadened.
- Community-based sites and organisations are better engaged to provide input on the conduct of clinical studies and to promote diversity in patient populations through inclusive enrolment practices.
- Regulators, health technology assessment bodies and payers benefit from better information on health technologies including medicinal products, medical devices benefit-risk profile across the patient populations for use in clinical practices.
- Data standards established in agreement with regulators. Standardisation of data standards for demographic descriptors across sponsors such as race, ethnicity, gender, sex, and other selected diverse factors for the defined underserved and under-represented populations are essential for consistent reporting and valid demographic measurement.

## Scope

Patient recruitment and retention remains a leading challenge in the efficient completion of clinical studies, including studies on medicinal products, medical devices, or IVDs. Furthermore, despite advancement of enrolment practices designed to better reflect the population most likely to use the health technologies in clinical practice, there is still only limited diversity within recruited patient populations. The under-representation of diverse populations (due for instance to their race and ethnicity, gender, age, socio-economic status, geographical location) creates knowledge gaps about the risks and benefits of health technologies for these specific populations.

This topic aims to develop a multi-faceted, intersectional approach to overcome the multifactorial barriers associated with the recruitment and retention of underserved patient populations in clinical studies and to contribute to transforming the way clinical studies are conducted in Europe.

To fulfil this aim, the following activities around the defined themes should be addressed.

## **Landscape**

- Agree a definition of “underserved” populations in Europe with regulators, that includes populations facing socio-economic, systemic, or cultural barriers that prevent equitable access to clinical studies. This may be broader than populations currently defined in the demographics that sponsors collect, such as age, sex, gender, race, and ethnicity. This could include rural populations, refugees, homeless, illiterate, disabled people, and those belonging to minority populations.
- Estimate the current participation of diverse study populations in clinical studies differentiated by success in recruitment and retention; identify and evaluate the factors that contribute to and limit existing initiatives to increase diversity of recruitment and retention in clinical studies.
- Define and develop country-, social- and culture- specific understanding of factors driving under-representation and underserved populations in Europe. Shape the development of guidance on how to reach and retain underserved populations in clinical studies in different settings and countries, and how to collect data in a GDPR<sup>63</sup>-compliant fashion across Europe.
- Establish a sustainable patient-centric digital platform (open to all sponsors) connecting the patients, patient support organisations, sponsors, and investigators at different sites (including in community settings, hospitals, primary physicians, etc). To ensure patient engagement, the platform should use lay language and make use of existing resources such as ClinicalTrials.gov information; patient support information developed by patient organisations, or Clinical Trials Information System (CTIS). This is important to ensure that the patient/community engagement activities undertaken lead to patients being directed to use the platform, leading to an improvement in participation of diverse patients. The needs of underserved populations with access barriers to digital platforms or language barriers should be considered.
- Define the governance structure and maintenance/ownership of the platform. The active involvement of underserved patients / patient representatives is expected in the planning and development of the platform, as well as governance activities.
- Understand the interface between international, regional, and local approaches from a patient-centricity perspective (while the strategies may need to be developed and implemented locally, they will be part of multi-regional/multi-country clinical studies conducted by sponsors).

## **Protocol design and clinical operations**

- Establish criteria for measuring ‘representativeness’, i.e. patients enrolled in the trial represent the prevalence of the disease in different sub-populations. For example:
  - Representation: age, sex, gender, race, ethnicity (measured against prevalence).
  - Inclusion: socioeconomic status, rural vs. urban access, sexual orientation, disability, payer status (private vs public), pregnancy/lactation status, etc.
- Identify and assess existing tools and solutions for patient recruitment and retention that could be used for recruitment and retention of a diverse population from a European perspective. Develop a set of

<sup>63</sup> General Data Protection Regulation

suitable tools, solutions, and strategies applicable for different types of clinical studies, including studies with medicinal products, medical devices, or IVDs.

- Identify and review aspects of study design such as narrow eligibility criteria, methodological approaches, logistical and other patient-related factors that could limit broader patient and communities' engagement, taking account of regulatory requirements; define recommendations for best practices.
- Explore and validate approaches that improve access, participation, recruitment, and retention of diverse patient populations, including innovative technology solutions, clinical research methodologies (e.g., adaptive, home based/hybrid), leveraging real world data sources etc.

### **Community engagement**

- Raise awareness, develop educational activities and inclusive toolkits to increase knowledge and trust of target populations towards clinical studies to overcome recruitment, participation, retention challenges and to enable early patient engagement.
- Develop targeted activities to foster community engagement and build trust with patients.
- Establish connections between different stakeholders in the community e.g. researchers, industry stakeholders, patients, caregivers, investigators, and healthcare providers.

### **Investigators / clinical sites**

- Build new site capabilities and develop training activities to increase the number of community-based sites and expand the pool of investigators, including investigators from under-represented communities and naïve investigators, to set them up in geographies where the infrastructure is missing.
- Create the necessary support mechanisms and define specialised training e.g. cultural competency training, naïve investigator training, etc. through existing clinical networks, medical institutions, patient organisations and community-based organisations. Existing resources such as Clinical Trials Transformation Initiative (CTTI), or other projects such as IMI (Innovative Medicines Initiative) projects connect4children (c4c) and EUPATI can be leveraged.

To ensure the applicability of the solutions/tools/recommendations, the applicants should test them in pilot use cases, which will be determined during the project based on the availability of cases from sponsor companies and in discussion with the consortium, in one or more disease areas of choice. The proposed disease areas should constitute an unmet public health need and a significant burden to patients, healthcare systems and society (e.g. breast cancer, prostate cancer, hypertension, lupus etc). Furthermore, the proposed areas should be representative to allow broad implementation across diverse disease areas, different cultural and geographical distributions, types of clinical research such as clinical studies on medical products, clinical investigations for medical devices, performance studies for IVDs, and studies testing non-pharmacological and rehabilitation interventions.

The purpose of the pilot use cases is to test tools and solutions for patient recruitment and retention, assess the functionality of the digital platform, and test the improvements brought by the digital platform on patient recruitment and retention. The focus will be on testing the robustness of the infrastructure to ensure the solutions put in place are "fit for purpose". The testing could establish the viability of the solutions, for example:

- number of new sites added to the platform;
- number of under-represented investigators trained through this initiative;

- number of investigators that serve underserved patient populations;
- effectiveness of community engagement activities as judged by patient support organisations;
- effectiveness of recruitment and retention activities via the platform, as experienced by investigators and patients;
- analysis of number of users of the platform and the type of content accessed by users.

Applicants are expected to consider the potential regulatory impact of the results and as relevant develop a strategy/plan for generating appropriate evidence, and to engage with regulators in a timely manner (e.g., through the EMA Innovation Task Force, qualification advice).

In their proposals, applicants should leverage and build on existing tools & solutions and best practice experiences that have already been developed at national European and/or international level, including tools developed in IMI/IHI projects.

### Why the expected outcomes can only be achieved by an IHI project

To achieve the transformation outlined above, a broad cross-sectoral collaboration is needed including healthcare professionals to give insights on their experience with the current technology utilisation and act as champions for the new developments, academic researchers, health economists, hospital management, public procurers, technology developers and vendors and patients, who will benefit from the solutions. Integrating data from multiple origins/sources requires the cooperation of data holders, both public and private, in a non-competitive, neutral setting like an IHI project. Improving clinical studies that address patients' needs is of paramount importance for the private and public sector. Recruitment, retention, and the insufficient participation of underserved patient populations in clinical studies are a challenge that the entire health industry faces, including large and small and medium-sized pharmaceutical and medical technology companies. Efforts to tackle those are riddled with complexities such as the geographical complexity (a solution appropriate in one country may be less appropriate in another). In addition, the multitude of healthcare partners in the health ecosystem hinders scalability of initiatives that can be put in place. Cultural barriers also exist that may result in the mistrust of under-represented and underserved patients towards clinical research.

An important paradigm change is needed to succeed in better including under-represented populations, requiring collaboration among stakeholders: patients, caregivers, academia, healthcare practitioners, clinical investigators, industry, sponsors, contract research organisations, regulators, health technology assessment bodies, payers, social scientists, and ethicists, etc. A cross-sectoral and multidisciplinary public-private approach is the only way to harness the insights from key stakeholders, consider all perspectives, and adjust the trajectory in real time. Increasing the recruitment and retention of underserved patient populations is a multistakeholder effort and the IHI provides the framework to bring together all sectors, and all involved in clinical research, including patients and caregivers to succeed in promoting more inclusive clinical studies.

### Pre-identified industry consortium

The pre-identified industry consortium that will contribute to this cross-sectoral IHI project is composed of the following pharmaceutical and medical technology industry partners:

- Abbvie
- AstraZeneca
- Bristol Myers Squibb
- Eli Lilly
- GlaxoSmithKline

- Janssen
- Novartis (Lead)
- Novo Nordisk
- Pfizer
- Roche
- Sanofi
- Takeda

In addition, the following contributing partner will participate in the IHI project:

- JDRF

In the spirit of partnership, and to reflect how IHI two-stage call topics are built upon identified scientific priorities agreed together with a number of proposing industrial beneficiaries, it is envisaged that IHI proposals and projects may allocate a leading role within the consortium to an industrial beneficiary. Within an applicant consortium discussing the full proposal to be submitted for the second stage, it is expected that one of the industrial beneficiaries may become the coordinator or the project leader. Therefore, to facilitate the formation of the final consortium, all beneficiaries are encouraged to discuss the weighting of responsibilities and priorities with regard to such leadership roles. Until such roles are formalised by execution of the Grant Agreement, one of the proposing industrial leaders shall facilitate as project leader an efficient drafting and negotiation of project content and required agreements.

### **Indicative budget**

The maximum financial contribution from IHI up to EUR 33 000 000.

The indicative in-kind contribution from industry partners is EUR 33 600 000.

The indicative in-kind and financial contribution from IHI JU contributing partner is EUR 250 000.

Due to the global nature of the participating industry partners, it is anticipated that some elements of the contributions will be in-kind contributions to operational activities from those countries that are neither part of the EU nor associated to the Horizon Europe programme.

The indicative in-kind contribution from industry partners may include in-kind contributions to additional activities (IKAA).

### **Indicative duration of the action**

The indicative duration of the action is 72 months.

This duration is indicative only. At the second stage, the consortium selected at the first stage, the pre-identified industry consortium and the contributing partner may jointly agree on a different duration when submitting the full proposal.

### **Contribution of the pre-identified industry consortium**

The pre-identified industry consortium and contributing partner expect to contribute to the IHI project by providing the following expertise and assets:

- Expertise in legal, ethics and compliance, regulatory, diversity, equity and inclusion (DEI) in clinical research and clinical study design both at a local and regional level.



- At a minimum, three use cases (in selected disease areas) are expected to be used as “pilots” to test the infrastructure that will be established during the project. There could be additional comparator use cases depending on testing criteria. Industry contributions will be based on the ‘disease/indication’ and total number of participants interacting with the solutions/platform put in place through this project. The contributions could extend to costs incurred to recruit and retain included patients (in Europe) in the pilots, such as investigator fees, site coordinator fees, digital recruitment/social media costs, reimbursement of patient costs (transportation, etc), community engagement activities, patient retention activities, etc. Costs that do not relate to recruitment and retention activities will be excluded such as costs linked to safety and efficacy assessments, therapeutic ingredients, and supply chain costs.
- Contribution to the elaboration of educational programme and training materials building on existing materials. Sharing potential expertise or technologies that are beneficial for the broader community to help reduce the burden of participating in clinical research.
- Leverage synergies with existing IMI/IHI initiatives and TransCelerate collaborations across industry.
- Capability to enable the platform to be used widely (and adopted as a single solution) by a variety of stakeholders that are currently funded by the pharmaceutical industry to run clinical studies, e.g. contract research organisations (CROs), sites, patient support and advocacy organisations.

The allocation of the EUR 200 000 financial contribution will be decided by the full consortium at the second stage when preparing the full proposal.

### Applicant consortium

The first stage applicant consortium is expected, in the submitted short proposal, to address the scope and deliver on the expected outcomes of the topic, considering the expected contribution from the pre-identified industry consortium and the contributing partner.

This may require mobilising the following expertise and/or resources.

- Knowledge of the existing clinical studies and site databases in Europe.
- Project management expertise in running cross-sectorial projects.
- Partners with expertise in building a patient-centric digital platform that connects various health ecosystem stakeholders, for e.g. patients, patient support organisations, sites, CROs, sponsors, registries.
- Expertise in gathering patient insights for clinical studies – such as input to protocol design, user acceptance testing of the platform, etc.
- Partners who have strong relationships with patient representatives / patient organisations to ensure patient-centricity at all levels of the project.
- Partners with relevant expertise like healthcare professionals, community organisations, sites, CROs.
- Public health experts, social scientists, behavioural scientists, to help change behaviours and mindsets. Communication expertise to reach underserved communities. Patient advocacy experts that in particular work across multiple disease areas and countries in Europe.

- Knowledge on the regulatory aspects (including good clinical practice of drug and medical device development).
- Experience with consumer-directed communications and/or interactions and/or patient advocacy (social media reach and expertise in health sector communications preferred).
- Experience with localised epidemiology data (i.e. incidence/prevalence) overlaid by demographics and/or local ethnopharmacology.
- Expertise in delivering capability-building activities and cultural competency training to the sites.
- Experience in onboarding naïve investigator sites.

At the second stage, the consortium selected at the first stage, the pre-identified industry consortium and the contributing partner will form the full consortium. The full consortium will develop in partnership the full proposal, including the overall structure of the work plan and the work packages, based upon the selected short proposal at the first stage.

### **Dissemination and exploitation obligations**

The specific obligations described in the conditions of the calls and call management rules under “Specific conditions on availability, accessibility and affordability” do not apply.

## Topic 4: Establishing novel approaches to improve clinical trials for rare and ultra-rare diseases

### Expected impacts to be achieved by this topic

The research and innovation (R&I) action (project) to be funded under this topic is expected to transform the clinical research landscape and boost drug development for rare diseases by enhancing patient access to clinical trials and trial preparedness of investigational sites, increasing acceptability of new tools and methods, and preventing research fragmentation across Europe.

It will have a direct impact not only on patients with rare and ultra-rare<sup>64</sup> diseases but also on all stakeholders involved in drug development. More specifically, the expected impact will include the following:

- New pathways co-created by all interested parties and new rules / best practices for early engagement will facilitate clinical development in 'white spot' areas<sup>65</sup> and increase the likelihood that pharmaceutical and biotech companies will test drugs originally intended for common diseases in rare/ultra-rare disease populations with a plausible disease-modifying mechanism of action (MOA).
- Patients with rare/ultra-rare diseases will benefit from cutting-edge clinical development of new health innovations in Europe (impacting the current situation of 95% of underserved rare diseases).
- By fostering the use of alternative innovative designs for randomised clinical trials, patients will have a higher probability of being assigned to active treatment, whether in Phase 2 and/or in Phase 3 registrational trials (especially critical for rare paediatric genetic diseases where the window of therapeutic intervention may be relatively narrow).
- Continuum of evidence generation accelerates authorisation and patient access / treatment / deployment.
- In line with the Accelerating Clinical Trials in EU<sup>66</sup> (ACT-EU) initiative, proactive delivery of patient-oriented medicines across populations including patients with rare/ultra-rare diseases will be increased. Europe is becoming more attractive for the clinical development of medicines for rare/ultra-rare diseases thanks to the uptake of innovative methodological approaches for conducting successful clinical trials for rare/ultra-rare diseases.
- Optimised and predictable referral of patients (physically and virtually) to expert centres, facilitated through incentives, while avoiding patients' disadvantages/burdens (e.g., travel etc.) and inconsistency between healthcare providers would help sponsors in their clinical development where appropriate.

Overall, the success of the project should be determined by measuring an increase in the use of innovative trials, including complex trials, designed to target selected populations with rare/ultra-rare diseases, and in the use and dissemination of playbooks<sup>67</sup>, which will optimise the current situation<sup>68</sup> and increase the number of new approved medicines targeting rare/ultra-rare diseases that are currently underserved.

<sup>64</sup> Ultra-rare diseases: diseases with a prevalence <1 per 50000 persons (<https://err.ersjournals.com/content/29/156/200195>)

<sup>65</sup> 'White spot': conditions for which there is no approved treatment option and where development is not currently commercially viable.

<sup>66</sup> <https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/accelerating-clinical-trials-eu-act-eu>

<sup>67</sup> Playbook: a book/guide including comprehensive guide on a technical topics, describing both overarching strategy and tactical approaches, and including all information relevant to the design, conduct, implementation and analyses of innovative CTs.

<sup>68</sup> <https://www.nature.com/articles/d41573-022-00019-z> / <https://irdirc.org/resources-2/rd-metrics/>

## Expected outcomes

The project generated from the topic should not only develop capacities and capabilities to execute innovative trial designs, but also plan to identify solutions to address scientific gaps as well as technical and operational challenges, and to collaborate / find synergies with relevant existing initiatives to establish a new, dedicated, rare disease specific and sustainable infrastructure. The project is expected to support innovation and optimise drug development for rare diseases with high unmet medical needs by focusing on clinical trials conducted for small populations and clusters of diseases with commonalities.

With a focus on addressing 'white spots'<sup>69</sup> in a subset of the 95% of underserved rare diseases, the R&I action to be supported under this topic should:

1. Deliver novel rare/ultra-rare disease-specific methodological approaches<sup>70</sup> to transform the way treatments are developed with a view towards accelerating approval and access.
2. Pressure-test new clinical trial designs by using the playbooks co-created with stakeholders through case studies and modelling, addressing up to four selected paediatric / rare disease (or clusters of ultra-rare diseases with commonalities) case studies, and different types of interventions (at least one for advanced therapy medicinal products (ATMP)).

In more detail, all the following outcomes are expected to be delivered:

- **Playbooks<sup>71</sup> for designing novel clinical trials (CT)** for rare diseases / clusters of diseases that can also be used for education and training. Jointly created with and validated by regulators, health technology assessment (HTA) bodies, these playbooks should include:
  - good practice recommendations for multinational innovative studies, electronic health records (EHRs) driven registries and longitudinal natural history studies;
  - standardised processes across all disease areas, countries and sites for fast and reliable feasibility processes, allowing – for example – for early feasibility assessment to support the design of feasible development programmes. Effectiveness assessment of optimised CT designs as compared to the 'gold-standard' CT design for rare diseases;
  - study protocols co-created by expert network(s) with regulators, HTA bodies, patients, and industry;
  - agreement on a minimum set of data variables to be included in every registry / newly designed real-world data (RWD) source (baseline patient characteristics, disease-related information, etc.) to ensure usability for regulatory decision-making and study planning;
  - information to support clinical research network set-up for conducting innovative trials including, for example, real world evidence (RWE), remote elements etc;
  - guidance from expert advice to developers on specific aspects when designing CTs.
- **Alignment and complementarity with the European Partnership on Rare Diseases** (in particular the 'Clinical Research Network') co-funded by Horizon Europe and Member States and Associated countries, to create synergies and avoid overlaps.

<sup>69</sup> 'White spots' - conditions for which there is no approved treatment option and where development is not currently commercially viable

<sup>70</sup> Framework defined as structured processes and methodologies

<sup>71</sup> Refer to footnote 67 (playbook).

- **Certified/qualified clinical trial sites** scientifically and operationally (especially in the areas of ATMPs) with readily available pools of patients ready to be recruited into CTs where appropriate; working to agreed site standards along comparable process and quality standards.
- **Structured and predictable system for referral of patient** (physically and virtually) to expert centres, facilitated through incentives and avoiding patient disadvantages (travel etc.) and incongruity amongst healthcare providers.

## Scope

Developing medicines for rare diseases involves complexities and challenges beyond those typically seen for common conditions, in particular:

- for most rare diseases, disease aetiology, biology and natural history are insufficiently understood, while there are often no established endpoints for use in clinical trials;
- enrolling, engaging and retaining patients, including patients who may be far apart geographically;
- designing and evaluating clinical trials, including using/identifying relevant outcome measures;
- ensuring the quality of patient data, and enabling re-use of data (e.g. registries);
- underdeveloped and fragmented clinical trial infrastructure for the conduct of clinical studies, including those using ATMPs and for cell and gene therapies;
- an evolving and internationally fragmented global regulatory and landscape.

The evaluation of the regulations on Orphan Medicinal Products and Paediatric Medicines by the European Commission has concluded that those regulations have boosted the development of new therapies for rare diseases but have not yet adequately managed to direct research and innovation towards the areas of greatest unmet medical need. There is clearly a need for holistic and inclusive solutions to address the persisting root causes of these unmet medical needs and to deliver more medicines for patients with rare diseases. This topic, which contributes to the Rare Disease MOONSHOT Initiative<sup>72</sup>, is expected to be an important catalyst for innovation for patients affected by some of the 95% of rare diseases without treatment options. Importantly, the project selected under this call would also align with the identified strategic priorities of the Horizon Europe co-funded Partnership on Rare Diseases that is expected to start in mid-2024 and to consolidate the Rare Disease (RD) research and innovation ecosystem.

The topic aims to unravel roadblocks on the current clinical development pathways and deliver methodological solutions for innovative clinical trial designs and analyses, including regulatory considerations.

To fulfil this aim, the proposal should:

- identify good practices for the design, use and implementation of innovative clinical trial (e.g., basket trials, platform trials, *in silico* trials) and of tools/methods (e.g., RWD, digital health technologies, quantitative approaches, trial with remote elements) developed for small populations and clusters of diseases, while also addressing scientific and statistical challenges with the generation and

<sup>72</sup> <https://www.eurordis.org/rare-disease-moonshot/>

interpretation of small, incomplete and/or heterogenous data sets to help support CT and product approval;

- identify good practices to address knowledge gaps including the collection of natural history data, the development of relevant new endpoints and patient reported outcomes (PROs) which should be incorporated into the CT design;
- benchmark new clinical trial designs (i.e. basket, platform CTs, shared control arm trials between different sponsors...) that should be assessed and compared to the existing 'gold standard' CT model for rare diseases (i.e. single arm);
- focus on paediatric and adult rare diseases ('white spots');
- develop appropriate capacity and capability for innovative clinical trials as well as education and training programmes based on lessons learnt from existing initiatives and developers' experience so that best practices to optimise drug development in rare diseases can be shared and disseminated, and playbooks deployed;
- develop a virtual platform for knowledge and tool sharing, which could be also used for playbook deployment;
- identify clinical trial sites which are certified/qualified scientifically and operationally (especially in the areas of ATMPs) with readily available pools of patients ready to be recruited into CTs where appropriate. Taking into account the cohort size of such clinical trials it will be quite important to ensure the cultural and geographical distribution of the CT at EU level;

To be successful and deliver according to the objectives, it is important:

- to capitalise on past public investments and collaborate with relevant stakeholders, e.g. with the European Reference Networks (ERNs) and their registries, the European Joint Programme on Rare Diseases (EJP RD<sup>73</sup>) and the future European partnership on rare diseases (RDP) to foster a more cost-effective pathway for the development of treatments for patients with rare diseases in Europe. The ERNs<sup>74</sup> are being established under the Directive on patients' rights in cross-border healthcare, with their registries under the supervision of the Member States<sup>75</sup>, and therefore any plan for collaboration between ERNs and industry should be compatible with the principles<sup>76</sup> set up by the ERN Board of Member States and the Commission services. Hence the need to identify solutions to unlock industry collaboration with ERNs (e.g., leveraging on ERNs' clinical expertise, ERN registries, etc.) should be in line with these principles;
- to utilise the European Commission's infrastructure for the RD registry data and clinical cohorts ecosystem, namely the European Platform on Rare Disease Registration (EU RD Platform) for clinical data management;

<sup>73</sup> EJP RD (European Joint Programme on Rare Diseases): <https://www.ejprarediseases.org/>

<sup>74</sup> [https://health.ec.europa.eu/european-reference-networks/overview\\_en](https://health.ec.europa.eu/european-reference-networks/overview_en)

<sup>75</sup> [https://health.ec.europa.eu/european-reference-networks/board-member-states\\_en](https://health.ec.europa.eu/european-reference-networks/board-member-states_en)

<sup>76</sup> [https://health.ec.europa.eu/system/files/2020-03/statement\\_industry\\_conflictofinterest\\_en\\_0.pdf](https://health.ec.europa.eu/system/files/2020-03/statement_industry_conflictofinterest_en_0.pdf)

- to leverage key learnings from existing ongoing initiatives, e.g., the Bespoke Gene Therapy Consortium<sup>77</sup>, IMI EU-PEARL<sup>78</sup>, EUnetHTA21<sup>79</sup>, or of the IRDIRC "Orphan Drug Development Guidebook" project<sup>80</sup> which aims at creating a simple guidebook for academic and industrial drug developers describing the available tools and initiatives specific for rare disease development and how best to use them;
- to build upon the results of Horizon 2020 (H2020) research projects such as the European Rare disease research Coordination and support Action (ERICA) and FP7 projects developing methodologies for clinical trials for small populations<sup>81</sup>, namely IDEAL<sup>82</sup>, InSPiRe<sup>83</sup> or ASTERIX<sup>84</sup>. It will be crucial to optimise their findings (if necessary) based on new scientific/technological progress and find synergies with other existing projects, whether completed or ongoing;
- to build synergies with the new cluster of Horizon Europe projects on developing new effective therapies for RD with no approved options (expected to start in Q3 2023) and to partner with existing projects/initiatives, e.g., IMI (Innovative Medicines Initiative) Screen4Care<sup>85</sup>, IMI conect4children (c4c)<sup>86</sup>, Remedi4All<sup>87</sup>, C-Path RDCA-DAP<sup>88</sup>;
- to help overcome the fragmentation of the clinical trial environment across Europe;
- to identify solutions to overcome hurdles in the implementation of cross-border patient participation in clinical trials;
- to develop best practices to support the development of innovative and 'regulatory-grade' clinical trials and generate the appropriate evidence for regulatory and HTA decision-making.

Once developed and established, the playbooks and related infrastructures will be pressure-tested through case studies and modelling, using up to four selected paediatric/rare diseases (with at least one ultra-rare disease or clusters of diseases) and different types of interventions (at least one being an ATMP).

### Why the expected outcomes can only be achieved by an IHI project

To tackle the challenges, and in line with the IHI objectives, a multidisciplinary public-private partnership driving innovative and solution-driven science and technology is the only way to harness expertise from all the relevant stakeholders (i.e., patients, academia, regulators, health industry representatives, etc.) and to consider all relevant perspectives and adjust the trajectory in real time. IHI provides frameworks for a structured dialogue among stakeholders including regulatory, HTA bodies and healthcare authorities, and succeeds in creating clinical trials / research initiatives reflective of global populations.

There is a need to break down existing silos and bring together the expert ecosystem and stakeholders. This should help in optimising and streamlining the development of assets relevant for paediatric / rare diseases by removing key technical bottlenecks and identifying best practices. Therefore, collaboration and

<sup>77</sup> <https://ncats.nih.gov/programs/BGTC>

<sup>78</sup> <https://eu-pearl.eu/>

<sup>79</sup> <https://www.eunetha.eu/eunetha-21/>

<sup>80</sup> <https://irdirc.org/activities/task-forces/orphan-drug-development-guidebook-task-force/>

<sup>81</sup> <https://cordis.europa.eu/search?q=contenttype%3D%27project%27%20AND%20programme%2Fcode%3D%27HEALTH.2013.4.2-3%27&p=1&num=10&srt=/project/contentUpdateDate:decreasing>

<sup>82</sup> IDEAL – Integrated DEsign and AnaLysis of clinical trials in small population groups (rwth-aachen.de): <https://www.ideal.rwth-aachen.de>  
<https://cordis.europa.eu/project/id/602552>

<sup>83</sup> InSPiRe (Innovative methodology for small populations research): <https://cordis.europa.eu/project/id/602144>

<sup>84</sup> ASTERIX (Advances in Small Trials designs for Regulatory Innovation and eXcellence): <http://www.asterix-fp7.eu/>

<sup>85</sup> <https://screen4care.eu/>

<sup>86</sup> <https://conect4children.org/>

<sup>87</sup> <https://remedi4all.org/>

<sup>88</sup> <https://portal.rdca.c-path.org/>

synergies between the experts from industry, academia, patients' organisations, not-for-profit organisations, biotech, research institutions, clinics, and small and medium-sized enterprises (SMEs), will be essential for this project. Similarly, patients' involvement and connection with clinicians, health care providers and rare disease networks will be essential as well as collaboration with regulators to ensure appropriate development and implementation of the playbooks.

### **Pre-identified industry consortium**

The pre-identified industry consortium that will contribute to this cross-sectoral IHI project is composed of the following pharmaceutical and medical technology industry partners:

- AstraZeneca (Lead)
- Bayer
- Boehringer-Ingelheim
- Ipsen
- Janssen
- Novartis
- Roche
- Sanofi
- Servier
- UCB

In the spirit of partnership, and to reflect how IHI two-stage call topics are built upon identified scientific priorities agreed together with a number of proposing industrial beneficiaries, it is envisaged that IHI proposals and projects may allocate a leading role within the consortium to an industrial beneficiary. Within an applicant consortium discussing the full proposal to be submitted for the second stage, it is expected that one of the industrial beneficiaries may become the coordinator or the project leader. Therefore, to facilitate the formation of the final consortium, all beneficiaries are encouraged to discuss the weighting of responsibilities and priorities with regards to such leadership roles. Until such roles are formalised by execution of the Grant Agreement, one of the proposing industrial leaders shall facilitate as project leader an efficient drafting and negotiation of project content and required agreements.

### **Indicative budget**

The maximum financial contribution from IHI is up to EUR 8 500 000.

The indicative in-kind and financial contribution from industry partners is EUR 9 100 000.

Due to the global nature of the participating industry partners, it is anticipated that some elements of the contributions will be in-kind contributions to operational activities from those countries that are neither part of the EU nor associated to the Horizon Europe programme.

The indicative in-kind contribution from industry partners may include in-kind contributions to additional activities.

### **Indicative duration of the action**

The indicative duration of the action is 60 months.

This duration is indicative only. At the second stage, the consortium selected at the first stage and the pre-identified industry consortium will jointly agree on a different duration if needed, when submitting the full proposal.

### **Contribution of the pre-identified industry consortium**



The pre-identified industry consortium expects to contribute to this IHI project by providing the following expertise and resources to:

- build solution components that are sustainable and scalable;
- generate site standards and quality processes to support the build-up and training of research network hubs and expert sites;
- engage and raise awareness amongst patient groups;
- provide regulatory expertise, to help with other experts to build playbooks;
- provide anonymised data that could be used as control arms;
- support virtual trial platform providers, directly or indirectly;
- support sustainability of existing trial networks and/or data sources, directly or indirectly;
- aid centres in building referral networks;
- provide support for the conduct of natural history studies for ultra-rare diseases, identification of standard of care – patient flow, and development of patient registries;
- seek expert input/advice for ultra-rare diseases.

The allocation of the EUR 575 000 financial contribution will be decided by the full consortium at the second stage when preparing the full proposal.

### **Applicant consortium**

The first stage applicant consortium is expected, in the submitted short proposal, to address the scope and deliver on the expected outcomes of the topic, considering the expected contribution from the pre-identified industry consortium.

This will require mobilising the following expertise and/or resources among others:

- for the development of new endpoints, biomarkers in rare/ultra-rare and paediatric diseases;
- for epidemiology and natural history diseases;
- for translational science;
- for data management and standards;
- for devices, digital health and registries;
- for clinical operations, and in engagement with patient representatives and other interest organisations within the area of public health;
- for education and training;
- for European Research Networks;
- for project management expertise in running cross-sectorial projects.

Applicant consortia should bring together partners with relevant expertise such as regulators, healthcare professionals, patient representatives / organisations, health technology developers, research organisations, academia, biostatisticians, legal experts, ethicists. Participation of SMEs with expertise in clinical development in small populations and/or in the use of digital health technologies is encouraged. The composition of the consortium should also ensure a broad geographical representation of EU member states. For the development of the playbooks, input from other relevant stakeholders, in particular HTA bodies, would be necessary.

At the second stage, the consortium selected at the first stage and the pre-identified industry consortium and contributing partners will form the full consortium. The full consortium will develop in partnership the full proposal, including the overall structure of the work plan and the work packages, based upon the selected short proposal at the first stage.

To successfully deliver according to the objectives, it is important to engage with stakeholders within the health (research) ecosystem such as health authorities, health technology assessment (HTA) bodies and regulatory bodies, starting with the European Medicines Agency (EMA).

### **Dissemination and exploitation obligations**

The specific obligations described in the conditions of the calls and call management rules under 'Specific conditions on availability, accessibility and affordability' do not apply.

## Topic 5: Safe & Sustainable by Design (SSbD) packaging and single use device solutions for healthcare products

### Expected impacts to be achieved by this topic

The project is expected to strengthen and make more competitive the European healthcare industry by positioning it at the forefront of the development of medical technologies, products, and services of the future - those that generate less waste, require less waste treatment, have reduced carbon footprints, increased circularity, and other approaches that reduce the environmental impact of healthcare.

It aims to promote the development of new health products by integrating the principles of the safe & sustainable by design (SSbD) framework<sup>89</sup>, from the earliest design stages, and notably for packaging and device design including the end-of-life of a product. In the context of this call, packaging includes primary packaging in direct contact with products (e.g. drugs, medical devices, *in vitro* diagnostic reagents, etc.) and secondary packaging made of plastic polymer materials – excluding secondary and tertiary cardboard packaging. Medical devices refer to single-use plastic pharmaceutical and medical devices used for the administration of medicines such as pens used for insulin injection or devices used for surgeries such as trocars and staplers. They may contain additional components such as metals and electronic components as is the case of smart staplers, for example.

The project should as a minimum have all of the following impacts:

- Developers of health products (e.g. drugs, medical devices, *in vitro* diagnostic reagents, combination devices, etc.) are able to draw general lessons and best practices for their current research, and integrate research results on packaging and devices that generate less waste, make more efficient use of materials, and minimise the use of single-use components.
- Alignment with the European Green Deal objectives for healthcare systems, especially in the field of waste management and CO<sub>2</sub> reduction, as well as an improved competitive position for healthcare companies.
- Improving the recyclability of medical devices, independent of whether the material of construction (e.g. plastic, metals) is classified as non-hazardous or infectious waste.<sup>90</sup>
- Reduced carbon footprint of health products in alignment with the Paris Agreement on climate change and the European Green Deal (55 % by 2030, NetZero by 2050).
- Propose new solutions that are holistic in nature, and which do not create additional adverse ESG (environment, social & governance) issues.
- New solutions should facilitate circularity even if the end points are not a closed loop back into the healthcare sector and instead are used for other applications.
- Identify a range of physical, mechanical, chemical and/or composting recycling infrastructures such that packaging materials and single-use medical devices (e.g. pens used for insulin injection, surgical trocars) can be recycled.

<sup>89</sup> <https://publications.jrc.ec.europa.eu/repository/handle/JRC128591>

<sup>90</sup> <https://www.who.int/news-room/fact-sheets/detail/health-care-waste>

## Expected outcomes

The project should contribute to the following outcomes:

1. Paradigm shifts in standard materials to shape products of the future (e.g. reduced material usage by pushing the boundaries on material specifications such as down gauging foils/films, blending virgin and recycled polymers, inclusion of more sustainable materials as newly proposed from material suppliers, etc.).
2. Development of new and effective technologies, products and innovations that generate minimal waste from packaging and enable the recycling of used devices (including devices which have been in contact with human tissues, i.e. infectious waste<sup>91</sup>) throughout their lifetime of use in healthcare systems, by applying the principles of the safe & sustainable by design (SSbD) framework.
3. Alignment with the European Packaging and Packaging Waste<sup>92</sup> and Ecodesign of Sustainable Products<sup>93</sup> Directive proposals.
4. Such innovations – i.e. packaging materials & single-use medical devices (e.g., pens used for insulin injection, surgical trocars) are easily accessible in sufficient quantities to healthcare providers (e.g., hospitals, medical analysis laboratories, caregivers, and patient associations/organisations).
5. Environmentally-friendly packaging and device materials are designed from sustainable raw components and manufacturing processes with minimal carbon footprint.
6. Selective sorting procedures, implementable by healthcare providers.
7. The creation of short circuits for recycling packaging and device waste from healthcare providers' locations.

Healthcare systems more widely adopt a lifecycle assessment approach, enabling healthcare to become a more sustainable industry with closer and more circular recycling loops for packaging as well as single-use devices, including those which may have been contaminated (i.e. infectious waste).

Solutions should include a holistic approach such as:

1. adoption of biomass balanced materials that reduce environmental impacts, and
2. inclusion of advanced recycling technologies such as various chemical recycling technologies (hydrolysis, pyrolysis, solvolysis, etc.) if improvements to environmental impacts can be properly documented.

Patient outcomes and the safety/performance of medical products should not be compromised by the environmentally-friendly packaging and device solutions to be developed by the project.

Notably, these packaging solutions should be compliant with existing standards (e.g. primary packaging with sterile barrier: ISO 11607) to guarantee the safe use of medical products, i.e. maintenance of the safety and performance levels that are claimed throughout their intended shelf life.

<sup>91</sup> <https://www.who.int/news-room/fact-sheets/detail/health-care-waste>

<sup>92</sup> [https://environment.ec.europa.eu/publications/proposal-packaging-and-packaging-waste\\_en](https://environment.ec.europa.eu/publications/proposal-packaging-and-packaging-waste_en)

<sup>93</sup> [https://environment.ec.europa.eu/publications/proposal-ecodesign-sustainable-products-regulation\\_en](https://environment.ec.europa.eu/publications/proposal-ecodesign-sustainable-products-regulation_en)

- Depending on the use cases selected by the project, they must provide a sterile barrier, maintain controlled humidity, protect against light, etc. throughout their shelf life, including shipment from manufacturing site to end users.
- When used as a sterile barrier, they should be compatible with common sterilisation processes (e.g. steam, gas sterilisation such as hydrogen peroxide; radiation treatments such as e-beam, gamma irradiation, X-rays, etc.).
- When used as medical products for use in humans, existing safety & biocompatibility standards are met such as European Pharmacopeia (EP) compendia, ISO 10993, etc. (e.g. not generating extractible and leachable harmful products during the full shelf life of the products).
- The chemical and physical properties of the new material formulations should also guarantee the intended shelf life of the medical products (e.g. up to 5 years).
- Work with regulators (e.g. European Chemicals Agency (ECHA), European Directorate for the Quality of Medicines & HealthCare (EDQM), European Pharmacopeia (EP), US Pharmacopeia (USP), American Chemical Society (ACS), etc.) to create new or revised standards/monographs for new materials that are used in health products. By extension, this engagement should contribute to the generation of future product eco-design labels / green claims.
- For example, the use of packaging composed of biodegradable, recyclable and/or environmentally benign ingredients is favoured if the claimed performance and safety of the medical products are maintained.
- Improved and simplified protocols for the management, collection, and recycling of medical device waste (packaging and devices) to reduce waste management costs for healthcare providers and minimise the environmental impact of the medical waste generated by medical devices.
- Protocols for the collection of single-use devices and their packaging to drive circularity should be easily implementable by healthcare providers. Their adoption must be possible for the greatest number of healthcare providers, regardless of their location. They may potentially include the decontamination of products if they have been in contact with human tissues to allow their sorting and recycling under the safest conditions.
- Improved and simplified protocols for supply chains and logistics for sorting of packaging waste of health products for healthcare providers with a minimised carbon footprint.

The outcomes must be as cost-effective as possible so as not to burden health systems with prohibitive additional costs.

Overall, the project is expected to yield strong results from the use cases. The results should be taken as evidence to collaboratively shape European legislation on packaging and packaging waste and the eco-design of sustainable products for health technology industries.

## Scope

### Product development

The project should accelerate the implementation of alternative eco-packaging and device materials through collaborative work by including policy makers, regulators, and standards bodies. It should identify, characterise, and test new replacement materials according to specifications and in compliance with existing standards (e.g. primary packaging with sterile barrier: ISO 11607).

The project should examine the European landscape of materials, whether commercially available or under development, which may be acceptable as components of sustainable packaging and appliance solutions, from different perspectives, regulations, possibility to recycle with current and future waste management processes, and sustainability of industrial supply. Such a review can benefit from and partner with the European Partnership for the Assessment of Risks from Chemicals (PARC) and with the successor partnership of the M.ERA-NET III and the AMI2030 initiative. In addition, synergies with projects funded in the Horizon Europe Cluster 4 addressing SSbD could be envisaged (HORIZON-CL4-2023-RESILIENCE-01-21: Innovative methods for safety and sustainability assessments of chemicals and materials (RIA); HORIZON-CL4-2023-RESILIENCE-01-22: Integrated approach for impact assessment of safe and sustainable chemicals and materials (RIA); HORIZON-CL4-2023-RESILIENCE-01-23: Computational models for the development of safe and sustainable by design chemicals and materials (RIA)).

Health tech companies are expected to design and develop new packaging and devices (e.g. insulin pens, staplers) by starting from solutions that already exist or are at an advanced stage of development (e.g. available paper-based covers / packaging seals reinforced with polyolefins, or mixtures of virgin and chemically recycled polymers for the manufacture of blisters), and/or by selecting fully compostable or recyclable materials (for example, biomass balanced polymers as currently proposed and under development by chemical companies) to generate innovative packaging and device solutions. The polymers or materials to be selected must not only be recyclable/compostable, but also manufactured with a minimal environmental footprint.

The design and development of the new packaging and devices should apply and adapt circular economy principles and be guided by the SSbD framework. It should be done in close partnership with all players of the value chain from the manufacturers of the raw materials to the end users, the healthcare providers. The packaging and device use cases of the project are highly expected to improve and enrich the current SSbD framework, through concrete feedback to the European Commission and lessons learned. It is envisioned that this will necessitate regular interactions between the project and the developers of the SSbD framework at the European Commission.

## **Recycling**

The project should promote the management of waste from packaging and single-use devices (including complex devices) by end users, the healthcare providers, considered as key partners of the project. This should lead to the effective implementation of the sorting and recycling of waste through collaborative work, including technical, organisational, and regulatory aspects (e.g. allowing the reuse of plastics etc. after industrial disinfection and/or decontamination of infectious waste, development of new recycling processes, setting up composting units etc.). Preferably, healthcare providers should include not only hospitals, but also other end users such as nursing homes. Healthcare providers should preferably be from several EU Member States or associated countries (e.g. minimum 3 EU Member States or associated countries), given the great disparity of practices from one country to another, in terms of legislation and implementation of waste sorting and recycling.

Importantly, the project should extend existing life cycle assessment (LCA) based metrics systems to packaging and devices, by considering the life cycle of the packaging materials, from their manufacturing to their recycling / composting. The LCA study must be carried out by an independent institution. Key performance indicators are expected to come from comparing LCA metrics with the implementation of the SSbD framework, which should lead to better packaging and device recyclability and more favourable life cycle outcomes.

Another key element of the project is expected to come from an active partnership with European non-profit packaging associations, single-use plastic, and waste management associations and, possibly, standards

bodies and approval bodies responsible for marketing authorisations. These institutions should work with European policy makers to support evidence-based policy making based on the findings of the different use cases of the project. The development and implementation of recyclable packaging and device solutions should also be articulated by the health tech trade associations, at the European (i.e. EFPIA, COCIR, MedTech Europe, EuropaBio and Vaccines Europe) or national levels, in particular with their working groups on sustainability and the circular economy.

General lessons / best practices and results will be shared as far as possible (e.g. peer-reviewed articles, white papers, press releases, web media, report deliverables, etc.). Communicating project results is essential to collaboratively shaping the acceptability, adoptability, and implementation of European legislation on packaging and packaging waste and the eco-design of sustainable products for health technology industries.

Besides this topic, another topic in this IHI call entitled “Sustainable circular development and manufacturing of healthcare products and their quantitative environmental impact assessment” will aim to improve the manufacturing efficiency of drug substances of chemical/biological origin (covering all chemical drug substances, proteins, oligonucleotides, vaccines or polypeptides etc.) by developing new manufacturing technologies, saving natural resources like water and fossil or fossil-based raw materials, and reducing waste in accordance with circularity principles (reduce, reuse, refine, recycle).

To jointly develop new strategies to ensure a greener healthcare industry along the whole value chain, and to avoid overlaps, a close collaboration between the two topics is essential and should be reflected by providing dedicated resources in both projects to align on common life cycle assessment (LCA) methodologies and LCA data.

### **Why the expected outcomes can only be achieved by an IHI project**

To fully develop and foster the adoption of recyclable packaging and device recycling solutions to drive a circular economy for healthcare products, it is essential that different industry sectors come together and exchange knowledge and best practices to find optimal solutions. Combining expertise from various industrial and research sectors is critical to the success of this project.

It is essential that health tech industry partners from different sectors, e.g. the pharmaceutical industry, medical device manufacturers, *in vitro* diagnostic, biotech & vaccine companies, etc. exchange knowledge and experience and provide complementary use cases.

Healthcare providers (HCPs) are identified as key stakeholders as end users of healthcare products. Packaging and device management goes through HCPs with the implementation of selective sorting solutions to integrate them into appropriate recycling channels. HCPs should be from different European Union countries, preferably a minimum of three countries of different sizes.

This cross-sectorial collaboration is expected to include circular economy specialists, notably for life cycle assessment (LCA), European not-for-profit packaging, single use plastics and waste recycling associations, and, possibly, standardisation bodies. Such institutions and all partners of the project are committed to working with European policy makers to support evidence-based policy making.

Beyond classical health tech industries, the project may be even more impactful by including as partners other industry players of the value chain, notably from the materials and packaging industries.

This will ensure optimal implementation of the technical and scientific innovations expected to stem from this topic. IHI JU offers a unique opportunity to break down existing silos along the packaging and device value

chain for a measurable impact on adopting recyclable packaging and device materials and reducing waste from packaging & device materials.

### **Pre-identified industry consortium**

The pre-identified industry consortium that will contribute to this cross-sectoral IHI project is composed of the following pharmaceutical and medical technology industry partners:

- Boehringer Ingelheim
- Eli Lilly
- Fresenius Medical Care
- J&J
- Medtronic (Lead)
- Novo Nordisk
- Pfizer
- Takeda

In the spirit of partnership, and to reflect how IHI two-stage call topics are built upon identified scientific priorities agreed together with several proposing industrial beneficiaries, it is envisaged that IHI proposals and projects may allocate a leading role within the consortium to an industrial beneficiary. Within an applicant consortium discussing the full proposal to be submitted for the second stage, it is expected that one of the industrial beneficiaries may become the coordinator or the project leader. Therefore, to facilitate the formation of the final consortium, all beneficiaries are encouraged to discuss the weighting of responsibilities and priorities regarding such leadership roles. Until such roles are formalised by execution of the Grant Agreement, one of the proposing industrial leaders shall facilitate as project leader an efficient drafting and negotiation of project content and required agreements.

### **Indicative budget**

The maximum financial contribution from IHI is up to EUR 8 300 000.

The indicative in-kind and financial contribution from industry partners can go to EUR 8 300 000.

Due to the global nature of the participating industry partners, it is anticipated that some elements of the contributions will be in kind contributions to operational activities from those countries that are neither part of the EU nor associated to the Horizon Europe programme.

The indicative in-kind contribution from industry partners may include in-kind contributions to additional activities (IKAA).

### **Indicative duration of the action**

The indicative duration of the action is 48 months.

This duration is indicative only. At the second stage, the consortium selected at the first stage and the pre-identified industry consortium may jointly agree on a different duration when submitting the full proposal.

### **Contribution of the pre-identified industry consortium**

The industry consortium is not limited to health tech companies (i.e. pharmaceutical, medical devices, *in vitro* diagnostic & imaging companies, etc.).

The industry consortium expects to contribute to the IHI project by providing the following expertise and assets.



- Grant administration & project management
  - To provide legal support for project-related tasks.
  - To support project management.
- Packaging & single-use pharmaceutical and medical device use cases
  - To design and develop safe & sustainable packaging solutions and to apply the safe & sustainable by design (SSbD) framework. For example, such activities should consider from project start, i) recycling routes; and ii) if relevant, second life of packaging and devices.
  - To implement and execute flagship projects guided by the SSbD framework by including recyclable materials as components of sustainable packaging and appliance solutions.
  - To identify materials not yet marketed and/or under development, but compatible with the regulatory and normative requirements of the industrial manufacture of health products.
  - If the design and development stages are successful, industrialisation activities are expected to lead to the implementation of new pilot and/or industrial manufacturing lines.
  - To be inspired by and learn from other industries by possibly exploiting synergies, with the food industry for example.
  - To look for cost-effectiveness: new and innovative sustainable solutions should be reasonably cost-efficient compared to existing solutions.
  - To identify implementable sustainable solutions: New and innovative sustainable solutions should be still acceptable and adoptable by end-users (e.g. patients, nurses / caregivers, healthcare providers [HCPs], etc.), or even better compared to existing solutions.
  - To compare the performance of the sustainable packaging & device solutions with existing solutions and determine if they are suitable to be used with current products, according to specifications and standard requirements. It is essential that the sustainable packaging and device solutions do not compromise the safety and performance of the medical products.
- Recycling
  - To contribute to the definition of “recyclable” vs. “recycle-ready” with all partners of the project. Recycling activities may be preceded by decontamination procedures in case of contact with human tissues.
  - As a first intent, “recyclable” means that a product is likely to be recycled and the infrastructure exists such that the “recycle-ready” product can be recycled.
  - Physical, mechanical, and chemical recycling and composting are recycling solutions that are considered in scope.
  - Burning and landfill solutions should be avoided as much as possible.

- Recyclable “at all” is good enough, but it does not have to be a closed loop in the health tech industry. Raw materials can also be re-used in other industries. The primary goal is re-use of recycled packaging and device materials.
- To understand drug-product interactions and biological contamination as potential limitations to recycling and propose solutions to overcome them.
- From waste management audits of HCPs, the industry and the public consortia will work together to make recommendations to improve the sorting and recycling of packaging and single-use devices.

The allocation of the EUR 400 000 financial contribution will be decided by the full consortium at second stage, when preparing the full proposal.

### **Applicant consortium**

The first-stage applicant consortium is expected, in the submitted short proposal, to address the scope and deliver on the expected outcomes of the topic, considering the expected contribution from the pre-identified industry consortium.

Beyond grant administration and project management, the applicant consortium is expected to address all the research objectives and make key contributions to the defined deliverables in synergy with the industry consortium. It should include any relevant public and private organisations.

### **Grant administration**

- To provide financial administration, submission of deliverables, periodic reports etc.

### **Project management**

- To coordinate internal communication and meetings, general oversight and management of communication, exploitation and dissemination activities, risk management.
- To provide and maintain an IT infrastructure, to develop and implement an efficient data governance and management strategy of the joint consortium according to adequate standards and deliver the “data management plan”.
- To coordinate networking, joint activities and synergies with other European initiatives, or other relevant groups (e.g. Horizon Europe and IHI projects, etc.).
- To develop a strategy for the exploitation and sustainability of project results and outcomes and deliver the “exploitation and sustainability plan”.
- To prepare relevant documents / reports of the results being generated by the project (e.g. briefing books, guidance documents, etc.) to be shared with any stakeholders committed to the development, evaluation and regulation of packaging and single-use solutions including European regulators, policymakers and standards organisations.

### **Project activities**

- Consortium to review, evaluate and recommend materials (already existing or under development at the pilot scale) which can be selected as safe and sustainable packaging and single-use devices, according to the regulatory landscape and current specifications / standards for packaging and single-use devices.

- Consortium to review and evaluate the waste management process solutions of the recommended list of materials with a focus on existing recycling schemes, at the industrial level or at a pilot scale, which can be leveraged by healthcare providers. The review should provide a European landscape assessment and highlight any regional disparities. It should also integrate the national and European regulations and incentives of waste management and recycling.
- The consortium should be acquainted with planned activities under the European Partnership for the Assessment of Risks from Chemicals (PARC) and take advantage of the partnership as a facilitator for open data and methodology sharing with risk assessors and their scientific networks.
- Healthcare providers (HCP) including hospitals, medical analysis laboratories, caregivers, and patient associations to contribute to the identification, evaluation and implementation of sorting and waste management solutions of packaging and single use devices. HCPs are also expected to generate audit reports on the waste they generate by categories (non-hazardous & hazardous) and by materials (e.g. plastic, metal, paper). The report should also include quantitative data on waste volumes / costs per category, identification of waste minimisation, opportunities / potential cost savings, facility walk through / stream analysis of waste, application of waste reduction principles (e.g. 10 R's rule<sup>94</sup>), improvement plans for compliance with regulation and waste minimisation goals set at the national level (e.g. see the Dutch example of Green Deal Sustainable Care 2.0<sup>95</sup>) or European level.
- From the waste management audit reports, recommendations to optimise waste management should be made by all actors of the value chain, including HCPs and health tech industries.
- HCPs with their external waste management partners are expected to run pilot studies of waste management from the use cases provided by the healthcare industries.
- Policy makers, health tech trade associations, notified bodies (for medical devices and *in vitro* diagnostic products), European Medicines Agency (EMA) and/or organisations working with EMA, environmental health, and sustainability (EHS) institutions, advocacy groups, standards organisations as partners or members of the advisory board, to work in partnership with all partners of the project on the acceptability, applicability and implementation of regulations on safe and sustainable packaging and single use devices.
- European non-profit packaging, single-use plastics & waste recycling societies or associations as partners to work with the industry consortium, policy makers and standards organisations to support evidence-based policy making from the findings of the project. These societies or associations are also expected to provide data and insight on trends of eco-design and waste management of health tech products, but also of products from other industries when possibly benefiting the health tech industries.
- Small and medium-sized packaging companies will co-develop innovative, safe and sustainable solutions with the industry consortium.
- Small and medium-sized health tech companies including vaccines and biotech players are also invited to develop their own packaging and / or device solutions.
- Consortium – public and/or private entities – to assist the physical, chemical characterisation of new safe and sustainable solutions for packaging and single use devices, including compliance with the regulatory packaging and device requirements.

<sup>94</sup> <https://www.sciencedirect.com/science/article/pii/S0921344919304598>

<sup>95</sup> <https://www.government.nl/topics/sustainable-healthcare/more-sustainability-in-the-care-sector>

- Consortium – public and/or private entities – to evaluate the biocompatibility and toxicity of the new packaging and single-use devices according to regulatory and standard requirements (e.g. analysis of extractables and leachable compounds).
- To contribute to the regulatory landscape for life cycle assessment (LCA) standards in the EU and in other non-EU European countries.
- In conjunction with industry, to discuss with regulatory authorities, standards organisations, and advocacy groups the acceptability and implementation of the LCA metrics and in the EU and harmonisation with efforts in other non-EU European countries and the US.
- Evaluate the life-cycle assessment, including the costs in a comparative way (sustainable vs. current solutions).
- To evaluate the environmental impact of the new packaging and single-use device solutions with a holistic view, by including:
  - environmental toxicity of the end products;
  - environmental impact of the manufacturing process of the starting materials and their transformation into packaging and single-use devices.
- Standards bodies to adapt, revise, change current standards to accommodate the use of the sustainable solutions from the evidence generated by the use cases of the project and, possibly, other findings, notably captured by the different European non-profit packaging, single-use plastics and waste societies or associations.

Subject to the rules of the IHI Horizon Europe Model Grant Agreement applicable to IHI, all major findings of the project – except for confidential information, notably pertaining to generated intellectual property – should be publicly disseminated and communicated. They should provide strong evidence to shape the acceptability, adoptability and the implementation of the future European regulations on packaging and single use devices.

- The project may include the question of certification or green claims of the materials used for the packaging and device solutions and also of the packaging and device solutions themselves.

### **Dissemination and exploitation obligations**

The specific obligations described in the Conditions of the calls and calls management rules under “Specific conditions on availability, accessibility and affordability” do not apply.

## Topic 6: Sustainable circular development and manufacturing of healthcare products and their quantitative environmental impact assessment

### Expected impacts to be achieved by this topic

This project will pave the way for European healthcare industries to collaborate cross-sectorially to improve the manufacturing efficiency of drug substances of chemical/biological origin (covering all chemical drug substances, proteins, oligonucleotides, vaccines or polypeptides etc.) by saving natural resources like water and fossil or fossil-based raw materials and consumables, in addition to reducing waste in accordance with circularity principles (reduce, reuse, refine, recycle).

Healthcare industries in the Organization for Economic Cooperation and Development (OECD) countries are responsible for 3-8% of natural carbon dioxide emissions<sup>96</sup>. The invention of new and creative technology in the field of chemistry and biotechnology will make Europe the central driver of innovation for the supply of drugs made of renewable resources. The ultimate goal of the project is to significantly reduce the environmental impact of the manufacture of medicines.

Based on life cycle assessment, most of the environmental impact of a typical medicine is generated during manufacturing operations. This project will address gradual changes in the reduction of virgin resource consumption, greenhouse gas emissions (GHG), waste generation and water consumption and minimise contaminating effluents from industry. This would be achieved by the development/introduction of shorter manufacturing routes, lower energy processes, reductions in solvent and chemical use, the introduction of biorenewable materials, and the replacement of substances of concern (e.g. PFAS = poly- and perfluorinated alkyl substances, chlorinated organic solvents) with more benign alternatives (which may be commercially available or under development) like aqueous-based reagents.

Establishing diversified sustainable supply chains of raw materials that are independent of volatile market situations will promote the security of medicines as finished products by the European healthcare industry and contribute to the health of European citizens by safeguarding the continuous availability of drugs for patients. The new chemical technologies developed will provide access to newly discovered fine chemicals and pharma building blocks. This will allow industries to become independent of fossil-based raw materials like crude oil and strengthen the European science and technology community.

The harmonisation of environmental sustainability assessment methodologies across the whole healthcare sector will influence European environmental regulations to make life cycle assessments (LCA) comparable between different pharmaceutical manufacturing processes and will contribute to establishing a novel European LCA guideline, aligned with the EU Product Environmental Footprint<sup>97</sup> methodology and its underlying relevant methods and standards.

The project will provide a recognised contribution from the life science sector to the Green Deal<sup>98</sup> and Chemicals Strategy for Sustainability<sup>99</sup> of the European Union, in line with the Pharmaceutical Strategy for Europe<sup>100</sup>.

<sup>96</sup> Environmental considerations in the selection of medical staplers: A comparative life cycle assessment, Journal of Cleaner Production, 371, 2022, 133490.

<sup>97</sup> [https://eplca.jrc.ec.europa.eu/permalink/PEF\\_method.pdf](https://eplca.jrc.ec.europa.eu/permalink/PEF_method.pdf)

<sup>98</sup> [https://ec.europa.eu/info/strategy/priorities-2019-2024/european-green-deal\\_en](https://ec.europa.eu/info/strategy/priorities-2019-2024/european-green-deal_en)

<sup>99</sup> [https://environment.ec.europa.eu/strategy/chemicals-strategy/implementation\\_en](https://environment.ec.europa.eu/strategy/chemicals-strategy/implementation_en)

<sup>100</sup> <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:52020DC0761>

## Expected outcomes

We expect all of the following outcomes to be generated from the topic.

1. Generation of novel, process-intensified manufacturing methods and unit operations according to safe and sustainable by design (SSbD) principles with the following goals.
  - a. Reducing solvent volumes in chemical synthesis and cleaning operations: Large volumes of pure and high-quality organic solvents are required for pharmaceutical manufacturing without ever being reused or recovered. The goal is to identify ways to either eliminate solvents, by increasing the usage of water-based reactions; reuse solvents; or more preferably avoid entirely the use of high solvent volumes. Innovative methods (e.g. surface functionalisation) of cleaning and rinsing techniques (equipment, medical devices) need to be developed to minimise solvent waste.
  - b. Replacement of substances of concern:
    - i. by either replacing reagents with less toxic chemicals, e.g. replacements of chlorinated solvents, toxic reagents, heavy metal based homogeneous catalysts;
    - ii. by identifying alternative routes to target the chemical transformation, e.g. through catalytic or biocatalytic rather than stoichiometric chemical transformations, or by reducing the overall number of steps (e.g. through cascade reactions) with a significant impact on the use of solvents and chemicals.
  - c. Reducing total water volumes in fermentation processes (both upstream and downstream) by innovative fermentation designs, e.g. continuous manufacturing, perfusion technology and reusable downstream processing aids, or preferably by reducing or recycling the purified water (PW), and particularly high quality water (e.g. sterile water for injection (WFI)) volumes.
  - d. New fermentation/cultivation and purification technologies (e.g. alternatives to chromatography or innovative chromatography technologies, buffers and resins) with reduced water and energy demands.
  - e. Reducing energy consumption in chemical or biotechnological processes: Heating, cooling and sterilisation / cleaning in place (CIP/SIP) operations are energy intensive. Use of alternative chemical transformation steps or sterilisation techniques should help to reduce energy consumption.
  - f. Harvesting new sources of raw materials other than fossil sources to have reliable access to readily-available starting materials, solvents, reagents, homogeneous catalysts (where possible transition metal based or, if necessary, rare earth metal based) or biocatalysts (enzymes for catalytic chemical transformations).
  - g. Changing biomanufacturing<sup>101</sup>: Many biotechnological manufacturing processes rely on single-use equipment, consumables and materials, and this contributes to an increase in solid waste generation, especially plastics. Novel single-use materials will be developed from renewable sources with the possibility of recovering valuable materials like transition metals/rare earth metals from electronic

<sup>101</sup> The term "biomanufacturing" describes all manufacturing methods that utilize prokaryotic or eukaryotic cell systems to produce biomolecules for use in medicines (e.g. therapeutic proteins, monoclonal antibodies (mABs), mRNA for vaccines) or chemical synthesis (e.g. enzymes).

components of single-use equipment (single-use reactors, electrodes, probes etc.) or using single-use equipment manufactured from renewable resources.

2. According to the World Economic Forum 2022 report, the pharmaceutical industry is fuelling the climate crisis where the sector is responsible for 4.4% of global emissions and its CO<sub>2</sub> footprint is forecast to triple by 2050<sup>102</sup>. Reducing the generation of greenhouse gases (mainly CO<sub>2</sub>, methane, nitrous oxide) is a key element to preventing climate change. Any attempt to improve the efficiency and environmental compatibility of a manufacturing process under development is expected to reduce the generation of GHGs everywhere on the planet. A thorough assessment of the origins and the life cycles of all chemicals, reagents, solvents and API (active pharmaceutical ingredient) drug substances procured must be performed to have a complete cradle-to-gate analysis of the GHG generation to be measured as GHG footprint per mass/dose/treatment. All changes in manufacturing processes should include considerations of the economic impacts. This includes the development of thresholds for the recovery and reuse of solvents.
3. All aspects of process designs should be quantified in standardised assessment systems comprising as many influence factors as possible to describe the full environmental impact of a single drug product on everybody's environment. Artificial intelligence (AI) / machine learning (ML) driven technology should help to sharpen the full picture of the environmental impacts from material supplies via manufacturing to the consumer and waste (= cradle-to-gate analysis). A publicly accessible digital toolbox will be developed that guides development chemists, biotechnologists and engineers to create the best possible manufacturing processes that produce safe and high-quality products with the minimum environmental impact possible.
4. The harmonisation of assessment systems<sup>103</sup> across the healthcare industry is expected to be incorporated into European environmental guidelines, and standards aligned with existing standards outside the scope of the EC.

## Scope

Many programmes launched on green chemistry and green pharmaceuticals (e.g. Innovative Medicines Initiative [IMI] projects like CHEM21 and iCONSENSUS, or HORIZON-HLTH-2021-IND-07-01 projects) aim to demonstrate the technical feasibility of applying new methods to improve the overall efficiency and robustness of single manufacturing steps and how to assess their impact on the environment.

The scope of this topic is as follows.

- To transfer approaches from green chemistry and technology into biomanufacturing by developing new types of upstream and downstream processing methods with increased efficiency, more balanced energy consumption and less waste (stainless steel vs. single-use equipment), continuous manufacturing (perfusion cell cultures vs. fed-batch), and the production of enzymes as process reagents in the manufacture of pharmaceutical products.
- To apply innovative technology to the chemical synthesis of e.g. small molecules, oligonucleotides, peptides and vaccines, by removal of hazardous chemicals, and streamline manufacturing processes and energy consumption, mainly by introducing new production and analytical technologies using "greener" solvents, smaller solvent volumes (e.g. mechanochemistry, alternatives to chromatography),

<sup>102</sup> <https://www.weforum.org/agenda/2022/11/pharmaceutical-industry-reduce-climate-impact>

<sup>103</sup> Assessment System means a set of measures that collects and analyses data of raw materials, consumables, equipment performance, and unit operations to evaluate and improve the performance of inputs, the unit, and its output.



continuous manufacturing processes (e.g. flow-chemistry) and emphasising catalysis and enzymatic chemistry. More sustainable sterilisation processes as alternative to ethylene oxide sterilisation for devices.

- To identify, characterise and test novel replacement materials for single-use equipment and process aids (tubing, bags, PVCs (polyvinyl chlorides)) based on materials from renewable sources, e.g. BioPET (biorenewable polyethylene terephthalate).
- To create new life cycle assessments (LCA) of drug substances and drug products of all (including new modalities<sup>104</sup>) to gain a holistic view of the end-to-end environmental impact of all materials, energies, chemicals and wastes involved in the production of medicines, with the ultimate goal of achieving comparability of diverse manufacturing processes, technologies and products, e.g. chemical entities (tablets / liquid formulations) or biologics (lyophilised / liquid formulations).
- To promote diversified value/supply chains resulting in a shift away from dependencies on specific suppliers and ingredients, thereby promoting the security and resilience of the European pharmaceutical and healthcare industry and the health of European citizens.
- To harmonise and standardise the definitions, manufacturing ontologies, methodologies and frameworks for environmental impact assessment (e.g. LCA standards) of healthcare, including pharmaceutical products, across the European healthcare sector, and align with industries outside the EU (north America, Asia, UK etc.).
- To evaluate the applicability and relevance of the proposed solutions, existing impact assessments (e.g. life cycle assessments, based on existing industry standards, e.g. the standard developed by the Sustainable Markets Initiative, SMI) should be performed to show superiority in comparison to existing approaches.

Previous and current projects (cf. HORIZON-HLTH-2021-IND-07-01 projects IMPACTIVE, ENVIROMED, ETERNAL, SusPHARMA and TransPharm) have a strong focus on the environmental impact of current and new manufacturing technologies at low technology readiness level (TRL) using life cycle assessments. In this project, the industrialisation of new technology is pursued more intensively and on a larger scale at higher TRL by all partners. In this project, the standardisation of environmental impact assessment methodologies (e.g. LCA) of industrial processes is prioritised rather than the individual assessment of new technologies.

Continuous alignment and exchange with the relevant projects from the existing Horizon Europe and IMI programmes will avoid duplication of the work and allow for the harmonisation of scientific efforts.

Resources and learnings from previous and ongoing initiatives (e.g. projects funded under IMI1 / IMI2<sup>105</sup> or other Horizon 2020, Horizon Europe, NextGenEU and EU4Health projects) should also be taken into consideration.

Current projects like IMI project PREMIER<sup>106</sup> demonstrate the impact of drug substances, by bioaccumulation, in living organisms and mobility across the environment. In contrast, the aim of this project

<sup>104</sup> The term “modality” includes biologically active macromolecules like proteins, oligopeptides, oligonucleotides/mRNA, vaccines, and protein conjugates.

<sup>105</sup> Findings from the IMI-funded projects [CHEM21](#) and [iCONSENSUS](#) may be relevant. The CHEM21 project aimed to identify reactions and methodologies that addressed bottlenecks in the sustainability of processes applied to the synthesis of active pharmaceutical ingredients (APIs). The iCONSENSUS project aims to develop innovative analytical, hardware, software and high-throughput tools for the development, monitoring and control of mammalian cell cultivation processes for the production of biopharmaceuticals.

<sup>106</sup> <https://imi-premier.eu/>



is to avoid the accumulation or distribution of any substances of concern in nature and therefore identify new transformations that can replace stoichiometric or catalytic use of toxic reagents or catalysts, respectively.

Most fine chemicals originate from fossil sources. Creative utilisation of new sources is the key to directing our future manufacturing efforts into a more sustainable production of second-generation fine chemicals and drugs. Developing new skills and technologies by exploring renewable sources for the bulk production of chemical starting materials of high quality based on European research networks promotes and facilitates Europe's independence from raw material sources outside Europe and diversifies global supply chains. This will make sensitive supply chains more stable and guarantee reliable patient care in Europe.

The compilation of life cycle assessment data is a time-consuming and cost intensive process, requiring the collection of a large amount of data on raw materials, consumables, transport, manufacturing utilities, devices and other materials needed during the use phase and waste treatment of pharmaceutical products. Therefore, LCAs are created when the asset has already reached a mature development state. Early involvement of product environmental data can help guide development scientists in a more sustainable and overall impactful direction of manufacturing processes and technologies. While ongoing projects such as TransPharm<sup>107</sup> focus on developing new impact assessment methodologies for assessing the sustainability of pharmaceuticals, the project in this call will be complementary by applying harmonised standards for LCA. A harmonised set of standard data will be applied in close collaboration with SMI (Sustainable Markets Initiative) in this project based on a common set of product category rules (PCR), which will be fed into a shared database and digital planning tool that enables a non-expert user to investigate the environmental impact of new process designs, or later process or product changes. EU PEF / PEFCR (= product environmental footprint / product environmental footprint category rules) will be a key reference and over-arching starting point for a medicine-specific Product Environmental Footprint standard.

This project will therefore focus on the standardisation and harmonisation of assessing and scoring the environmental performance of systems across industry: healthcare and API manufacturing by chemical and biotech companies. They have developed a strong commitment to sustainability by design approaches over the past years with individually developed life cycle assessment methodologies to evaluate the environmental impact of their respective process developments and improvements. All methodologies lack a common framework of metrics and quantitative sets of descriptors to allow comparability of identical unit operations with different assessment systems.

The Chemicals Strategy for Sustainability has as its objective the transition towards safer and more sustainable chemicals in line with the SSbD principles. It will require that industry minimises, substitutes as far as possible, and phases out the most harmful chemicals in healthcare products whilst at the same time ensuring the sustainability / availability, safety, quality and efficacy of these products.

The early involvement of European regulatory authorities, both related to environmental footprinting requirements and from a medicine manufacturing perspective, are essential for the harmonisation of standards with existing European directives.

Besides this topic, another topic in this IHI call entitled "Safe & sustainable by design (SSbD) packaging and single use device solutions for healthcare products" will cover the reduction of waste, the recyclability and circularity as well as renewable feedstock of packaging materials. The impact of innovative packaging and device materials on the life cycle assessment (LCA) of the healthcare products will be investigated in this SSbD project. In order to jointly develop new strategies to ensure a greener healthcare industry along the whole value chain, and to avoid overlaps, a close collaboration between the two topics is essential and

<sup>107</sup> <https://transforming-pharma.eu/>

should be reflected by providing dedicated resources in both projects to align on common LCA methodologies and LCA data.

### Why the expected outcomes can only be achieved by an IHI project

Public partners/ small and medium-sized enterprises (SMEs): European science and technology is extremely powerful at collaborating on very basic research in order to create new manufacturing technologies and identifying alternatives to substances of concern (reagents/chemicals) used for manufacturing or as components of materials with direct contact to drug substances (e.g. primary packaging, process aids etc). The development of innovative and truly sustainable manufacturing technology and chemistry requires a highly skilled and modern academic research and innovation network that comprises university research groups, publicly funded research institutes and SMEs. The transformation of industrial manufacturing processes can only start with new knowledge developed and learnings shared from within independent research laboratories in science, engineering and novel therapeutic technologies. The wide scientific and industrial network of the partners in this consortium should serve as a starting point for an exchange with external partners in order to be able to implement the innovations more efficiently.

SMEs with unique platform technologies will feed new aspects into well-established material supply chains and manufacturing.

A project management office will provide administrative support to run the project.

Fine chemical and API manufacturers are the link between pharmaceutical or biotechnological industries and raw material suppliers. They play a key role in the overall life cycle of drug substance manufacturing as providers of chemical building blocks, bulk reagents, solvents and process materials.

Industrial partners will transfer research outcomes into industrial manufacturing practice and demonstrate the scalability of processes and validate the usability of new materials. Industry partners will assess any new ideas for their transferability into a commercial and scalable process to maintain the quality and safety of products and guarantee the safety and efficiency of a novel manufacturing process.

All partners, in combination with regulators, will eventually establish a cross-sectoral, harmonised standard life cycle assessment tool to quantify the environmental impact of different manufacturing routes in development that allows decisions to be made based on data rather than the experience of scientists. This tool should have the capacity to quantitatively support the selection of the most efficient and environmentally benign process by using real world data and innovative digital capabilities such as AI and ML.

### Pre-identified industry consortium

The pre-identified industry consortium that will contribute to this cross-sectoral IHI project is composed of the following pharmaceutical and medical technology industry partners:

- AstraZeneca
- Abbvie
- Boehringer Ingelheim
- GlaxoSmithKline
- Janssen
- Medtronic

- Merck KGgA
- Novo Nordisk
- Olon
- Pfizer
- Sanofi (Lead)
- Servier
- SwiftPharma

In the spirit of partnership, and to reflect how IHI two-stage call topics are built upon identified scientific priorities agreed together with a number of proposing industrial beneficiaries, it is envisaged that IHI proposals and projects may allocate a leading role within the consortium to an industrial beneficiary. Within an applicant consortium discussing the full proposal to be submitted for the second stage, it is expected that one of the industrial beneficiaries may become the coordinator or the project leader.

Therefore, to facilitate the formation of the final consortium, all beneficiaries are encouraged to discuss the weighting of responsibilities and priorities with regard to such leadership roles. Until such roles are formalised by execution of the Grant Agreement, one of the proposing industrial leaders shall facilitate as project leader an efficient drafting and negotiation of project content and required agreements.

### **Indicative budget**

The maximum financial contribution from IHI is up to EUR 20 550 000.

The indicative in-kind and financial contribution from industry partners is EUR 20 550 000.

Due to the global nature of the participating industry partners, it is anticipated that some elements of the contributions will be in kind contributions to operational activities from those countries that are neither part of the EU nor associated to the Horizon Europe programme.

The indicative in-kind contribution from industry partners may include in-kind contributions to additional activities (IKAA).

### **Indicative duration of the action**

The indicative duration of the action is 60-72 months.

This duration is indicative only. At the second stage, the consortium selected at the first stage and the predefined industry consortium may jointly agree on a different duration when submitting the full proposal.

### **Contribution of the pre-identified industry consortium**

The industry consortium expects to contribute to the IHI project by providing the following expertise and assets:

- Expertise in the development of drug substance and product manufacturing processes, aspects of environmental and occupational safety, cost efficiency, procurement of materials, energies and manufacturing equipment (e.g. supply chains, transportation, energy supply).
- Manufacturing equipment to scale up innovative technologies into the pilot plant scale and run test batches.
- Chemistry, manufacturing and controls (CMC) expertise in the development of new chemical entities or new modalities in terms of quality, patient safety, patient drug delivery systems and economy.
- Provide specifications on product categories and product data to feed the harmonised LCA methodology.

- Provide user requirements, delivery of manufacturing data to generate and feed the LCA tool.
- Provide user requirements to lead the development of new planning tools for safe and sustainable by design (SSbD) tools.
- The overall split of efforts should be 70%-80% investigation of new technologies, and 20%-30% creation of new standards/LCA tools in this project.
- Collaboration with other initiatives, e.g. SMI (Sustainable Markets Initiative), the ACS GCI Pharmaceutical Round Table, the British Standards Institute (BSI) and PEG (Pharmaceutical Environment Group) to harmonise efforts to define new standards of PCR (product category rules) and LCA.

## Applicant consortium

The first stage applicant consortium is expected, in the submitted short proposal, to address the entire scope and deliver on the expected outcomes of the topic, taking into account the expected contribution from the pre-identified industry consortium.

The applicant consortium is expected to address all the research objectives and make key contributions to the defined deliverables in synergy with the industry consortium.

A project management office is expected to be member of the applicant consortium to provide the administrative support to run the project.

Applicants should clearly outline their approach for data capture, storage and sharing within the consortium as well as sharing results through peer-reviewed publications or other mechanisms. They must ensure that the relevant results and data repositories will be sustainable after the end of the project and made public.

Applicant consortia shall in addition provide the following expertise or resources.

### Grant administration

To provide financial administration, submission of deliverables, periodic reports etc.

### Project management

- To coordinate internal communication and meetings, general oversight and management of communication, exploitation and dissemination activities, risk management.
- To provide and maintain an IT infrastructure, to develop and implement an efficient data governance and management strategy of the joint consortium according to adequate standards and deliver the “data management plan”.
- To coordinate networking, joint activities and synergies with other European initiatives, or other relevant groups (e.g. Horizon Europe and IHI projects).
- To develop a strategy for the exploitation and sustainability of project results and outcomes and deliver the “exploitation and sustainability plan”.

**Interactions with regulatory authorities, health technology assessment (HTA) bodies, payers, policy makers, and advocacy groups**

- To contribute to the regulatory landscape for life cycle assessment standards in the EU and in other non-EU European countries.
- In conjunction with industry, to discuss with regulatory authorities, standards bodies, and advocacy groups the acceptability and implementation of the LCA metrics in the EU and harmonisation with efforts in other non-EU European countries and the US.
- To prepare relevant documents regarding the approach used and the results generated by the project (e.g. briefing books, European Medicines Agency [EMA] guidance documents).

## Technology

- Continuous manufacturing technology (flow chemistry, perfusion cell culture) in combination with online monitoring and in-process control.
- Innovative technology in manufacturing new chemical entities (NCE):
  - demonstrated expertise in pharmaceutically relevant chemical chemistry;
  - compulsory expertise: chemo catalysis and biocatalysis;
  - optional expertise: photochemistry, mechanochemistry, cell-based chemical transformations (oxidations, functionalisations).
- Innovative technology in manufacturing new biological entities (NBE):
  - new fermentation/cultivation technology with low volumes/low energy;
  - demonstrated expertise in pharmaceutically relevant expression systems;
  - innovative chromatography technologies, alternative purification technologies or other purification technologies replacing chromatography;
  - low energy utility preparation (e.g. WFI, steam);
  - ontologies in biomanufacturing.
- Innovative technology in manufacturing new medical devices (MD):
  - cleaning technology avoiding the use of solvents and detergents;
  - sustainable sterilisation processes (e.g. irradiation, supercritical CO<sub>2</sub>);
  - analytical methods to track chemical residues in medical devices;
  - checking the safety of new cleaning and/or sterilisation processes according to ISO10993 requirements;
  - cleaning & sterilisation process design based on SSbD framework principles.
- Innovative chromatography.

- Low energy, low solvent volume processes including reactions in/on water and recycling technologies.
- Utilisation and supply of raw materials, fine chemicals, consumables and solvents from renewable sources.
- Reuse technology of organic and aqueous solvents and catalysts to address waste reduction.
- Replacement of substances of concern to avoid regrettable substitutions.
- Expertise in conducting life cycle assessments of pharmaceutical products.
- Knowledge about existing LCA standards, tools and data for chemical and (bio)pharmaceutical products.
- AI/ML supported process design based on SSbD principles.
- Network with healthcare providers and regulatory stakeholders.

At the second stage, the consortium selected at the first stage and the pre-identified industry consortium will form the full consortium. The full consortium will develop in partnership the full proposal, including the overall structure of the work plan and the work packages, based upon the selected short proposal at the first stage.

### **Dissemination and exploitation obligations**

The specific obligations described in the conditions of the calls and call management rules under “Specific conditions on availability, accessibility and affordability” do not apply.

<p><b>HORIZON-JU-IHI-2023-04-01</b></p> <p><b>Expanding translational knowledge in minipigs: a path to reduce and replace non-human primates in non-clinical safety assessment</b></p>	<p>The maximum financial contribution from IHI is up to EUR 8 500 000.</p> <p>The indicative in-kind contribution from industry partners is EUR 8 910 000.</p> <p>The indicative in-kind and financial contribution from IHI JU contributing partners is EUR 492 000.</p>	<p>Research and Innovation Action (RIA)</p> <p>Two-stage submission and evaluation process.</p> <p>Only the applicant consortium whose proposal is ranked first at the first stage is invited for the second stage.</p>
<p><b>HORIZON-JU-IHI-2023-04-02</b></p> <p><b>Patient-centric blood sample collection to enable decentralised clinical trials and improve access to healthcare</b></p>	<p>The maximum financial contribution from IHI is up to EUR 4 500 000.</p> <p>The indicative in-kind and financial contribution from industry partners is EUR 3 574 000.</p> <p>The indicative in-kind contribution from IHI JU contributing partners is EUR 300 000.</p>	<p>Research and Innovation Action (RIA)</p> <p>Two-stage submission and evaluation process.</p> <p>Only the applicant consortium whose proposal is ranked first at the first stage is invited for the second stage.</p>
<p><b>HORIZON-JU-IHI-2023-04-03</b></p> <p><b>Inclusive clinical studies for equitable access to clinical research in Europe</b></p>	<p>The maximum financial contribution from IHI is up to EUR 33 000 000.</p> <p>The indicative in-kind contribution from industry partners is EUR 33 600 000.</p> <p>The indicative in-kind and financial contribution from IHI JU contributing partners is EUR 250 000.</p>	<p>Research and Innovation Action (RIA)</p> <p>Two-stage submission and evaluation process.</p> <p>Only the applicant consortium whose proposal is ranked first at the first stage is invited for the second stage.</p>
<p><b>HORIZON-JU-IHI-2023-04-04</b></p> <p><b>Establishing novel approaches to improve clinical trials for rare and ultra-rare diseases</b></p>	<p>The maximum financial contribution from IHI is up to EUR 8 500 000.</p> <p>The indicative in-kind and financial contribution from industry partners is EUR 9 100 000.</p>	<p>Research and Innovation Action (RIA)</p> <p>Two-stage submission and evaluation process.</p> <p>Only the applicant consortium whose proposal is ranked first at the first stage is invited for the second stage.</p>

<p><b>HORIZON-JU-IHI-2023-04-05</b></p> <p><b>Safe &amp; Sustainable by Design (SSbD) packaging and single use device solutions for healthcare products</b></p>	<p>The maximum financial contribution from IHI is up to EUR 8 300 000.</p> <p>The indicative in-kind and financial contribution from industry partners is EUR 8 300 000.</p>	<p>Research and Innovation Action (RIA)</p> <p>Two-stage submission and evaluation process.</p> <p>Only the applicant consortium whose proposal is ranked first at the first stage is invited for the second stage.</p>
<p><b>HORIZON-JU-IHI-2023-04-06</b></p> <p><b>Sustainable circular development and manufacturing of healthcare products and their quantitative environmental impact assessment</b></p>	<p>The maximum financial contribution from IHI is up to EUR 20.550.000.</p> <p>The indicative in-kind and financial contribution from industry partners is EUR 20.550.000.</p>	<p>Research and Innovation Action (RIA)</p> <p>Two-stage submission and evaluation process.</p> <p>Only the applicant consortium whose proposal is ranked first at the first stage is invited for the second stage.</p>



## 6.3 IHI JU call 5

### Topic 1: Accelerating the implementation of New Approach Methodologies and other innovative non-animal approaches for the development, testing and production of health technologies

#### Expected impacts to be achieved by this topic

The work supported under this topic seeks to pursue the aims of Directive 2010/63/EU<sup>108</sup> on the protection of animals used for scientific purposes. It also contributes to the implementation of the 3Rs principles to “replace, reduce and refine the use of animals”, and ultimately helps progress towards no use of animals or animal-sourced materials in research, innovation and development, which is an expectation of society.

The following impacts are expected.

- Break down silos between technological areas and disciplines, and bring together different stakeholders (e.g. health industry, academia, small and medium-sized enterprises (SMEs), patients, regulators, non-governmental organisations (NGOs) and policy makers) to foster the use of new approach methodologies<sup>109</sup> (NAMs) and other non-animal approaches in the efficient development, testing and production of safe and effective innovative health technologies<sup>110</sup> (e.g. medicinal products, medical devices, biopharmaceuticals, vaccines, *in vitro* diagnostics) and their combinations.
- Improve public health as patients will benefit faster from safe and effective health technologies developed using NAMs and other non-animal approaches that, where relevant, provide more human-relevant data and are more predictive than current approaches.
- Foster the development of health policies and standards on the use of NAMs and other non-animal approaches in health technologies which will positively affect public health.
- Enhance the competitiveness of the European health industry that will benefit from high quality innovative approaches and methodologies for the development and production of new health technologies, which can reduce the time and costs of processes while significantly reducing the use of animals or animal-sourced biomaterials.
- Help to make the EU more sustainable/autonomous by achieving regulatory validation and uptake of NAMs and other non-animal approaches for the development, testing and production of health technologies that are not dependent on shortages/issues with animal supply.

#### Expected outcomes

- Research and innovation (R&I) actions (projects) to be supported under this topic must contribute to all the following outcomes.
- Researchers will benefit from the implementation of NAMs and other innovative non-animal approaches which have been assessed and validated for their performance and found to be relevant, reproducible, predictive, and standardised, ultimately leading, as relevant, to their regulatory acceptance for use in

<sup>108</sup> DIRECTIVE 2010/63/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 22 September 2010 on the protection of animals used for scientific purposes (OJ L 276, 20.10.2010, p. 33) <https://eur-lex.europa.eu/eli/dir/2010/63/2019-06-26>.

<sup>109</sup> New approach methodologies, as defined in <https://www.frontiersin.org/articles/10.3389/ftox.2022.964553/full>

<sup>110</sup> Health technology, as defined in the [IHI Strategic Research and Innovation Agenda](#), means a medicinal product, a medical device, or medical and surgical procedures, as well as measures for disease prevention, diagnosis or treatment used in healthcare.

infectious and/or non-communicable disease applications. The new approaches should lead to an improvement in the assessment of health technologies (and animal to human translation where relevant) and/or production processes, and to a significant reduction in the number of animals used. In addition, these approaches may answer questions that current methods cannot, and improve the predictability and robustness of evidence generated for regulatory decision-making.

- European industry will benefit from the establishment and availability of NAMs and other innovative non-animal approaches for the testing, development and/or production of health technologies that are fit-for-purpose to support regulatory decision making.
- Researchers and developers of innovative healthcare solutions will have access to high-quality data, new recommendations and best practices to incentivise the use of NAMs and other non-animal approaches and their integration in industrial processes. This should be supported by an appropriate digital repository to ensure both the sustainability and scalability of the knowledge base.
- Regulators and policy makers will gain knowledge and have access to high-quality data on the characteristics and use of NAMs and other innovative non-animal approaches in the production and development of health technologies to foster the development of harmonised guidance and requirements, as well as uptake or translation into health policies.

## Scope

Animals and animal-derived materials are widely used in biomedical research and in the production and development of health technologies. This raises serious ethical concerns, and there is growing societal pressure to move towards alternative approaches and methods. Besides major ethical concerns, there is also scientific evidence that supports moving away from animal-based approaches and finding more human-relevant methods and strategies for both the assessment of safety and efficacy of new health technologies and for manufacturing. Animal testing requires time-consuming protocols, high costs for animal supply, and the results are not always reproducible and applicable to humans. In addition, for the development and production of health technologies (e.g. *in vitro* diagnostics) as well as in biomedical research in general, materials of animal origin are required (e.g. biomolecules, sera). These animal-derived products require large amounts of animals for their production. Therefore, also in this context, there is a need to foster progress towards new alternatives (e.g. synthetic matrix, recombinant proteins, optimisation of production processes via artificial intelligence) to reduce the overall number of animals that are bred for these purposes.

NAMs and other innovative non-animal approaches have high potential to improve the development and/or production of health technologies, while contributing to the reduction and replacement of the use of animals. Recent improved biological knowledge, technological advances, computer simulations and innovative non-animal approaches and methods (e.g. organoids, complex 3D cell models, microphysiological systems<sup>111</sup>, *in silico* models, non-animal derived antibodies and other biomolecules<sup>112</sup>) provide the opportunity to move forward with safer and more effective tools for protecting human health and preventing/treating diseases that would in parallel entail an improvement of animal to human translation or better production processes, as well as helping progress towards the replacement of animals used in biomedical research in general.

While the potential for using non-animal approaches for the production, development and testing of new health technologies is enormous, more evidence and high-quality data for their performance evaluation in

<sup>111</sup> [Microphysiological Systems: Stakeholder Challenges to Adoption in Drug Development - PMC \(nih.gov\)](#)

<sup>112</sup> [EURL ECVAM Recommendation on Non-Animal-Derived Antibodies](#)

comparison with established animal-based approaches for a specific application (such as a production process, primary pharmacology, or next-generation-risk-assessment – NGRA) and for their validation are required by the industry and regulators to implement these alternative approaches in R&D and decision-making processes. In addition, policy makers require a large body of up-to-date, high-quality knowledge to inform relevant health policies and ensure the long-term goal of full transition to non-animal approaches.

The current topic seeks to address these challenges by exploiting the latest relevant scientific advancements to develop NAMs and other non-animal approaches, which could be more readily available and more efficient than those involving animals, and which should improve either the development, including efficacy and safety assessment, of new health technologies for infectious/non-communicable diseases or the production processes of such technologies.

The projects funded under this topic should aim to do the following.

- Develop new NAM/s or other non-animal approach/es (or a combination of those) or use existing ones in an innovative way to improve (early-stage) assessment of new health technologies (and animal to human translation where relevant), or to improve the production processes of health technologies (such as bio/pharmaceuticals, vaccines, medical devices including *in vitro* diagnostics, and radio-chemicals).
- Specify the context of use (e.g. primary pharmacology, toxicology, safety, quality control, production processes) of the novel approach/es, how it/they can be integrated efficiently in the relevant workflows and propose and implement a plan to carry out their performance evaluation and validation, as well as demonstrate their added value in comparison to relevant established animal-based approaches.
- Make a comparative evaluation of the different approaches to replace, reduce and refine animal use, including the identification and assessment of parameters that influence their usefulness such as their reliability, reproducibility, robustness and fitness for purpose.
- Generate evidence on the robustness, reliability, and applicability of these novel approaches in an industrial research and development (R&D) context and to support regulatory decision making in testing, development or production of health technologies, as relevant. Accordingly, applicants should develop a strategy/plan for generating appropriate evidence to support regulatory acceptance and engage with regulators in a timely manner (e.g. through the European Medicines Agency [EMA] Innovation Task Force or qualification advice).
- Gather and produce high quality datasets to generate a solid knowledge base for supporting the use of NAMs and other non-animal approaches in the field of health technology and drive 3Rs implementation. To ensure the sustainability of the results and foster future development and validation of innovative non-animal approaches, applicants should develop a fit-for-purpose scalable digital data repository. Applicants should consider and leverage as much as possible existing infrastructures.
- Establish a collaboration platform between all relevant stakeholders from public and private sides, including regulatory agencies and policy makers, to exchange information, prepare white papers and guidelines to foster uptake or translation into health policies, supporting an adequately reflected transition to full implementation of non-animal approaches in health technology development and manufacturing. Patients and/or patient organisations may be included and actively contribute to such activities by providing, for example, their insight on the use of human-derived samples, as relevant.

- Accelerate the broad implementation of the NAMs and other non-animal approaches in research through a strong communication and dissemination plan, fostering also exchanges and cross fertilisation with other projects funded in this area.

Projects funded under this topic are expected to contribute to relevant EU health policy initiatives such as the new Industrial Strategy for Europe, the European Health Emergency and Response Authority (HERA) and the EC proposal on the European Health Data Space (EHDS).

Furthermore, applicants are expected to explore and/or implement synergies<sup>113</sup> and complementarities with relevant initiatives/projects, at national, European and international level. They should also consider, as relevant, the activities of the 3Rs Working Party of EMA<sup>114</sup>.

### Why the expected outcomes can only be achieved by an IHI project

Animals and animal-derived materials are widely used by several industry sectors (pharmaceutical, medical devices, *in vitro* diagnostics, vaccines), academia, as well as SMEs for their R&D or manufacturing activities. There is a need to move towards alternatives and accelerate the development and use of NAMs and other non-animal approaches in health technologies.

The exchange of data, expertise and knowledge is currently limited, for example, between the chemical and the pharmaceutical sectors concerning toxicological testing or between different areas of basic and applied research. Therefore, there is a need to generate, compile and share data and knowledge, as well as expertise, across biomedical and health technology sectors.

This topic requires cross-sectorial multidisciplinary private-public partnerships to help address the scientific challenges and accelerate the development and use of effective NAMs and other non-animal approaches in the testing, development, and production of health technologies.

The involvement of patients, regulators and policy makers is also needed to guide and advise on regulatory acceptance criteria, foster acceptance, and to facilitate their uptake or translation into health policies.

### Indicative budget

Applicant consortia will be competing for a maximum financial contribution from IHI up to EUR 30 000 000.

IHI estimates that an IHI financial contribution of between EUR 12 000 000 and EUR 15 000 000 would allow a proposal to address these outcomes appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.

Applicant consortia should ensure that at least 45 % of the action's eligible costs and costs for action-related additional activities are provided by contributions [In-kind contributions to operational activities (IKOP), financial contribution (FC), in-kind contributions to additional activities (IKAA)] from private members and / or contributing partners and the constituent or affiliated entities of the private members and/or of the contributing partners. Contributing partners may not contribute IKAA. Additional activities from industry members and their constituent or affiliated entities may also contribute towards this 45 % threshold, providing these activities are related to the project. Contributing partners do not contribute additional activities. See call conditions for further information.

<sup>113</sup> Examples of synergies at European level (not exhaustive list): [RISK-HUNT3R RISK](#), [Precision Tox](#), [ONTOX](#), projects that will be generated from [HORIZON-HLTH-2024-TOOL-05-06-two-stage topic](#), [HORIZON-HLTH-2024-IND-06-09](#)

<sup>114</sup> [3Rs Working Party \(3RsWP\) plenary meeting - Public session on the 2023 work plan](#)

### **Indicative duration of the actions**

Applicants should propose a project duration that matches the project's activities and expected outcomes and impacts.

### **Dissemination and exploitation obligations**

The specific obligations described in the Conditions of the calls and calls management rules under "Specific conditions on availability, accessibility and affordability" do not apply.

## Topic 2: Development and proof of principle of new clinical applications of theranostics solutions

### Expected impacts to be achieved by this topic

- Improved availability of effective treatments for patients based on multi-modal theranostic<sup>115</sup> solutions.
- Stronger resilience and improved strategic autonomy of Europe's health systems, for example, by implementing new manufacturing capabilities for medical radioisotopes and radiopharmaceuticals (in accordance with the EU SAMIRA<sup>116</sup> action plan).
- Depending on the disease area of the application, contributing to the objectives of Europe's Beating Cancer Plan and the Horizon Europe Mission on Cancer.

### Expected outcomes

Research and innovation (R&I) actions to be supported under this topic must contribute to at least three of the following outcomes:

- Patients will benefit from increased treatment efficacy, reduction of time-to-treat, fewer side effects, and reduced duration of hospitalisation.
- Healthcare professionals benefit from education, training on theranostic treatment approaches, recommendations, and clinical guidelines on the most appropriate use of theranostic solutions.
- European healthcare systems benefit from a broader spectrum of theranostic treatments and improved cost-effectiveness and affordability of theranostic solutions due to scale effects and more robust European supply chains.
- Technology developers, healthcare professionals and patients benefit from increased information on the sensitivity, quantification, stratification and staging of diseases.

### Scope

Multi-modal theranostic solutions, currently dominated by radionuclide-based therapy and companion diagnostics, are emerging as safe, personalised, and effective approaches for the treatment of several diseases. However, the use of such therapies is limited to a few specialised centres with the need to increase clinical treatment capacities, and to widen the arsenal of theranostics, possibly including novel non-nuclear approaches, e.g. enabled by nanotechnologies.

To address this challenge, project(s) funded under this topic should aim at developing new, or innovative combinations of existing multi-modal theranostic solutions including radiopharmaceuticals and/or non-radioactive theranostic solutions. Applicants should clearly identify a disease(s) of unmet public health need, (e.g., oncology, neurology and/or advanced multi-disease conditions) and explain their choice with relevant evidence where possible.

In particular, for the selected disease(s), the project(s) funded under this topic are expected to address all the following objectives:

<sup>115</sup> Theranostics refers to the pairing of diagnostic biomarkers with therapeutic agents that share a specific target in diseased cells or tissues.

<sup>116</sup> The [SAMIRA action plan](#) is the EU's first comprehensive plan for action to support a safe, high quality and reliable use of radiological and nuclear technology in healthcare.

- develop innovative theranostic solutions and consider conducting early phase clinical trial(s) as proof of concept(s) to demonstrate the added value of the proposed theranostic solutions for patients;
- develop tools for the quantification of the chosen disease(s) through the development of novel modalities to ensure proper planning and monitoring of patient care, which may include imaging, artificial intelligence and pathology models;
- facilitate the development of tools to increase European theranostic manufacturing capabilities and treatment capacities, including guidance on quality assurance and improving logistics of supply at the EU level;
- develop education and training materials on the deployment of multi-modal theranostic solutions and their integration in clinical settings including recommendations for the organisation and composition of disease-specific medical expert boards.

In addition, applicants are expected to consider the potential regulatory impact of the results and if relevant develop a strategy/plan for generating appropriate evidence as well as engaging with regulators in a timely manner (e.g., through the EMA Innovation Task Force, qualification/scientific advice).

### **Why the expected outcomes can only be achieved by an IHI project**

Theranostic solutions require a highly multidisciplinary team of specialists for their clinical application and integration in a patient treatment workflow. Furthermore, the production of theranostic pharmaceuticals, based on radionuclides or nanomedicine products, involves and requires specialised knowledge and expertise. Therefore, a cross-sectorial collaboration is necessary for clinical deployment of theranostic solutions between academia, healthcare professionals as well as the health industry sectors which for instance contribute with the production of diagnostic and therapeutic agents and the development of imaging technologies. It is recommended to include regulators in all steps during development and related planning.

### **Indicative budget**

Applicant consortia will be competing for the maximum financial contribution from IHI of up to EUR 25 000 000.

IHI estimates that an IHI financial contribution of between EUR 10 000 000 and EUR 12 000 000 would allow a proposal to address these outcomes appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.

Applicant consortia should ensure that at least 45% of the action's eligible costs and costs for action-related additional activities are provided by in-kind contributions to operational activities (IKOP), financial contributions (FC), or in-kind contributions to additional activities (IKAA) from private members and/or contributing partners and the constituent or affiliated entities of the private members and/or of the contributing partners. Contributing partners may not contribute IKAA. See call conditions for further information.

### **Indicative duration of the actions**

Applicants should propose a project duration that matches the project's activities and expected outcomes and impacts.

### **Dissemination and exploitation obligations**

The specific obligations described in the conditions of the calls and call management rules under 'Specific conditions on availability, accessibility and affordability' apply.

## Topic 3: Improved prediction, detection, and treatment approaches for comprehensive stroke management

### Expected impacts to be achieved by this topic

- Patients will be offered accelerated access to the healthcare system through improved and holistic management of stroke including prevention, diagnosis, treatment, and rehabilitation that will lead to better outcomes for their health.
- Development of advanced visualisation approaches, connected artificial intelligence (AI)-based devices and modelling-based systems supporting health research and innovation (R&I), resulting in wider availability of personalised health interventions to end-users.
- Medical technology, pharmaceutical and biotechnology companies develop and offer integrated, advanced solutions for prevention, diagnosis, and treatment of stroke. This will facilitate coordinated decision-making by the different healthcare professionals involved in the stroke care pathway.
- Better implementation and scale up of existing treatments that have proven to be effective, ensuring wide coverage of the right treatment options for patients at the right time; also avoiding disparities in countries and regions.
- Contribute to the EC proposal for an 'European Health Data Space' (EHDS) by promoting better exchange of, and access to, different types of health data and data generated by health technologies.

### Expected outcomes

Research and innovation (R&I) actions (projects) to be supported under this topic must aim to deliver results that contribute to all the following expected outcomes.

- Patients will benefit from superior healthcare compared to the current standard of care through the availability of a clear pathway for prevention, diagnosis, and treatment of their stroke. This should be achieved by early and rapid diagnosis of stroke, more integrated and precise interventions, and treatment strategies with the patient in the centre.
- Healthcare professionals will have access to integrated patients' health data, improved visualisation, predictive computational models and clinical support decision systems for stroke, and benefit from efficient coordination among and within stages of care and clinical specialities.
- Healthcare systems will benefit from more effective organisation of stroke management and personalisation of care delivery. This will increase treatment and care effectiveness and efficiency.
- Researchers will benefit from access to integrated data, innovative modelling-based tools, and a more patient-centred definition of clinical outcomes after stroke (including patient reported outcome measurement and patient reported experience measurement), which will facilitate the continued improvement and development of future intervention strategies.
- Health care systems, researchers, and industry will benefit from new innovative modelling tools enabling integration and analysis of a wider, actionable range of patient-specific data, including federated analysis of data.



## Scope

Globally, stroke is the second leading cause of death and the third leading cause of disability. One in four people are in danger of stroke in their lifetime<sup>117</sup>.

In Europe in 2017, nearly 1.5 million people suffered a stroke, nine million Europeans lived with a stroke, and more than 430,000 people died due to a stroke. The total cost of stroke in that year was €60 billion. The number of new strokes and the number of people living with stroke is set to rise due to the ageing population of Europe, as age is the greatest, non-modifiable risk factor for stroke<sup>118</sup>.

Stroke is a heterogeneous, multifactorial disease regulated by non-modifiable (e.g., age, sex, family history) and modifiable risk factors (e.g., high density lipid-cholesterol, low density lipid-cholesterol, cigarette smoking) and underlying pathologies (such as diabetes, hypertension, atrial fibrillation) and as such, it requires a multi-factorial approach<sup>119</sup>. However, stroke is a preventable, treatable, and manageable disease and thus the potential to reduce its burden and its long-term consequences exists<sup>120</sup>.

The challenge in stroke management is the lack of efficient and comprehensive pathways along the whole continuum of the disease – including the variation of structural settings depending on the location of the patient (rural vs. central) and between countries. While several effective treatment approaches are available, there are still silos existing between the different stages of care (e.g., primary, acute care, intensive care, chronic hospitalisation, rehabilitation). The implementation of connected healthcare pathways will lead to an improvement in the outcome for the patients and thereby drive efficiency and effectiveness from a clinical and health resource perspective.

Better communication, sharing and integration of data along the whole stroke care pathway has the potential to be a game changer for stroke patients and for the healthcare professionals as well as payers.

Integrating data is key to allow for modelling, artificial intelligence (AI) and machine learning (ML)-based evaluation to identify groups and individual persons at risk and assure early recognition of stroke, thereby providing faster diagnosis and optimal, patient-specific treatment, resulting in better outcomes for patients. Effective, personalised and rapid care is critical and can make a substantial difference between full recovery and possible permanent impairment or death.

Moreover, comprehensive stroke management continues in the post-acute treatment setting and includes long-term follow-up for secondary prevention and rehabilitation. This is important, as a high percentage of patients are readmitted to the hospital or suffer a second stroke. More than a quarter of patients do not adhere to medication and/or have their blood pressure controlled. Patients frequently report that post-stroke follow up is impaired by siloed data between their generalist and specialist care.

Innovative solutions for faster acquisition, integration, and better retention of multiple types of data and better organisation among the various actors across the entire stroke pathway are crucial to achieve optimal prevention and treatment focused on the needs of patients. Use of novel technologies for federated data analytics and interpretation could help in this direction and assist in providing the right treatment to patients in a timely manner, improving their outcomes.

Applicants to this topic should address all the aims below in their proposals.

<sup>117</sup> Feigin VL et al. World Stroke Organisation (WSO): Global Stroke Fact Sheet 2022. *International Journal of Stroke*, 2022;17(1):18–29.

<sup>118</sup> The Economic Impact of Stroke – SAFE (Stroke Alliance Sor Europe) <https://www.safestroke.eu/wp-content/uploads/2020/10/03.-At-What-Cost-EIOS-Full-Report.pdf>

<sup>119</sup> Goldstein LB et al. Primary Prevention of Ischemic Stroke. *Stroke*, 2006;37:1583-1633.

<sup>120</sup> Norrving B et al. Action Plan for Stroke in Europe 2018-2030. *European Stroke Journal*, 2018;3(4):309-336.

- Develop approaches to integrate patient-relevant health data, from primary care / outpatient clinic, hospital, and rehabilitation settings, as relevant, improving data retention along the care pathway. Applicants could consider starting with a focus on patients at higher risk with the possibility to expand to other patients.
- Develop a next generation of systems that promote interoperability of data from different settings (including intensive and acute care units) and support better clinical decision making. Strategic approaches for integration with the EHDS and community-based, collaborative integrated care should be considered.
- Create solutions to foster better access to data for all involved healthcare professionals (primary care, hospital care and after hospital release e.g., rehabilitation) and support exchange of knowledge and information between the different actors – including at the level of algorithms and datasets that can be exchanged under ethically and legally sound conditions.
- Develop innovative tools and approaches, for example ‘virtual human twin’ model approaches and AI/ML for enhanced computational modelling, optimised for transparency to users and non-users, federated data analytics, and visualisation for enhanced output/results view and interpretation. These tools aim at appropriate risk stratification, timely prediction of stroke and stroke recurrence, faster diagnosis, and treatment.
- Propose innovative approaches to improve and expedite diagnostic and treatment decisions for streamlining operations and guiding patients in the continuum of stroke care in a patient-centric way. This should include consideration of the complexity of the organisational dimension.
- Propose approaches to improve implementation and scale-up of treatment in Europe relying on multimodal clinical data capture and their better interpretation and use in patient management and clinical decision-making. This should include consideration of the regional differences in stroke management and access to treatment options across Europe.
- Propose approaches to enhance precision of care delivery as well as improving patient experience and quality of life using new technologies, tools, and educational means (e.g., education on identification of risk factors, signs of stroke, treatment adherence).

### Why the expected outcomes can only be achieved by an IHI project

This topic requires cross-sectorial collaboration, including contributions from all the different healthcare professionals, health data specialists, patients and their care network, academia, as well as the different industry sectors, including medical technology (e.g., focusing on connected care and medical devices) and pharma sector (providing pharmaceutical interventions for stroke). Such a cross-sectional public-private partnership is needed to break the silos in care, bring the necessary diverse expertise together and combine different types of resources to address the challenge of delivering an efficient and comprehensive stroke management focused on patients’ needs.

### Indicative budget

Applicant consortia will be competing for the maximum financial contribution from IHI of up to EUR 40 000 000.

IHI estimates that an IHI financial contribution of between EUR 10 000 000 and 13 000 000 would allow a proposal to address these outcomes appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.

Applicant consortia should ensure that at least 45% of the action's eligible costs and costs for action-related additional activities are provided by contributions [In-kind contributions to operational activities (IKOP), financial contributions (FC), in-kind contributions to additional activities (IKAA)] from private members and/or contributing partners and the constituent or affiliated entities of the private members and/or of the contributing partners. Contributing partners may not contribute IKAA (see call conditions for further information).

### **Indicative duration of the actions**

Applicants should propose a project duration such that it matches project activities and expected outcomes and impacts.

### **Dissemination and exploitation obligations**

The specific obligations described in the conditions of the calls and calls management rules under "Specific conditions on availability, accessibility and affordability" apply.

## Topic 4: Maximising the potential of synthetic data generation in healthcare applications

### Expected impacts to be achieved by this topic

To exploit the full potential of digitalisation and data exchange in health care, this topic is expected to contribute to the following expected impacts:

- wider availability of interoperable, synthetic data generation methodologies and/or datasets facilitating research and development of integrated products and services that will benefit patients;
- improved insight into real-life behaviour and challenges of patients with complex, chronic diseases and co-morbidities thanks to m-health and e-health technologies;
- advanced analytics / artificial intelligence tools supporting health research and innovation resulting in: a) better clinical decision support for increased accuracy of diagnosis and efficacy of treatment; b) faster prototyping and shorter times-to-market of personalised health interventions; and c) better evidence of the added value from new digital health and AI tools, including reduced risk of bias due to improved methodologies.

### Expected outcomes

The proposals should contribute to all of the following expected outcomes:

- academic and industrial researchers should have access to relevant, robust, and generalisable synthetic data generation methodologies, including open source when relevant, to create and share pools of synthetic patient data in specific use cases;
- academic and industrial researchers should have access to relevant, high quality synthetic datasets;
- thanks to better availability of robust synthetic datasets for training data models, healthcare providers and industry should have a wider range of performant AI-based and other data-driven tools to support diagnostics, personalised treatment decision-making and prediction of health outcomes.

### Scope

Healthcare research using individual patient data is often constrained due to restrictions in data access because of privacy, security, intellectual property (IP) and other concerns. Synthetic health data, i.e., data that is artificially created to mimic individual patient data, can reduce these concerns, leading to more rapid development of reliable data-driven methods including diagnostic, precision medicine, decision support and patient monitoring tools. However, while many synthetic data generation (SDG) methods are currently available, it is not always clear which method is best for which use case, and SDG methods for some types of data are still immature. Furthermore, it is still unclear whether highly detailed synthetic data, which are often needed for research, can be categorised as anonymous.

To address these challenges and maximise the opportunity offered by synthetic data, projects funded under this topic should address the following objectives:

- assemble a cross-sectoral public-private consortium including synthetic data experts, public and private data owners, and healthcare solution developers;
- using high-quality public and private datasets, develop / further develop and validate reliable SDG methods for relevant healthcare use cases. The use cases to be explored must be described and justified in the proposal, complement work that is already ongoing, and should:

- ensure the broad applicability of the SDG methods developed and include data types that are not currently adequately addressed, such as device data, image data, genomic data etc;
- include methods to generate: a) fully synthetic datasets that do not contain any real data; b) hybrid datasets composed of a combination of data derived from both real and synthetic data; and c) synthetically-augmented datasets.
- pay particular attention to bias, both in source data and in the SDG methods.
- validate the synthetic data generation methods applied in the project using source data. This should include assessing the risk of re-identification;
- demonstrate the quality and applicability of the synthetic data generated in the project through the development of relevant models;
- encourage the uptake of the results of the project through a strong communication and outreach plan.

Applicants are expected to consider allocating appropriate resources to explore synergies with other relevant initiatives and projects, including the EC proposal for an European Health Data Space (EHDS)<sup>121</sup> when it becomes operational.

### Why the expected outcomes can only be achieved by an IHI project

Development and validation of synthetic data generation methods and tools for data-driven applications requires multidisciplinary collaboration across private and public entities, including public and private data owners, healthcare solution developers, and synthetic data experts.

### Indicative budget

Applicant consortia will be competing for the maximum financial contribution from IHI up to EUR 20 000 000.

IHI estimates that an IHI financial contribution of around EUR 10 000 000 would allow a proposal to address these outcomes appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.

Applicant consortia should ensure that at least 45% of the action's eligible costs and costs for action-related additional activities are provided by in-kind contributions to operational activities (IKOP), financial contributions (FC), or in-kind contributions to additional activities (IKAA) from private members and/or contributing partners and the constituent or affiliated entities of the private members and/or of the contributing partners. Contributing partners may not contribute IKAA. See call conditions for further information.

### Indicative duration of the actions

Applicants should propose a project duration that matches project activities and expected outcomes and impacts.

### Dissemination and exploitation obligations

The specific obligations described in the conditions of the calls and call management rules under 'Specific conditions on availability, accessibility and affordability' do not apply.

<sup>121</sup> [https://health.ec.europa.eu/ehealth-digital-health-and-care/european-health-data-space\\_en](https://health.ec.europa.eu/ehealth-digital-health-and-care/european-health-data-space_en)

<p><b>HORIZON-JU-IHI-2023-05-01</b></p> <p><b>Accelerating the implementation of New Approach Methodologies and other innovative non-animal approaches for the development, testing and production of health technologies</b></p>	<p>Applicant consortia will be competing for the maximum financial contribution from IHI of up to EUR 30 000 000.</p> <p>Applicant consortia must ensure that at least 45 % of the action's eligible costs are provided by contributions from industry members, their constituent or affiliated entities, and contributing partners.</p>	<p>Research and Innovation Action (RIA)</p> <p>Single-stage submission and evaluation process.</p> <p>Proposals submitted will be evaluated and ranked in one single list. Several proposals might be invited to conclude a Grant Agreement, depending on the budget availability and their ranking.</p>
<p><b>HORIZON-JU-IHI-2023-05-02</b></p> <p><b>Development and proof of principle of new clinical applications of theranostics solutions</b></p>	<p>Applicant consortia will be competing for the maximum financial contribution from IHI of up to EUR 25 000 000.</p> <p>Applicant consortia must ensure that at least 45 % of the action's eligible costs are provided by contributions from industry members, their constituent or affiliated entities, and contributing partners.</p>	<p>Research and Innovation Action (RIA)</p> <p>Single-stage submission and evaluation process.</p> <p>Proposals submitted will be evaluated and ranked in one single list. Several proposals might be invited to conclude a Grant Agreement, depending on the budget availability and their ranking.</p>
<p><b>HORIZON-JU-IHI-2023-05-03</b></p> <p><b>Improved prediction, detection, and treatment approaches for comprehensive stroke management</b></p>	<p>Applicant consortia will be competing for the maximum financial contribution from IHI of up to EUR 40 000 000.</p> <p>Applicant consortia must ensure that at least 45 % of the action's eligible costs are provided by contributions from industry members, their constituent or affiliated entities, and contributing partners.</p>	<p>Research and Innovation Action (RIA)</p> <p>Single-stage submission and evaluation process.</p> <p>Proposals submitted will be evaluated and ranked in one single list. Several proposals might be invited to conclude a Grant Agreement, depending on the budget availability and their ranking.</p>
<p><b>HORIZON-JU-IHI-2023-05-04</b></p> <p><b>Maximising the potential of synthetic data generation in healthcare applications</b></p>	<p>Applicant consortia will be competing for the maximum financial contribution from IHI of up to EUR 20 000 000.</p> <p>Applicant consortia must ensure that at least 45 % of the action's eligible costs are provided by contributions from industry members, their constituent or affiliated entities, and contributing partners.</p>	<p>Research and Innovation Action (RIA)</p> <p>Single-stage submission and evaluation process.</p> <p>Proposals submitted will be evaluated and ranked in one single list. Several proposals might be invited to conclude a Grant Agreement, depending on the budget availability and their ranking.</p>



## Contact

Tel +32 (0)2 221 81 81  
infodesk@ihi.europa.eu

**Postal address:**  
IHI JU - TO56  
1049 Brussels – Belgium

**Visiting address:**  
Ave de la Toison d'Or 56-60  
1060 Brussels – Belgium

[ihi.europa.eu](http://ihi.europa.eu)

 [@IHIEurope](https://twitter.com/IHIEurope)