innovative health initiative

IHI

11th Call for proposals

Two-stage call

COCIR efpia EuropaBio MedTech Europe from diagnosis to cure Vaccines Europe Co-funded by the European Union

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Introduction

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 and builds on the experience gained from the Innovative Medicine Initiative 2 Joint Undertaking (IMI2 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.

Call conditions for single stage and two-stage calls

For Call 11 please refer to the conditions relevant to the two-stage call

The submission deadline for short proposals (SPs) will be 09/10/2025 and the full proposals (FPs) submission deadline will be 29/04/2026.

Scientific evaluation of the SPs and FPs under the two-stage call will be completed by 2026. GAP will be completed within 3 (three) 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).

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 2023-2025 shall apply *mutatis mutandis* to the calls for proposals covered by this amended Work Programme, including the "Restrictions for the protection of European communication networks" under General Annex B. 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 amended 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.

GENERAL CONDITIONS RELATING TO THE IHI JU CALLS

Admissibility conditions	The conditions are described in General Annex A.
Eligibility conditions	The conditions are described in General Annex B.
Financial and operational capacity and exclusion	The conditions are described in General Annex C.
Award criteria	The criteria are described in General Annex D.
Documents	The documents are described in General Annex E.
Procedure	The procedure is described in General Annex F.
Legal and financial set-up of the grant agreements	The conditions are described in General Annex G.

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

STANDARD ADMISSIBILITY CONDITIONS, PAGE LIMITS AND SUPPORTING DOCUMENTS

General Annex A ('Admissibility') to the Horizon Europe Work Programme 2023-2025 shall apply *mutatis mutandis* for the calls for proposals covered by this amended 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 the first stage of a two-stage call, the limit for RIA short proposals is 20 pages;
- at the second stage 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 2023-2025 shall apply *mutatis mutandis* for the calls for proposals covered by this amended Work Programme unless otherwise provided in this amended Work Programme.

Per the above and by way of derogation from General Annex B of the Horizon Europe Work Programme 2023-2025:

According to Article 119 of the Council Regulation (EU) 2021/2085, for indirect actions selected under calls for proposals covered by this amended 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 the 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:
  - Twenty percent (20%) for IHI JU Call 9[1];
  - One hundred percent (100%) for IHI JU Call 10;
  - One hundred percent (100%) for IHI JU Call 11.

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[2].

[1] Even if this threshold of 20% is not intended as an eligibility condition *per se*, proposals recommended for funding that will feature a non-EU IKOP amount higher than the 20% of IKOP, will be requested to remove the exceeding part. If this is the 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.

[2] It has to be noted that, pursuant to 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.

ENTITIES ELIGIBLE FOR FUNDING

In relation to the single-stage calls for proposals covered by this amended Work Programme, the relevant provisions of the General Annex B to the Horizon Europe Work Programme 2023-2025 shall apply *mutatis mutandis*.

By way of derogation, in relation to the two-stage calls for proposals covered by this amended 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 or as constituent or affiliated entities of either.

- 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.

- 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 – 2025,

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.

Where specified in the call topics conditions, with reference to the Trade and Cooperation Agreement between the EU and the UK including its Protocol I, establishing the UK's association to the Horizon Europe Programme, more particularly to article 2(2) of that Protocol; and Regulation (EU) 2085/2021,

more particularly article 174.14, and Commission Delegated Regulation (EU) 2019/887, specifically article 6.5 ('Principle of Annuality'):

- legal entities established in the UK shall not be eligible to receive funding.

Where specified in the call topic's conditions, with reference to agreement between the European Union and Canada on the participation of Canda in Union programmes, more particularly to articles 6 and 21; and regulation (EU) 2085/2021, more particularly article 174.14; and Commission Delegated Regulation (EU) 2019/887, specifically article 6.5 ('Principle of Annuality'):

- legal entities established in Canada shall not be eligible to receive funding.

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 amended Work Programme will take into account any application of Art 22(5) of the Horizon Europe Regulation as well as Union legislation and guidance relevant for its application 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 2023-2025 shall apply *mutatis mutandis* for the calls for proposals covered by this amended Work Programme.

EVALUATION RULES

General Annex D ('Award Criteria') to the Horizon Europe Work Programme 2023-2025 shall apply *mutatis mutandis* for the calls for proposals covered by this amended Work Programme with the following additions: The relevant calls for proposals launched under this amended 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:

	Excellence Aspects to be taken into account to the extent that the proposed work corresponds to the topic description in the work programme:	**Impact** Aspects to be taken into account to the extent that the proposed work corresponds to the topic description in the work programme:	**Quality and efficiency of the implementation** Aspects to be taken into account to the extent that the proposed work corresponds to the topic description in the work programme:
First stage evaluation of two-stage procedure	• Clarity and pertinence of the project's objectives, and the extent to which the proposed work is ambitious, and goes beyond the state of the art. • Soundness of the overall methodology.	• Credibility of the pathways to achieve the expected outcomes and impacts specified in the work programme, and the likely scale and significance of the contributions due to the project.	• Quality and effectiveness of the outline of the work plan. • Capacity of each participant, and extent to which the consortium as a whole brings together the necessary expertise.
Single-stage and second stage of two-stage procedure	• Clarity and pertinence of the project's objectives, and the extent to which the proposed work is ambitious, and goes beyond the state of the art.	• Credibility of the pathways to achieve the expected outcomes and impacts specified in the work programme, and the likely scale and significance of the contributions due to the project.	• Quality and effectiveness of the work plan, assessment of risks (including risk of falling below 45% contribution threshold), appropriateness of the effort assigned to work packages, and the resources overall.

	• Soundness of the proposed methodology, including the underlying concepts, models, assumptions, interdisciplinary approaches, appropriate consideration of the gender dimension in research and innovation content, and the quality of open science practices, including sharing and management of research outputs and engagement of citizens, civil society and end users where appropriate.	• Suitability and quality of the measures to maximise expected outcomes and impacts, as set out in the dissemination and exploitation plan, including communication activities.	• Capacity and role of each participant, and extent to which the consortium as a whole establishes a public-private collaboration and brings together the necessary expertise. If relevant capacity and role of the contributing partner(s) to the consortium. • Clearly defined and effective integration of in-kind and financial contributions of IHI JU private members, their constituent or affiliated entities to enable a successful public-private partnership. If relevant clearly defined and effective integration of in-kind and financial contribution of contributing partner(s).

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;
- 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 procedure, evaluated proposals will be ranked in one single list. With the exception of those provisions herein for establishing priority order for proposals with the same score within the same budget envelope, General Annex F ('Procedure') to the Horizon Europe Work Programme 2023-2025 shall apply *mutatis mutandis.*

For proposals with the same score within a single budget envelope (with the exception of the first stage of two-stage submissions) the method to establish the **priority order** is as follows:

Starting with the group achieving the highest score and continuing in descending order:

1) Proposals that address aspects of the call that have not otherwise been covered by more highly ranked proposals will be considered to have the highest priority.
2) The proposals identified under 1), if any, will themselves be prioritised according to the scores they have been awarded for 'Excellence'. When those scores are equal, priority will be based on scores for 'Impact'.
3) Proposals that include the highest number of IHI JU private members and constituent and affiliated entities of the IHI JU private members.
4) Proposals that provide the highest percentage of contributions (IKOP, IKAA and financial contributions) from the IHI JU private members and contributing partners and the constituent and affiliated entities of both, of the proposal's eligible costs and costs for the related additional activities.
5) If necessary, the gender balance among the researchers named in the researchers table in the proposal, will be used as a factor for prioritisation.

6) If necessary, any further prioritisation will be based on geographical diversity, defined as the number of Member States or Associated Countries represented in the proposal, not otherwise receiving funds from projects higher up the ranking list (and if equal in number, then by budget).

7) If a distinction still cannot be made, the panel may decide to further prioritise by considering other factors related to the objectives of the call, or to IHI JU in general. These may include, for example, enhancing the quality of the project portfolio through synergies between projects or, where relevant and feasible, involving SMEs. These factors will be documented in the panel report.

8) The method described in 1) to 6) will then be applied to the remaining equally ranked proposals in the group.

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 second stage proposal. This notification must be accompanied by a joint report clearly stating the reasons why a second stage 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 second stage 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 (first stage) 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[3].

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

1) clarify the proposals and help the panel establish their final assessment and scores, and/or;

2) 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.

[3] Failure to observe this restriction may result in IHI JU rejecting either the breaching participant or the full proposal per Article 141 point 1, letter (c) of the REGULATION (EU, Euratom) 2018/1046 of the European Parliament and of the Council of 18 July 2018 on the financial rules applicable to the general budget of the Union, amending Regulations (EU) No 1296/2013, (EU) No 1301/2013, (EU) No 1303/2013, (EU) No 1304/2013, (EU) No 1309/2013, (EU) No 1316/2013, (EU) No 223/2014, (EU) No 283/2014, and Decision.

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 2023-2025 shall apply *mutatis mutandis* for the calls for proposals covered by this amended Work Programme.

BUDGET FLEXIBILITY

General Annex F to the Horizon Europe Work Programme 2023-2025 shall apply *mutatis mutandis* to the calls for proposals covered by this amended 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[4]

Under the single-stage submission procedures and for the second stage 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[5].

SPECIFIC CONDITIONS ON AVAILABILITY, ACCESSIBILITY AND AFFORDABILITY (3A)[6]

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

[4] 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 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).

[5] 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

[6] Article 125(3) of the Council Regulation (EU) 2021/2085.

activities of the selected project, will be broadly[7] 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[8], 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.[9]

  b) At the project interim review stage, if relevant[10], 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.

  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.[11]

  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[12] 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 2023-2025 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.

[7] This covers EU Member States and countries that are associated to Horizon Europe at the time of call opening.
[8] 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.
[9] 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.
[10] 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.
[11] 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.
[12] Cognisant of IP sensitivities, confidential info, and commercial realties, 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.

FINANCIAL SUPPORT TO THIRD PARTIES

Financial support for third parties in IHI projects is allowed for the call(s) covered by this amended Work Programme. The additional conditions contained in General Annex B to the Horizon Europe Work Programme 2023-2025 for Financial Support to Third Parties shall apply *mutatis mutandis.*

Topics Overview

HORIZON-JU-IHI-2025-11-01 **Towards precision medicine: platform for transdiagnostic stratification of brain dysfunction**	The maximum financial contribution from IHI JU is up to EUR 20 202 000. The indicative in-kind contribution from industry partners is EUR 13 987 940. The indicative in-kind contribution from IHI JU contributing partners is EUR 6 642 533. The indicative in-kind contribution from industry partners may include in-kind contributions to additional activities.	Research and Innovation Action (RIA). Two-stage submission and evaluation process. Only the applicant consortium whose proposal is ranked first at the first stage is invited for the second stage.
HORIZON-JU-IHI-2025-11-02 **Understanding how infections foster and induce non-communicable diseases**	The maximum financial contribution from IHI JU is up to EUR 7 127 000. The indicative in-kind contribution from industry partners is EUR 8 167 000. The indicative in-kind contribution and financial from the philanthropic organisation is EUR 1 020 000. The indicative in-kind contribution from industry partners may include in-kind contributions to additional activities.	Research and Innovation Action (RIA). Two-stage submission and evaluation process. Only the applicant consortium whose proposal is ranked first at the first stage is invited for the second stage.
HORIZON-JU-IHI-2025-11-03 **AI-Powered Signal Detection in Pharmacovigilance**	The maximum financial contribution from IHI JU is up to EUR 8 906 000. The indicative in-kind and financial contribution from industry partners is EUR 11 418 645. The indicative in-kind contribution from industry partners may include in-kind contributions to additional activities.	Research and Innovation Action (RIA). Two-stage submission and evaluation process. Only the applicant consortium whose proposal is ranked first at the first stage is invited for the second stage.
HORIZON-JU-IHI-2025-11-04 **Leveraging Europe's Expertise to accelerate Cell Therapy for Type 1 Diabetes**	The maximum financial contribution from IHI JU is up to EUR 8 825 000. The indicative in-kind and financial contribution from industry partners is EUR 2 300 000. The indicative in-kind and financial contribution from IHI JU contributing partners is EUR 7 340 000. The indicative in-kind contribution from industry partners may include in-kind contributions to additional activities.	Research and Innovation Action (RIA). Two-stage submission and evaluation process. Only the applicant consortium whose proposal is ranked first at the first stage is invited for the second stage.
HORIZON-JU-IHI-2025-11-05 **Establishing Ortho and Cardiology Ambulatory Surgical Centres in Europe**	The maximum financial contribution from IHI JU is up to EUR 12 351 000. The indicative in-kind and financial contribution from industry partners is EUR 12 351 000. The indicative in-kind contribution from industry partners may include in-kind contributions to additional activities.	Research and Innovation Action (RIA). Two-stage submission and evaluation process. Only the applicant consortium whose proposal is ranked first at the first stage is invited for the second stage.

Topic 1: Towards precision medicine: platform for transdiagnostic stratification of brain dysfunction

Expected outcomes

The action generated by this topic is expected to contribute to all the following outcomes:

1. A sustainable and collaborative large, multimodal data platform that can identify novel transdiagnostic candidate markers and endpoints for the symptom domains of reward/motivation (including anhedonia) and impulsivity (RM&I) [1],[2] in neuropsychiatric, neurodegenerative, and physical health disorders. Relevant disorders include Alzheimer's disease (AD), major depressive disorder (MDD) and obesity (priority areas). Other relevant disorders/diseases include but are not limited to substance use and associated disorders, schizophrenia, bipolar disorder, borderline personality disorder and Parkinson's disease. For a disorder/disease to be relevant, there must be evidence to show that reward/motivation and/or impulsivity are clinically significant symptom domains;
2. Novel transdiagnostic candidate markers and endpoints are identified and progressed towards validation. Learnings are applied in drug discovery to increase probability of success (PoS);
3. A clear roadmap to achieve full validation of candidate markers and endpoints by regulatory and health technology assessment (HTA) bodies. Clinical best-practice guidelines are developed, and recommendations are made to the current diagnostic classifications[13] to expedite the adoption of precision medicine;
4. A greater understanding of the biological foundations of RM&I symptom domains and their role in AD, MDD, obesity and other relevant disorders, enabling the generation of novel therapeutic approaches by industry;
5. Closer alignment between psychiatry, neurology, and physical health disciplines to enable dialogue between healthcare professionals (HCPs) and other medical specialists to optimise outcomes, particularly for individuals with complex healthcare needs and comorbidities.

Scope

Current diagnosis and patient stratification in health disorders with Central Nervous System (CNS)-driven symptoms are based on DSM-5 / ICD-11 codes, which are not aligned with underlying biological processes and mechanisms. Subsequent suboptimal disease classification and patient stratification is a key reason for the low PoS of clinical development and the historical lack of new and more efficacious treatments. This topic aims to address these challenges by adopting a holistic, transdiagnostic approach [3] focused on the common underlying biology of RM&I symptom domains across the relevant disorders listed in the first expected outcome.

The topic seeks to build on an existing federated data platform to consolidate, curate, link and analyse robust, multimodal datasets from relevant patient populations. Thus, activities related to building a new platform or a biorepository from scratch are out of scope. The data platform must enable data/sample discovery, access, and support advanced computational analysis including artificial intelligence (AI)/ machine learning (ML) technologies while ensuring interoperability with other global data platforms to illuminate the biological basis of the RM&I symptom domains and identify related candidate markers and endpoints. The hypotheses will be prospectively tested in clinical case studies focusing on but not limited to AD, MDD, and obesity. Post-project, the platform will be available as open access for ongoing research and validation.

The topic also priorities collaboration with relevant stakeholders, including people with lived experience (LE), carers, HCPs, providers, regulators, HTA bodies and payers, to prepare the healthcare system for

[13] Diagnostic and Statistical Manual of Mental Disorders (DSM) and International Classification of Diseases (ICD)

this transformative shift. People with LE can provide unique insights and expertise that comes as the result of first-hand experience of health challenges. Integrating LE expertise improves research by bringing an understanding beyond academic and clinical knowledge. The perspectives of people with LE across the relevant symptom domains must be represented within the consortium and applied wherever appropriate.

Applicants must outline their approach to inclusive and equitable practices throughout the initiative, possibly through a risk register and appropriate mitigations. Example areas for consideration include data representation, bias mitigation, stakeholder engagement, ethics, and feedback mechanisms.

Objectives of the topic

Applicants are expected to address all four main objectives of the topic in their proposal:

1. Adapt and extend an existing federated data platform that is sustainable, enabling collaborative curation, access and analysis of clinical datasets and samples (as mentioned above). Consolidate existing multimodal datasets and samples from cohorts with relevant disorders[14] into the adapted platform;
2. Collect additional new clinical datasets and samples to address gaps and integrate these into the adapted platform;
3. Test hypotheses for candidate markers and endpoints within a defined context (e.g. patient selection, diagnosis, or treatment monitoring) in a transdiagnostic patient population presenting symptom domains of RM&I, including those with AD, MDD, and obesity;
4. Establish a collaborative platform to bring together people with LE, HCPs, regulators, HTA bodies and payers to achieve consensus on the value of candidate markers and endpoints, how to operationalise them into new diagnostic and treatment frameworks and achieve readiness in the healthcare system.

Activities under objective 1:

The success of this topic hinges on access to a large of amount of high-quality, multimodal data and biological samples collated from applicants and other partners (including industry). The applicants must list the datasets and samples that they will bring and confirm that they will be made accessible to the whole public-private partnership (PPP) from the start of the action.

1.1 Collate existing multimodal, longitudinal and transdiagnostic datasets at an individual level, including relevant parameters outlined under 1.2. These datasets can come from public or private databases, observational studies, clinical trials, real-world evidence (RWE) studies, biobanks, electronic health records, registries, and/or other digital health technologies and platforms. In their short proposal applicants must include a strategy to utilise relevant data from the European Platform for Neurodegenerative Diseases (EPND) catalogue[15] as much as possible as well as other relevant datasets available from previous projects (including pre-clinical data).

1.2 Relevant multimodal datasets ideally include as many as possible from the following: neurophysiology data (e.g. electroencephalography (EEG), magnetoencephalography (MEG)), brain imaging data (e.g. functional magnetic resonance imaging (fMRI), MRI), qualitative subjective assessments, behavioural data, real-world data, medical claims and billing data, routine clinical data (from medical and psychological assessments including data on metabolic status), physiological/activity monitoring data (polysomnography, actigraphy, digital data from wearables, etc.), speech/language data, patient reported outcome data (e.g. questionnaires), molecular biodata (e.g. “-omics”), and potentially data gained via therapeutic protocols (drugs,

[14] Relevant disorders: Alzheimer’s disease, major depressive disorder and obesity are priority areas for this topic. Other relevant disorders/diseases include but are not limited to substance use disorders, schizophrenia, bipolar disorder, borderline personality disorder and Parkinson’s disease. For a disorder/disease to be relevant, there must be evidence to show that reward/motivation and/or impulsivity are clinically significant symptom domains.
[15] https://discover.epnd.org/catalogue/studies

neuromodulation (deep brain stimulation, transcranial magnetic stimulation, transcranial functional ultrasound, etc.)). Biological samples (e.g. blood, urine, stools, cerebrospinal fluid) from biobanks should be leveraged. Datasets should be from individuals with relevant disorders as well as healthy controls.

1.3 Propose a strategy to integrate and connect the datasets from different sources.

1.4 Outline an approach to inclusive and equitable practices, including data representation, including but not limited to gender, ethnicity, and age (e.g. paediatric and adolescent populations).

1.5 Adapt and extend a federated data platform by building on existing infrastructures proven effective in PPPs, including the AD Workbench[16] and the EPND hub[17] (made available via the pre-identified industry consortium). The adapted platform should leverage available resources (including standard operating procedures) from EPND [4]. The adapted platform must be scalable and adaptable to curate high-quality, multimodal, retrospective, prospective and longitudinal data as mentioned under 1.1 and 1.2. It must enable data/sample discovery, access, and support AI analysis, while ensuring interoperability with other global data platforms.

1.6 Ensure high data quality by verifying the robustness of methodologies before integration into the adapted platform. This could be achieved by establishing a Data Quality Assessment Committee.

1.7 Implement fair and transparent governance for data- and sample-sharing including model interpretability, data provenance, and traceability of AI decision-making processes. Applicants must explain how they will develop a consensus on data sharing principles, complying with legal and ethical standards (e.g. General Data Protection Regulation (GDPR) and intellectual property rights (IPR)) and ensuring robust protection of data volunteers' rights. For example, leveraging the Data Sharing Playbook[18] and setting up a Data Access Review Committee.

1.8 Review the collated dataset to identify key gaps and develop a strategy to guide new data collection under Objective 2.

1.9 Identify potential algorithms for activities under 3.3 in Objective 3.

1.10 Ensure platform sustainability by creating a strong value proposition and user ecosystem beyond the consortium, with a clear strategy for a long-term, AI-powered platform accessible to the broader research community, including the healthcare industry. Relevant activities need to be in place from the start of the action.

Activities under objective 2

2.1 Collect new prospective multimodal and ideally longitudinal data from transdiagnostic cohorts, focussing on individuals affected by RM&I abnormalities in the relevant disorders, and ideally also collect biological samples. The datasets should close data gaps identified under 1.8 and be integrated into the adapted platform, meeting the same criteria described in objective 1.

2.2 Continue to recognise and fill data gaps to expand and maintain the adapted data platform, keeping it current with technological and scientific advancements. Whenever appropriate, utilise AI/ML, such as synthetic data generation, image analysis, natural language processing etc., to enhance the dataset.

2.3 Continue identification of potential algorithms for activities under 3.3 in Objective 3.

[16] https://www.alzheimersdata.org/ad-workbench
[17] https://epnd.org/news-and-resources
[18] Data Sharing Playbook: https://www.ihi.europa.eu/sites/default/files/uploads/Documents/ProjectResources/IMI_IHI_DataSharingPlayBook_2024.pdf

Activities under objective 3

3.1 The short proposal should propose an initial pilot clinical case study designed to test a scientifically robust and data-supported hypothesis on candidate markers and/or endpoints in RM&I symptom domains during the project's initial year. It must include transdiagnostic populations from AD, MDD, and obesity. The case study must include as a minimum neurophysiological data (e.g. EEG or MEG) and brain imaging data (e.g. MRI, fMRI) from each subject. In addition, datasets should include as many parameters as possible from the list described in 1.2. The precise scope of the initial clinical case study will be developed by the full consortium during the preparation of the full proposal. (Additional case studies are described under 3.4).

3.2 In the first 6 months, prepare a systematic literature review (white paper) of the available potential markers in RM&I symptom domains in relevant disorders to support hypothesis generation and subsequent testing. This should be kept up to date throughout the action.

3.3 Apply suitable statistical methods, advanced computational analytics (including, whenever appropriate, AI/ML as part of the statistical/analytical toolbox), modelling, and simulation across the multimodal data in the adapted platform to cluster biologically similar subjects across disorders/diseases, stratified independently of their conventional diagnostic classification. This should enable to identify and confirm clinically significant, quantitative candidate markers for RM&I symptom domains in relevant disorders, incorporating hypothesis-driven and data-driven approaches. It should also establish the foundation for a new transdiagnostic framework based on phenotypes/biotypes to enable detection of factors for susceptibility, risk stratification, diagnostic precision, disease monitoring, treatment response prediction, and overall patient outcomes. In addition, it should elucidate the biological underpinnings of the relationship between psychiatric and physical health (e.g. for obesity, understanding the interplay between metabolic disturbances, mental health and eating behaviours).

3.4 Test putative transdiagnostic markers and endpoint hypotheses derived from 3.2 and 3.3 through additional non-sequential pilot clinical case studies, incorporating insights from stakeholder consultations as mentioned in objective 4. These case studies must test the same transdiagnostic marker/endpoints in separate pre-defined patient populations in two or more of the relevant disorders to strengthen the transdiagnostic approach. As a preference, the three priority disorders should be included in at least one study each as a lead indication. For instance, one study with AD, one with MDD and one with obesity as the lead indication, each including at least one additional relevant disorder. Each study must include neurophysiological and brain imaging data and include as many other parameters as possible from the list outlined under 1.2. Studies must be powered sufficiently to allow analyses both within and across the included disorders. All results must be integrated into the adapted platform. The studies should enhance the platform's ability to accelerate hypothesis testing of new candidate markers and endpoints within a defined context of use (e.g. patient selection, diagnosis, or treatment monitoring) in representative patient populations. These studies must not involve the development of new *in vitro* diagnostic tools or digital sensors. The resulting evidence from pilot case studies (including the initial pilot clinical study under 3.1) should:

- be verifiable and applicable for patient stratification and/or monitoring in future clinical trials;
- demonstrate clinical utility to foster new patient pathways and clinical guidelines;
- contribute to bridging the gap between health care needs and capacity.

Activities under objective 4

4.1 Create an efficient collaborative platform to support seamless communication and collaboration among key stakeholders in the field of the relevant disorders. This includes innovators, researchers, clinicians, people with LE, carers, patient advocates, HCPs, regulators, scientific societies, HTA bodies, payers, and policy makers to collectively define and implement a new framework for the diagnosis and treatment of these disorders.

4.2 Form advisory/working groups comprising different stakeholders to support activities under objectives 1, 2 and 3, and co-create solutions. Ensure active and meaningful participation of people with LE, carers, and advocacy organisations throughout the activities and governance.

4.3 Engage with regulators (via experts with relevant expertise), e.g. EMA and/or national competent authorities, proactively initiating early consultations as appropriate. This should set the basis for continuation towards full validation of markers and endpoints beyond the action. Applicants are expected to consider the potential regulatory impact of the results and as relevant, develop a regulatory strategy and interaction plan early on to define a strategic approach to evidence collection and analysis where feasible (including case studies under objective 3) for generating appropriate evidence, as well as engaging with regulators in a timely manner (e.g. national competent authorities, EMA Innovation Task Force, qualification advice). Similarly, appropriately engage with HTA bodies and payers on the value of new transdiagnostic framework, candidate markers and endpoints when used to support claims of effectiveness of new therapies, paving the way for future reimbursement.

4.4 Craft evidence-based clinical guidelines through consultations with stakeholders, including people with LE, regulators, HTA bodies, payers, and medical organisations. Achieve consensus on best practices for implementing the new transdiagnostic framework. Develop recommendations and provide proposals for updates to the classification of disorders[19].

4.5 Design and implement a comprehensive training programme for HCPs to adopt the new transdiagnostic framework. Create educational materials and implement trainings for people with LE, families and carers in multiple languages, ensuring readiness across the healthcare system for the paradigm shift in healthcare delivery throughout Europe and helping to reduce stigma.

Applicants are expected to leverage and build on the learnings and outputs from previous and ongoing relevant PPPs[20] and other relevant global, European and national initiatives. They should consider synergies with the future European Genomic Data Infrastructure (GDI)[21], part of the European 1+Million Genomes Initiative[22], the future European Partnership for Brain Health[23] and other relevant upcoming projects[24].

Expected impacts

The action under this topic is expected to achieve the following impacts:

Data platform for precision medicine: A comprehensive, sustainable data-driven health platform linking behaviours and symptoms to quantitative biological markers. This will deliver much-needed refinements to existing diagnostic frameworks and treatment paradigms, providing a clear step towards personalised healthcare for CNS-driven symptoms. This platform could be a model for other disease areas where there is need for more biology-driven precision medicine.

Advancing mechanistic understanding: Clarification of the biological basis of CNS transdiagnostic symptoms expediting the identification of novel and more effective precision therapies across the relevant

[19] Relevant disorders: Alzheimer's disease, major depressive disorder and obesity are priority areas for this topic. Other relevant disorders/diseases include but are not limited to substance use disorders, schizophrenia, bipolar disorder, borderline personality disorder and Parkinson's disease. For a disorder/disease to be relevant, there must be evidence to show that reward/motivation and/or impulsivity are clinically significant symptom domains.

[20] EPND, PRISM/ PRISM2, RADAR-CNS, RADAR-AD, MOBILISE-D, IDEA-FAST, EU-PEARL, SOFIA, READI, AIMS-2-TRIALS, EHDEN, PROMINENT, PREDICTOM, AD-RIDDLE, among others.

[21] Synergies with the future European Genomic Data Infrastructure (GDI) are encouraged. https://gdi.onemilliongenomes.eu/

[22] https://gdi.onemilliongenomes.eu/ ; https://digital-strategy.ec.europa.eu/en/policies/1-million-genomes

[23] https://www.brainhealth-partnership.eu/about/

[24] IHI Call 11 T1: Understanding how infections foster and induce non-communicable diseases as well as relevant projects funded under IHI Call 9.

disorders, boosting the competitiveness of European industry and beyond. Advanced mechanistic understanding will also galvanise innovation in diagnostics.

Patient outcomes and stigma: A significant improvement in care quality (more integrated and personalised care) and in health outcomes for people within the RM&I driven relevant disorders. This includes healthcare innovations arising from improved understanding of the relationship between psychiatric and physical health and their underlying biology with far-reaching implications for patient health beyond psychiatry and neurology. This will also lead to reduction of stigma and provide opportunities for early intervention.

Efficiency in the healthcare system: Precision treatments reduce avoidable waste in healthcare resources, leading to overall cost reduction, higher productivity, and a positive economic impact on the European health care budget. Overall, a transformative shift towards a more integrated and personalised approach to healthcare will benefit patients across Europe and beyond.

The action will also support the EU political priority to boost European competitiveness and contribute to a number of European policies/initiatives, which include the European Health Data Space Regulation (EHDS)[25], the EU Artificial Intelligence Act[26] and the European Commission's Communication on a comprehensive approach on mental health[27] and the Healthier Together- EU Non-Communicable Diseases initiative[28].

Why the expected outcomes can only be achieved by an IHI JU action

The development of a scalable, sustainable, public-private federated data and biobanking infrastructure, as well as the collation of multimodal, transdiagnostic data, is crucial to address the current marker/endpoint challenges in neuropsychiatric, neurodegenerative, and physical health disorders including AD, MDD and obesity. Acquisition and harmonisation at this scale is beyond the capacity of a single organisation. The Innovative Health Initiative (IHI) provides an ideal model for creating such an initiative, integrating all relevant stakeholder groups in a focussed and collaborative framework. This public-private consortium will collate resources, share knowledge, and coordinate efforts to transform the diagnosis, treatment, categorisation and understanding of disorders driven by the RM&I symptom domains.

Pre-identified industry consortium and contributing partner

The pre-identified industry consortium that will contribute to this cross-sectoral IHI JU project is composed of the following medical technology industry beneficiaries ('constituent or affiliated entities of private members'):

- AbbVie
- Boehringer Ingelheim (Lead)
- Gates Ventures LLC (Co-lead)
- iFAB
- Novo Nordisk
- Roche

[25] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:L_202500327

[26] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32024R1689

[27] https://commission.europa.eu/strategy-and-policy/priorities-2019-2024/promoting-our-european-way-life/european-health-union/comprehensive-approach-mental-health_en

[28] https://health.ec.europa.eu/non-communicable-diseases/healthier-together-eu-non-communicable-diseases-initiative_en

In addition, the following contributing partners will participate in the IHI JU action:

- Wellcome Trust

In the spirit of partnership, and to reflect how IHI JU two-stage call topics are built upon identified scientific priorities agreed together with a number of proposing industry beneficiaries (i.e. beneficiaries who are constituent or affiliated entities of a private member of IHI JU), it is envisaged that IHI JU proposals and actions may allocate a leading role within the consortium to an industry beneficiary. Within an applicant consortium discussing the full proposal to be submitted for stage 2, it is expected that one of the industry beneficiaries may become the project leader. Therefore, to facilitate the formation of the final consortium, all beneficiaries, affiliated entities, and associated partners are encouraged to discuss the weighting of responsibilities and priorities regarding such leadership roles. Until the role is formalised by execution of the Grant Agreement, one of the proposing industry beneficiaries shall, as project leader, facilitate an efficient drafting and negotiation of project content and required agreements.

Indicative budget

- The maximum financial contribution from the IHI JU is up to EUR 20 202 000.
- The indicative in-kind and financial contribution from industry beneficiaries is EUR 13 987 940.
- The indicative in-kind and financial contribution from IHI JU contributing partners is EUR 6 642 533.

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 (IKOP) from those countries that are neither part of the EU nor associated to the Horizon Europe programme.

The EUR 2 600 000 financial contribution (FC) from industry beneficiaries and EUR 5 940 550 from the contributing partner is further described under the section *Contribution of the pre-identified industry consortium and contributing partners.*

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

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 predefined industry consortium may jointly agree on a different duration when submitting the full proposal.

Contribution of the pre-identified industry consortium and contributing partner

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

- the AD Workbench[29], which has already been leveraged in EPND, will be made available as well as facilitation of access to EPND hub infrastructure including the EPND catalogue[30];
- expertise and capabilities for data management, biostatistics and data science, development of processes for data and sample collection, quality assurance/control, and data analyses; contributions to implementation of data analysis algorithms and large language models (LLM) and other AI methodologies;
- contributions to systematic literature reviews;

[29] https://www.alzheimersdata.org/ad-workbench
[30] https://discover.epnd.org/catalogue/studies

- activities to make available multimodal datasets and (if possible) samples collected from historical clinical trials and activities to collect data in prospective clinical trials (e.g. placebo and potentially comparator data from Phase I/II/III trials in relevant disorders);
- clinical trial, translational, digital health, and medical expertise and guidance related to clinical protocol design, clinical operations, clinical and real-world data collection and analysis;
- expertise in legal, ethics, compliance, and representativeness in research/study design;
- expertise in regulatory strategy, policy and decision making, HTA assessment and reimbursement, involvement of LE expertise; support for integration of their requirements;
- contribution to the elaboration of educational and training programmes for HCPs, people with LE and carers.

Furthermore, the industry consortium will provide both the project leader and legal support during the project and help with data and knowledge management and communication/dissemination of results. It will also provide contributions to joint meetings and steering committees, networking, exploitation and sustainability.

Full details regarding the FC of EUR 2 600 000 from industry partners and of EUR 5 940 550 from the contributing partner will be provided in the full proposal. A part of the FC from industry beneficiaries will be allocated to activities related to the pilot clinical case studies.

Applicant consortium

The first stage applicant consortium is expected, in the 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 partner.

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

- project management expertise and capabilities in running multi-stakeholder cross-sector projects;
- data platform expertise and capabilities to leverage the AD Workbench to establish an extended version of the EPND platform, including data privacy, ethics, and legal expertise, development of principles and processes for data and sample collection, ensuring equitable and inclusive data practices, quality assurance/control, and an approach for the platform's sustainability;
- data capture / data management and analysis expertise and capabilities to import, curate and integrate existing and prospective datasets and ideally samples from public and private sources into the data platform; expertise and capabilities in data science, to develop and apply advanced AI supported analytics, modelling and simulation, and bias mitigation, and conduct multimodal analyses at scale to develop hypotheses of new candidate markers and endpoints;
- proven expertise and capabilities in the conduct of transdiagnostic pilot clinical case studies: i) expertise in RM&I symptom domains, translational, digital and clinical science, development and validation of new markers/endpoints; ii) systematic literature reviews of potential transdiagnostic markers and endpoints and hypotheses generation; iii) design and conduct of all pilot studies including regulatory and ethics approvals, setting up sites, recruitment in AD, MDD and obesity, collection and storage of data and samples, and measurement of all parameters described above. The outline of the first pilot clinical case study must be included in the short proposal (to be finalised by the full consortium during the preparation of the full proposal; study protocols of additional pilot clinical studies will be finalised by the full consortium during the proposed action);
- involvement of LE and patient advocacy groups/organisations as consortium members;
- resources to engage with people with LE, carers, HCPs to prepare training programmes and educational materials;
- expertise and capabilities in interacting with regulatory authorities, HTA bodies, payers, policy makers, medical societies, organisations of people with LE, and patient advocacy groups.
- regional health care centres with a centre of excellence in the relevant disorders.

At the second stage, the selected public consortium, the predefined industry consortium and contributing partners will form the full consortium. The full consortium will develop the full proposal in partnership, including the overall plan and the work packages, based on the selected short proposal.

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.

UK based legal entities' eligibility to receive funding

Legal entities established in the United Kingdom are eligible to receive funding in this topic.

Canadian legal entities' eligibility to receive funding

Legal entities established in Canada are eligible to receive funding in this topic.

References

[1] Nusslock R, and Alloy L B (2017) Reward Processing and Mood-Related Symptoms: An RDoC and Translational Neuroscience Perspective. J Affect Disord. 4;216:3–16. doi: https://www.sciencedirect.com/science/article/abs/pii/S0165032716310011?via%3Dihub

[2] Mata F, Treadway T, Kwok A, et al. (2017) Reduced Willingness to Expend Effort for Reward in Obesity: Link to Adherence to a 3-Month Weight Loss Intervention. Obesity 25 (10): 676-1681: https://onlinelibrary.wiley.com/doi/full/10.1002/oby.21948

[3] Towards a consensus roadmap for a new diagnostic framework for mental disorders, European Neuropsychopharmacology, 2025, 90: 16-27, https://doi.org/10.1016/j.euroneuro.2024.08.515

[4] The European Platform for Neurodegenerative Diseases (EPND) https://doi.org/10.1002/alz.079164

Topic 2: Understanding how infections foster and induce non-communicable diseases

Expected outcomes

The action under this topic must contribute to all of the following outcomes:

1. **Accelerated access to interventions:**

   A better understanding of the potential causal links between infections and non-communicable diseases and their accompanying biomarkers could:

   - more precisely define a person's level of risk for long term health complications
   - lead to the development of better diagnostic approaches such as early detection and monitoring strategies that will make preventive medicine more effective for the benefit of patients.

2. **Development of vaccine strategies:**

   A better understanding of the potential causal links between infections and chronic diseases could lead to the generation of vaccine strategies with the capacity to prevent the development of one or more chronic diseases over the course of a person's life, significantly reducing the long-term burden of disease.

3. **Early intervention strategies:**

   A clear understanding of the mechanisms of action used by infections to cause chronic diseases could more precisely define which cellular processes, metabolic pathways, enzymatic activities, and gene expression changes should be the focus of early intervention strategies. These strategies could halt or potentially reverse the progression of chronic diseases and would aim to replace many current treatments that only manage symptoms.

4. **Improved quality of life:**

   A better understanding of the potential causal links between infections and chronic diseases, as well as the biomarkers and mechanisms of action involved, could more precisely define development strategies for prophylactic vaccines, early diagnosis, and early intervention therapeutics that could significantly improve the quality of life of individuals by preventing health decline and avoiding escalating healthcare costs.

5. **Adoption of innovative approaches:**

   The establishment of a more systematic collaborative approach to mining existing research cohorts and biobanks to determine potentially causal links between infections and chronic diseases by combining multi-omics, artificial intelligence, and pre-clinical model verification to potentially accelerate the development of prophylactic vaccine, early diagnostic and early intervention strategies.

Scope

Infectious agent (IA) and non-communicable disease (NCD) interplay has driven effective prevention strategies. However, a growing field of research suggests that there are many unexplored connections between IAs and NCDs that could be utilised to develop better diagnostic, preventative, and therapeutic approaches to burdensome diseases. A cohort analysis identified 96 distinct NCDs correlated to IAs [1]. Other cohort analyses identified neurodegenerative diseases, defined as the progressive loss of neurons resulting in loss of motor function or cognition, with links to viral infection [2], including Alzheimer's disease, amyotrophic lateral sclerosis, dementia, vascular dementia, Parkinson's disease and multiple sclerosis. IA links to cardio-metabolic NCDs such as HSV (Herpes simplex viruses) and coronary artery disease [3], CMV (cytomegalovirus), EBV (Epstein-Barr virus), VZV (varicella-zoster virus), influenza and

parvovirus B19 have been shown to induce cardiomyopathies [4], and *H. pylori* infections may drive myocardial infarction [5].

While cancer, autoimmune, neurological, and cardiometabolic NCDs all have significant links to IAs, the scope of this topic is focused on neurodegenerative and cardiometabolic diseases, which carry significant disease burdens, potentially caused by direct, immune-mediated, or microbiota-gut-brain-axis damage/dysregulation, and lack early intervention strategies. Via the action funded under this topic, Europe's research community could potentially find more infection-based approaches for diagnosing, preventing, and treating NCDs.

The action funded under this topic aims to identify potential causal links and biomarkers leading to mechanism of action (MoA) studies. The literature [6][7][8] demonstrates research cohorts' utility in exploring the interplay between IAs and NCDs, increasing the likelihood of success. For instance, causative links were determined for oncolytic viruses, EBV [9] and human papillomavirus (HPV) [10], using Hill's causation criteria. The action funded under this topic should:

- develop methodologies to demonstrate non-carcinogenic IA to NCD causal relationships;
- consolidate data in one repository of IA/NCD causal relationships, biomarkers, and MoAs.

Applicants are expected to define a strategy to assess non-carcinogenic infection-associated NCD causative links and related biomarkers, incorporating a modelling perspective alongside AI-assisted data mining, appropriate statistical methodologies, and prioritisation approaches for the exploration of mechanisms of action (MoA). Applicants should also detail their methodological approach and data collection procedures, providing preliminary data to show potential for success and strategies for mitigating main methodological risks and limitations.

- As part of the first objective of proposed activities, applicants should work toward generating robust evidence toward proof of causality rather than only strengthening the known associations of IAs and NCDs. Applicants should take advantage of the available research cohorts, biobanks, and exposome data, including microbiota-gut-brain-axis samples from large general population studies, neurodegenerative disease cohorts, or cardiovascular disease cohorts. Association strength, consistency, and specificity should be indicated by similarity of measurement across different cohorts. Insurance data could be used to analyse temporality where infection occurs prior to medically attended disease. Cohorts from patients that have received transplants or immunosuppressive treatments with longitudinal data could demonstrate temporality and biological gradient effects from opportunistic infections, the strength of the immune response to IAs to demonstrate elements of causality driven by immune-mediated damage. Selection of research cohorts should prioritise data sets with populations from diverse ethnicities, socio-economic statuses, and balanced for gender. Applicants should develop/use pre-clinical models for causal link plausibility verification. Applicants are expected to follow and comply with all relevant ethical and data privacy standards for research. Applicants are also expected to conduct their consortium work with full transparency, clearly communicating data provenance, model interpretability, traceability, and limitations, especially when using AI modelling and decision-making.
- The second objective is identifying novel biomarkers, ideally to classify associated IAs, to better stratify individuals (children, adults, the elderly) who are at risk of developing NCDs post infection. This could be done using immune or metabolic markers, host and microbiome metabolomics, sequencing, etc. This pillar can utilise the same cohorts, biobanks, and exposome data used for pillar 1 if sufficient, but should supplement with additional cohorts where needed. To ensure outcomes within the 5-year timeframe of the project, the launch of new prospective cohorts is out of scope but limited recruitment to fill specific data gaps in existing cohorts could be considered.
- The third objective is to define the MoA that IAs use to drive NCD development. MoA identification would require tissue samples from pillars 1 & 2, as well as pre-clinical or *in silico* experimentation according to the targeted conditions or diseases.

No product development is expected from this action in the proposed timeline.

Applicants are expected to consider the potential regulatory impact of the results and, as relevant, develop a regulatory strategy and interaction plan for generating appropriate evidence as well as engaging with regulators in a timely manner. Additionally, applicants should anticipate engaging regional healthcare systems and authorities to prepare for clinical implementation and outcome acceptance when necessary.

Applicants should include in their proposal a strategy to ensure sustainability of the outputs of the project beyond the funding period.

The funded project should explore synergies with the funded project from IHI Call 11 Topic 'Towards precision medicine: platform for transdiagnostic stratification of brain dysfunction' (once the funded projects are awarded) to increase impact. Applicants are also expected to consider synergies with other relevant global, European and national initiatives including projects generated from Cluster Health topic "Relationship between infections and non-communicable diseases (HORIZON-HLTH-2023-DISEASE-03-07).

Expected impacts

The action under this topic is expected to achieve the following impacts:

- accelerate the EU's access to more cost-effective interventions for the most burdensome diseases;
- decrease the risk of developing serious diseases later in life by defining specific prevention strategies;
- contribute to halting the progression of chronic diseases by using biomarkers in early interventions;
- improve the quality of life for healthy individuals and patients by preventing further health decline, avoiding escalating care costs, and properly stratifying individuals and patients earlier in the diagnostic pathway;
- accelerate the adoption of innovative approaches to diagnostic, preventative, and therapeutic strategies, strengthening the EU positioning as an innovator in healthcare.

The action will also support the EU political priority to boost European competitiveness and contribute to a number of European policies/initiatives, which include the European Commission's European Health Data Space Regulation (EHDS)[31] and the EU Artificial Intelligence Act[32].

Why the expected outcomes can only be achieved by an IHI JU action

Elucidating the potentially complex relationships between infectious agents and non-communicable diseases can take decades using traditional research structures. In order to accelerate the understanding of how infectious agents drive non-communicable diseases, a multi-disciplinary approach is necessary to bring together multi-omics data, AI modelling, and existing cohort resources. This will shorten the timelines required to design appropriate studies and analyse longitudinal samples, making translational outcomes for the work feasible in the timeframe of a project. As many of these disease areas do not traditionally overlap with infectious disease research, the understanding of the interplay between infection and chronic disease also requires a dedicated partnership between academic researchers with expertise in microbiology, multi-omics approaches and NCDs and private companies currently pursuing preventative and therapeutic options for the selected disease areas. This new collaborative partnership

[31] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:L_202500327
[32] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32024R1689

could be an extremely fruitful way to develop preventative and therapeutic interventions over the long-term.

The greatest advantage of the IHI model is that it increases the access of all players in the ecosystem to existing research cohorts, biobanks, and exposome datasets, including the microbiome. Such datasets, whether privately held by industry players or largely publicly available, may need to be compared directly to effectively extract biomarkers, pathways activated and novel pathogen information. Additionally, biomarker identification in at-risk populations may lead to the development of diagnostic strategies for early intervention. The unravelling of the MoAs will inform on the right clinical endpoint diagnostics in time for clinical development of new prophylactic/therapeutic strategies.

Pre-identified industry consortium

The pre-identified industry consortium that will contribute to this cross-sectoral IHI JU project is composed of the following medical technology industry beneficiaries ('constituent or affiliated entities of private members'):

- Gates Ventures LLC
- Sanofi (Lead)

In addition, the following philanthropic organisation will participate in the IHI JU action:

- Novo Nordisk Foundation

In the spirit of partnership, and to reflect on how IHI JU two-stage call topics are built upon identified scientific priorities agreed together with a number of proposing industry beneficiaries (i.e. beneficiaries who are constituent or affiliated entities of a private member of IHI JU), it is envisaged that IHI JU proposals and actions may allocate a leading role within the consortium to an industry beneficiary. Within an applicant consortium discussing the full proposal to be submitted for stage 2, it is expected that one of the industry beneficiaries may become the project leader. Therefore, to facilitate the formation of the final consortium, all beneficiaries, affiliated entities, and associated partners are encouraged to discuss the weighting of responsibilities and priorities regarding such leadership roles. Until the role is formalised by execution of the Grant Agreement, one of the proposing industry beneficiaries shall, as project leader, facilitate an efficient drafting and negotiation of project content and required agreements.

Indicative budget

- The maximum financial contribution from the IHI JU is up to EUR 7 127000.
- The indicative in-kind and financial contributions from industry beneficiaries is EUR 8 167 000.
- The indicative in-kind and financial contributions from the philanthropic organisation is EUR 1 020 000.

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 (IKOP) from those countries that are neither part of the EU nor associated to the Horizon Europe programme.

The allocation of the EUR 1 000 000 financial contribution (FC) from industry beneficiaries will be decided by the full consortium at the second stage when preparing the full proposal.

The allocation of the EUR 1 000 000 financial contribution (FC) from the philanthropic organisation will be decided by the full consortium at the second stage when preparing the full proposal.

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

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 predefined industry consortium may jointly agree on a different duration when submitting the full proposal.

Contribution of the pre-identified industry consortium

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

1) Expertise and Assets:
    - **Expertise and access to cohorts and patients' data in Disease Areas of Interest**:
        - Neurodegenerative diseases (e.g., Parkinson's disease, Alzheimer's disease); especially access to the European Platform for Neurodegenerative Diseases (EPND) data hub
        - Cardiometabolic/cardiovascular diseases.
    - **Pillars of Interest**:
        - Infectious agent target discovery expertise and methodology;
        - Tools and methodology for biomarker identification (infectious agents & health conditions);
        - Mechanisms of action.
    - **Resources**:
        - Data and cohort access;
        - Biomarker identification (multi-omics);
        - Immune profiling;
        - Microbiome expertise;
        - *In silico* modelling, preclinical investigations *in vitro* and *in vivo*;
        - Federated analyses;
        - Internal expertise, wet lab work;
        - Advanced multi-omics including immuno-proteomics, spatial proteomics, plasma proteomics, bioinformatics;
        - Expertise in analytics;
        - Initiatives focusing on the better use of health data and cohorts;
        - Knowledge transfer and early detection initiatives;
        - Artificial intelligence and machine learnings.
2) General Contributions:
    - **Data and cohort Access**: Access to large cohorts and biobanks for data mining and biomarker identification;
    - **Biomarker identification**: Expertise in multi-omics, immune profiling, and advanced proteomics, including artificial intelligence/bioinformatics;
    - **Therapeutic expertise**: Small molecule drug discovery, vaccines, and therapeutic interventions;
    - **Knowledge transfer**: Initiatives focusing on health data usage, early detection, and disease associations.

These contributions aim to leverage existing resources and expertise to advance the project's goals in understanding and addressing the interplay between infectious agents and NCDs.

Applicant consortium

The first stage applicant consortium is expected, in the short proposal, to address the scope and deliver on all the expected outcomes of the topic, taking into account the expected contribution from the pre-identified industry consortium and contributing partner(s).

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

Academic institutions can provide complementary expertise in neurodegenerative and cardiometabolic/cardiovascular diseases, as well as access to innovative assets and methodologies such as the following list of suggested, non-exhaustive capabilities:

Expertise:

1. **Infectious diseases:**
    - Microbiology expertise in virology, bacteriology or parasitology;
    - Preclinical model of infection to determine causality, pathogenesis and mechanisms of action;
    - Omics expertise: sequencing, spatial transcriptomics, proteomics to identify the infectious agents;
    - Immunology to study serostatus, immune profiling, cytokines and single cell ribonucleic acid (RNA) sequencing to understand the pathogenesis and mechanisms of action.
2. **Neurodegenerative diseases, cardiometabolic/cardiovascular**:
    - Cellular and molecular biology to understand molecular mechanisms;
    - Expertise in neuroscience, cardiometabolism to understand pathogenesis, especially the microbiota-gut-brain axis for neurodegenerative diseases;
    - Innovative preclinical models including organ-on-chip and/or organoid to understand mechanisms and pathogenesis;
    - Multi-omics expertise such as sequencing, epigenetics, transcriptomics, proteomics, lipidomics, metabolomics to identify biomarkers and expertise to understand pathogenesis and mechanisms of action.
3. **Bioinformatics and biostatistics**:
    - Expertise in data analysis, integration and modelling;
    - Original data mining techniques;
    - Statistical methodologies for data interpretation.
4. **Biomarker discovery**:
    - Expertise in identifying and validating biomarkers;
    - Expertise in designing, monitoring and diagnostics assay.

Assets:

1. **Large patient cohorts**:
    - Access to cohorts, databases, and patients;
    - Access to samples, databases, and cohorts available from relevant public-private European partnership platforms in neurodegenerative and cardiometabolic diseases.
2. **Enhanced Consortium Capabilities**:
    - Improved understanding and addressing of neurodegenerative and cardiometabolic/cardiovascular diseases;

- Access to digital twins for understanding how infections could increase risk for NCDs post infection.

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

Legal entities established in the UK

According to the conditions of the calls and call management rules under 'Entities eligible for funding', legal entities participating in this topic and established in UK are not eligible to receive funding.

Legal entities established in Canada

According to the conditions of the calls and call management rules under 'Entities eligible for funding', legal entities participating in this topic and established in Canda are not eligible to receive funding.

References

[1] Lape, Michael et al. "After the Infection: A Survey of Pathogens and Non-communicable Human Disease." medRxiv : the preprint server for health sciences 2023.09.14.23295428. 30 Dec. 2024, doi:10.1101/2023.09.14.23295428. Preprint.

[2] Levine, Kristin S et al. "Virus exposure and neurodegenerative disease risk across national biobanks." Neuron vol. 111.7 (2023): 1086-1093.e2. doi:10.1016/j.neuron.2022.12.029.

[3] Roivainen, M et al. "Infections, inflammation, and the risk of coronary heart disease." Circulation vol. 101,3 (2000): 252-7. doi:10.1161/01.cir.101.3.252.

[4] Martens, Colton R, and Federica Accornero. "Viruses in the Heart: Direct and Indirect Routes to Myocarditis and Heart Failure." Viruses vol. 13,10 1924. 24 Sep. 2021, doi:10.3390/v13101924.

[5] Zito, Francesco, et al. "Helicobacter pylori infection and the risk of myocardial infarction: Role of fibrinogen and its genetic control." Thrombosis and Haemostasis, vol. 82, no. 07, 1999, pp. 14–18, https://doi.org/10.1055/s-0037-1614622.

[6] Lape, Michael et al. "After the Infection: A Survey of Pathogens and Non-communicable Human Disease." medRxiv : the preprint server for health sciences 2023.09.14.23295428. 30 Dec. 2024, doi:10.1101/2023.09.14.23295428. Preprint.

[7] Levine, Kristin S et al. "Virus exposure and neurodegenerative disease risk across national biobanks." Neuron vol. 111.7 (2023): 1086-1093.e2. doi:10.1016/j.neuron.2022.12.029.

[8] Miklossy, Judith. "Alzheimer's disease - a neurospirochetosis. Analysis of the evidence following Koch's and Hill's criteria." Journal of neuroinflammation vol. 8 90. 4 Aug. 2011, doi:10.1186/1742-2094-8-90.

[9] Sugden, Bill. "Epstein-Barr virus: the path from association to causality for a ubiquitous human pathogen." PLoS biology vol. 12,9 e1001939. 2 Sep. 2014, doi:10.1371/journal.pbio.1001939.

[10] Bosch, F X et al. "The causal relation between human papillomavirus and cervical cancer." Journal of clinical pathology vol. 55,4 (2002): 244-65. doi:10.1136/jcp.55.4.244.

Topic 3: AI-powered signal detection in pharmacovigilance

Expected outcomes

Industry, regulators, researchers and other stakeholders have access to evidence-based and practical guidance, with aligned perspectives of public and private stakeholders, on the use of artificial intelligence (AI) for signal detection and other pharmacovigilance (PV) applications to ensure patient safety.

Patients and citizens will benefit from earlier and more accurate signal detection, which will lead to earlier risk communication and more effective measures to manage the risks.

More specifically the action under this topic must contribute to all of the following outcomes (which can be applied to various therapeutic areas irrespective of the size and composition of the safety database and to products under development as well as those in post-marketing setup):

- AI-powered algorithms and methods for faster and more accurate signal detection;
- a comprehensive list of data sources where AI methods could be used for improved signal detection, including a set of recommendations, along with principles to be followed to support a suitable common data model for simultaneous analyses of a wide range of different data sources (including clinical trials and post-marketing surveillance data) for the same purpose;
- AI-powered algorithms and methods for highly accurate risk prediction to help identify potential risks in the future before they escalate into significant public health issues and enable proactive measures to mitigate risks;
- recommendations, including practical considerations for implementing AI-powered signal detection and risk prediction systems in real-world scenarios, to enable effective and trusted use of AI;
- tools and templates for practical implementation of AI – power signal detection and risk predictions by the public and private stakeholders;
- training and user guides and other education materials on the implementation of the recommendations and the use of AI.

Central to the delivery of these outcomes are transparency, trustworthiness, and adherence to the ethical and legal principles of the use of patient-level data and any proprietary information.

Scope

Spontaneous reporting systems (SRSs) have been essential for signal detection in pharmacovigilance but suffer from low accuracy and delays, impacting patient safety. More recently, electronic health records (EHRs) have also been used for signal detection[33], but the performance needs to be improved [1]. A safety signal is information on a new or known adverse event that may be caused by a medicine and requires further investigation[34]. Signal detection is the identification of potential exposure-outcome relationships that warrant further consideration.

AI offers a promising solution by improving the efficiency, accuracy, and timeliness of signal detection using diverse and untapped data sources to allow for enhanced and timely benefit-risk profile evaluation. Recent regulatory developments include the FDA's January 2025 guidance on AI for decision-making (FDA Guidance AI), which provides recommendations for using AI in regulatory decision-making about drug safety and effectiveness. Additionally, the EMA's September 2024 reflection paper (EMA- Reflection

[33] Signal Identification Methods in the Sentinel System
[34] Signal management | European Medicines Agency (EMA)

paper on AI) discusses AI's role throughout the lifecycle of medicinal products, from drug discovery to post-authorisation.

Advances in digital technology and computer science, such as generative AI, machine learning, and predictive analytics, have the potential to enable faster and more accurate analysis of both traditional and emerging data sources, which will improve patient safety, provision of healthcare, and public health. There are different PV areas where AI could potentially be applied, including individual case safety report (ICSR) management, periodic reports, signal detection, and risk management. The scope of this topic focuses on the use of AI for signal detection and risk prediction. It also covers opportunities that may not be 'signal detection' per se but rather augmentations/support beyond signal detection for instance with the expanded use of data and AI-powered methods, including characterisation of cases that can provide context for interpreting an exposure-outcome relationship.

The use of AI for ICSR management and processing as well as periodic reports are out of the scope of this topic.

To fulfill this aim, the action funded under this topic should:

1. Evaluate, select, optimise and test AI algorithms using disparate data sources for signal detection. This implies:
    - carrying out a review of existing literature, including results from previous initiatives. and practical applications. This will help to understand the strengths and limitations of different approaches and identify a collection of systems, AI methods, and tools that have been tested on various data sources;
    - selecting the most effective algorithms for signal detection based on this review;
    - pilot testing the algorithms to evaluate their performance using a series of use cases against different business scenarios from different stakeholders' perspectives. Performance metrics include accuracy, reliability/repeatability, and trustworthiness. The criteria of the use case studies will be developed at an early stage of the project when promising algorithms and tools have been identified;
    - optimising AI algorithms to perform signal detection at the level of a medical concept or syndrome, with emphasis on transparency requirements, including model interpretability, data provenance, and traceability of AI decision-making processes.
2. Evaluate diverse data sources to be considered within a cohesive pharmacovigilance network for the purpose of signal detection. This implies:
    - identifying data sources and reference datasets needed to pilot test the algorithms. This will include EHRs (medical records, claims, registries) as one of the main data sources in this project and other data sources such as spontaneous reporting systems (EudraVigilance, FDA Adverse Events Reporting System FAERS and WHO Vigibase), social media and genomics;
    - evaluating these data sources addressing their overall quality, how fit they are for purpose, current limitations and future opportunities, such as electronic health records, social media platforms, and others. This includes evaluating them individually or simultaneously to ensure a holistic view of drug safety, enhancing the analysis and monitoring of adverse drug reactions for a more thorough understanding of drug safety;
    - developing a set of recommendations that could be utilised for simultaneous analyses of different data sources, along with the principles to be followed to support a common data model for evaluating different data sources for the same purpose.
3. Evaluate and develop predictive models to identify risks in the future (risk prediction).
    - based on the results from signal detection, develop predictive models using different data sources that may help identify potential risks in the future before they escalate into significant public health

issues. These models would use historical data and advanced analytics to forecast potential risks, potentially enabling proactive measures to mitigate risks.

4. Develop a recommendations document for implementing AI-powered signal detection and risk prediction systems in real-world scenarios
    - using the results from the pilot tests, design a recommendations document which will serve as a reference for implementing AI-powered signal detection and risk prediction systems in real-world scenarios. The recommendations will include a set of principles and practical considerations to enable effective, explainable, and trusted use of AI and will include ethical, legal, and governance considerations for the sharing and use of real-world data and AI-algorithms;
    - engage with the European Medicines Agency (EMA) to seek endorsement of the recommendations document via the “Qualification Procedure”.
5. Develop recommendations for human-in-the-loop (HITL) and human-on-the-loop (HOTL) AI in pharmacovigilance signal detection for optimal performance and oversight.
6. Develop templates and tools for practical implementation, including integration into existing PV systems of AI – power signal detection and risk prediction models by different stakeholders.
7. Develop training plans and education materials to disseminate the recommendations widely to the stakeholder community and develop a strategy for uptake.

For all these activities, applicants are expected to adhere to ethical and legal principles. For instance for trustworthy AI, human oversight and verifications will follow regulatory frameworks such as the Assessment List for Trustworthy Artificial Intelligence (ALTAI).

Applicants are expected to develop a regulatory strategy and interaction plan for evidence generation to support the regulatory qualification of the methodology as relevant and engage with regulators in a timely manner (e.g. national competent authorities, EMA Innovation Task Force, qualification advice).

Applicants are also expected to foster proactive and early involvement of regional healthcare systems and health authorities in all stages of the discussion and decision-making processes.

Expected impacts

The action under this topic is expected to achieve the following impacts:

- enhanced drug safety by improving the speed and accuracy of identifying adverse drug reactions (signal detection);
- proactive risk management by improving risk assessment and prediction, scalability in monitoring, and fostering collaboration among stakeholders;
- improved patient safety through an earlier and more effective risk management plan, risk communication, and risk mitigation;
- faster and more informed decision-making through AI-driven insights;
- increased efficiency through rapid processing of vast amounts of data at a much faster rate compared to traditional methods;
- streamlined processing by automating routine pharmacovigilance tasks, thereby reducing the manual workload for healthcare professionals, and the operational costs associated with these activities;
- support for future policies and the shaping of regulations through evidence generated on the use of AI in signal detection and pharmacovigilance to improve patient safety;
- increased consistency in approaches used by industry, academia and regulators.

The action will also support the EU political priority to boost European competitiveness and contribute to a number of European policies/initiatives, which include European policies and regulations on AI for signal detection, the Regulation on the European Health Data Space (EHDS)[35] through recommendations of data space for pharmacovigilance activities, the EU Artificial Intelligence Act[36] and the European Health Emergency Preparedness and Response Authority (HERA) through earlier risk communication and mitigation.

Why the expected outcomes can only be achieved by an IHI JU action

The successful integration of diverse data sources and the development of advanced AI algorithms necessitate a collaborative effort. This multi-disciplinary collaboration brings together expertise from various fields, including data science, pharmacovigilance, regulatory affairs, and clinical research. It is crucial to unite public and private sectors, along with different biopharma industries, to address these challenges effectively. The Innovative Health Initiative Joint Undertaking (IHI JU) plays a crucial role in facilitating this collaboration by providing a platform where experts from different disciplines can work together towards common goals.

Regulatory science and oversight are at the heart of pharmacovigilance and therefore the active involvement of regulators in this collaborative partnership is needed to foster shared confidence in AI tools, regardless of who is using them.

A public-private partnership is the ideal framework to bring all stakeholders, which includes patients, academics, industry, regulators to align on overarching principles to minimise risks.

Large-scale projects often require significant resources and infrastructure that individual organisations might find challenging to provide on their own. By bringing together public and private sectors, the IHI setting addresses this challenge by offering the necessary support, including funding, technological infrastructure, and access to a network of experts. This support enables the successful execution of ambitious projects that have the potential to make a substantial impact on the field.

Pre-identified industry consortium

The pre-identified industry consortium that will contribute to this cross-sectoral IHI JU project is composed of the following medical technology industry beneficiaries (‘constituent or affiliated entities of private members’):

- AbbVie
- Amgen
- Astellas
- AstraZeneca
- Biogen
- Bristol Myers Squibb
- GSK
- Johnson & Johnson
- Merck KGaA
- MSD

[35] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:L_202500327
[36] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32024R1689

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

In the spirit of partnership, and to reflect how IHI JU two-stage call topics are built upon identified scientific priorities agreed together with a number of proposing industry beneficiaries (i.e. beneficiaries who are constituent or affiliated entities of a private member of IHI JU), it is envisaged that IHI JU proposals and actions may allocate a leading role within the consortium to an industry beneficiary. Within an applicant consortium discussing the full proposal to be submitted for stage 2, it is expected that one of the industry beneficiaries may become the project leader. Therefore, to facilitate the formation of the final consortium, all beneficiaries, affiliated entities, and associated partners are encouraged to discuss the weighting of responsibilities and priorities regarding such leadership roles. Until the role is formalised by execution of the Grant Agreement, one of the proposing industry beneficiaries shall, as project leader, facilitate an efficient drafting and negotiation of project content and required agreements.

Indicative budget

- The maximum financial contribution from the IHI JU is up to EUR 8 906 000.
- The indicative in-kind contribution from industry beneficiaries is EUR 11 418 645.

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 (IKOP) from those countries that are neither part of the EU nor associated to the Horizon Europe programme.

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

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 predefined industry consortium may jointly agree on a different duration when submitting the full proposal.

Contribution of the pre-identified industry consortium

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

- AI and machine learning specialists:
  - data scientists to develop and implement AI, machine learning, and other AI-powered models for signal detection;
  - natural language processing (NLP) experts for processing and analysing unstructured data from various sources like medical literature and social media.
- Pharmacovigilance experts:
  - pharmacologists to understand drug safety and adverse event reporting;

- regulatory experts to ensure compliance with regulatory standards and guidelines.

- Ethics and data protection specialists
- Healthcare data analysts, real-world data/real-world evidence experts:
  - epidemiologists for analyses of trends and patterns in adverse event data and for validation of signals;
  - biostatisticians for statistical analysis and validation of signals.
- IT and data management professionals:
  - database administrators: to manage large datasets and ensure data integrity;
  - software engineers: to develop and maintain the infrastructure for AI applications.

Applicant consortium

The first stage applicant consortium is expected, in the 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, where available, building on existing structures.

This may require mobilising the following expertise:

- pharmacovigilance, epidemiology, biostatistics;
- data science, AI;
- risk modelling, risk assessment and risk management;
- data privacy and protection, ethics;
- experience in engaging with patients;
- regulatory and compliance Framework Standard Operating Procedures (SOPs): expertise for AI model validation and monitoring;
- project management experience for large multi-stakeholder European public-private partnerships.

Furthermore, the applicant consortium is expected to provide the below resources:

Technological infrastructure:

- high-performance computing for processing large volumes of data;
- data storage solutions to securely store and manage data from various sources.

Access in a GDPR-compliant (General Data Protection Regulation) manner to data sources:

- electronic Health Records (EHRs): comprehensive patient data for analysis;
- spontaneous reporting systems: voluntary reports of adverse drug reactions;
- medical literature;
- other emerging data sources arising from new advancements in digital technology and computer science (such as social media, laboratory outputs, radiology data, genomics): to be used for exploratory purposes and additional insights as well as other datasources currently in use, including chemometric, biologic;
- all project members need to have access in a GDPR-compliant manner to these data sources;
- data must comply with GDPR and informed patient consent regulations.

The applicant consortium is expected to enable effective collaboration with regulatory authorities, national competent authorities, and may consider, for instance, engaging them as consortium partners, or in an advisory capacity.

At the second stage, the applicant consortium selected at the first stage and the pre-identified industry consortium will form the full consortium. Considering the role of the European Medicines Agency (EMA) in coordinating the European Union (EU) pharmacovigilance system and operating services and processes to support pharmacovigilance in the EU, EMA is prepared to join the applicant consortium selected at the first stage along with the pre-identified industry consortium (the full consortium). EMA's provisions include substantial and unique data access and expertise, as well as sharing experience from ongoing activities with national competent authorities exploring AI use cases in pharmacovigilance.

The full consortium will develop the full proposal in partnership, including the overall structure of the work plan and the work packages, based upon the short proposal selected 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.

Legal entities established in the UK

According to the conditions of the calls and call management rules under 'Entities eligible for funding', legal entities participating in this topic and established in UK are not eligible to receive funding.

Legal entities established in Canada

According to the conditions of the calls and call management rules under 'Entities eligible for funding', legal entities participating in this topic and established in Canda are not eligible to receive funding.

References

[1] Taylor LG, Kürzinger ML, Hermans R, Enshaeifar S, Dwan B, Chhikara P, Li X, Thummisetti S, Colas S, Duverne M, Juhaeri J. Considerations for practical use of tree-based scan statistics for signal detection using electronic healthcare data: a case study with insulin glargine. Expert Opin Drug Saf. 2024 Aug 23:1-11. doi: 10.1080/14740338.2024.2393274. Epub ahead of print. PMID: 39162331.

Topic 4: Leveraging Europe's expertise to accelerate cell therapy for type 1 diabetes

Expected outcomes

The action under this topic must contribute to all of the following outcomes:

1. Researchers, industry, and healthcare providers will benefit from a standardised framework for impurity thresholds and manufacturing best practices, ensuring regulatory alignment, facilitating clinical translation, and supporting the scalable production of safe and effective beta-cell therapies for type 1 diabetes (T1D).
2. Regulatory authorities, academic researchers, healthcare professionals (HCP) and industry partners will have access to validated immune-modulating strategies that enhance graft survival and promote immune tolerance, alongside advanced models and biomarkers for assessing engraftment success, metabolic function, and immune responses.
3. Pharmaceutical companies, regulatory bodies, and payers will benefit from established, scalable and cost-effective manufacturing processes for beta-cell therapy, ensuring the production of high-quality, reproducible products that meet regulatory standards and support market approval and reimbursement.
4. Academic researchers, regulatory bodies, and healthcare providers will have improved preclinical models and clearly defined clinical criteria for different patient demographics, ensuring that beta-cell therapies are accessible, safe, and effective across diverse populations.
5. Healthcare providers, industry, and information and communication technology (ICT) companies will utilise AI-driven predictive models and real-time monitoring technologies to enhance the assessment of transplant success, immune responses, and metabolic function, enabling personalised treatment plans, optimised immunosuppression regimens, and reduced therapy failure.
6. Healthcare providers and regulatory bodies will adopt patient-centred clinical endpoints as key indicators of treatment success, accurately reflecting quality of life and disease burden in T1D.
7. Health technology assessment (HTA) bodies, people living with diabetes, payers, and policymakers will benefit from cost-effectiveness assessments, pilot reimbursement programmes, and policy recommendations that enable the establishment of a reimbursement framework, thus paving the way for the adoption of beta-cell therapies for T1D.
8. Healthcare providers, researchers, and policymakers will benefit from training programmes for endocrinologists, diabetologists, and transplant surgeons, enhancing expertise in cell therapy, immunosuppression, and post-transplant care. Collaboration with professional societies will drive the development of clinical pathways, ensuring the generation of appropriate evidence for integrating cell-based therapies into standard diabetes care.
9. Academia, industry, regulatory agencies, patient organisations, people living with diabetes and policymakers will collaborate through fully operational European innovation hubs, facilitating knowledge sharing, driving research advancements, and harmonising regulatory practices to accelerate the adoption and implementation of beta-cell therapies across Europe.
10. People living with diabetes will benefit from all these outcomes, as they will lead to improved treatment options, enhanced long-term health outcomes, better access to innovative therapies, and an overall improved quality of life.

It is expected that certain existing assets will be used as background in this action. Such background assets may include, but are not limited to, cell manufacturing technologies, gene editing platforms, scaffold materials, encapsulation systems, and delivery and release technologies, among others. The exact nature of the background to be brought into the project will depend on the proposals presented by the public consortia. Therefore, beneficiaries intending to participate in this action need to be comfortable with the principle that ownership of specific deliverables / project results which would be considered direct

improvements to a beneficiary's background asset, will need to be transferred back to the beneficiary who contributed the background asset to the project. Provision for and conditions relating to such transfers should be specified in the project's consortium agreement.

Scope

Challenges and Background

T1D is an autoimmune disease that destroys insulin-producing pancreatic beta-cells, leading to lifelong insulin dependence. Despite advances in technology, achieving stable blood glucose levels remains challenging, which increases the risk of severe complications, and this in turn impacts negatively on daily life, work productivity, and mental health, and contributes to stress, anxiety, and depression.

Beta-cell replacement therapy offers a promising path towards a functional cure, but critical challenges must be addressed, including the need for renewable cell sources, optimised islet preparations, standardised manufacturing protocols, robust monitoring tools, sustainable reimbursement models, and trained healthcare professionals to manage complex treatments. These challenges align with key priorities from the Draghi Report[37], emphasising harmonised regulatory pathways, early engagement with HTA bodies, standardised manufacturing processes, and patient-centred clinical endpoints. Without urgent action, the full potential of beta-cell therapies will remain unrealised.

Key Objectives:

1) Establishing standardised criteria and analytical methods:

This objective aims at developing standardised criteria and analytical methodologies to detect, quantify, and characterise unintended bystander cells and impurities in stem cell-derived or beta-cell therapies for T1D. This work is intended to support the field at large by generating reference materials, optimising detection technologies, and defining regulatory-compliant thresholds that can inform future research and development—not to advance a specific product. The focus is on creating translatable, broadly applicable tools and standards that ensure safety, consistency, and quality. Engagement with the European Medicines Agency (EMA) is encouraged to facilitate the regulatory relevance and potential adoption of these methodologies in preclinical and clinical research settings.

2) Enhancing graft survival and immune tolerance:

This objective aims at developing immune-modulating strategies that support the long-term survival of beta-cell grafts and promote immune tolerance. This work is intended to generate insights, tools, and models that advance scientific understanding and inform future therapeutic approaches. Activities will include retrospective analyses of human cadaveric islet transplantation cohorts from different European countries and healthcare systems to support biomarker discovery and predictive modelling. Key biomarkers – such as continuous glucose monitoring (CGM) metrics, C-peptide levels, HbA1c, inflammatory cytokines, immune cell subsets, beta-cell-specific autoantibodies, and gene expression profiles – will be explored to identify indicators of graft survival, immune tolerance, and beta-cell function. In addition, a prospective study may be designed to identify novel biomarkers related to glycaemic variability, immune regulation, insulin independence, beta-cell regeneration, and inflammatory pathways. These efforts are aimed at supporting the development of robust monitoring tools and decision-making frameworks, not at advancing a therapeutic candidate toward clinical use.

3) Advancing manufacturing and quality control:

The objective is to establish robust cryopreservation techniques that preserve the viability and functionality of beta-cells post-thaw, with an emphasis on the identification and validation of biomarkers to guide and assess these processes. Building on this, the applicants should aim to develop and optimise scalable, cost-effective manufacturing methodologies and quality control frameworks that support the

[37] Mario Draghi, 'The Future of European Competitiveness', European Commission, September 9, 2024

production of consistent, high-quality beta-cell therapy materials in a research and innovation context. The goal is to generate foundational knowledge, technical standards, and reference systems, not to develop specific commercial products. Additionally, the consortium should work toward establishing standardised criteria for the production and quality control of excipient raw materials used in beta-cell therapy delivery systems, to ensure their stability, safety, and suitability for future clinical applications.

4) Streamlining preclinical and clinical development:

This objective aims at enhancing preclinical models for allogeneic cell therapies, ensuring standardised approaches and consistent methodologies in transplantation science and surgery. The focus is on harmonised regulatory approval, defining patient demographics for broader accessibility, and tailoring treatment requirements for personalised care. Establishing definitions for insulin independence, investigating and working toward the regulatory acceptance of clinically meaningful endpoints, such as 'Time in Range (TIR)' and 'Time in Tight Range (TiTR)', and optimising clinical trial design for allogeneic therapies are essential components of the future project.

5) Implementing advanced monitoring and artificial intelligence (AI)-driven predictive tools:

Leveraging real-time monitoring technologies like continuous glucose monitoring (CGM) and biosensors to assess transplant success and metabolic function, this objective aims to integrate advanced techniques from various fields, including oncology. Specifically, immune monitoring strategies used in oncology, such as immune checkpoint inhibitors and tumour biomarker profiling, will be explored to enhance the understanding of immune responses in beta-cell transplantation. AI-powered predictive models will personalise treatment plans and optimise immunosuppression regimens. Additionally, non-invasive imaging techniques, such as magnetic resonance imaging (MRI) and positron emission tomography (PET), will track graft survival and immune responses, ensuring better monitoring and management of beta-cell therapies. The action should also reinforce transparency requirements, including model interoperability, data provenance, and traceability of AI decision-making processes.

6) Defining clinically meaningful and patient-centred endpoints using real-world evidence:

This objective aims at leveraging real-world data to define clinically meaningful endpoints that capture quality of life and disease burden in T1D. This includes identifying surrogate endpoints to enable clinical trials that demonstrate long-term benefits without requiring extended study durations. Additionally, generating data on the advantages of achieving normoglycemia in individuals already within target glucose ranges will help refine treatment goals and support regulatory decision-making. A small pilot study must be conducted to test these endpoints and gather initial data on their feasibility and impact.

7) Exploring reimbursement models for beta-cell therapies:

This objective aims at developing initial cost-effectiveness models that highlight the potential financial and healthcare benefits of beta-cell therapies, focusing on key aspects like reduced complications and improved quality of life. Early-stage collaboration with health technology assessment (HTA) bodies, payers, and policymakers must be sought to help build a foundation for understanding the value of these therapies, laying the groundwork for future integration into healthcare systems across Europe.

8) Integration of cell therapy into diabetes care and collaborative networks:

Beta-cell therapies should be integrated into standard diabetes care through specialised training for healthcare providers and the creation of a network of multidisciplinary centres across Europe. Clinical guidelines should be put in place to ensure a smooth transition from current treatments. Additionally, a network of European innovation hubs must be established to foster collaboration, knowledge exchange, and harmonised regulatory approaches, accelerating the development and clinical application of beta-cell therapies. It will also be crucial to collaborate with professional societies to define a clear clinical pathway, ensuring alignment with best practices and optimising patient outcomes across the region.

Additional key considerations:

Applicants are expected to consider a sustainability plan for the maintenance, update, and validation of the project's results beyond the project's duration to ensure long-term impact and continual improvements.

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

Applicants are expected to ensure transparent and open dissemination of outcomes, including models and tools, to enable their integration and reuse throughout the wider ecosystem.

Applicants should give adequate consideration in the ethical standards and data privacy frameworks applicable to the use of personal health data and biobanks.

The action funded under this topic is also expected to explore synergies with complementary initiatives to advance research and innovation in Europe, such as NHPIG[38], which is developing the first T1D autoimmune pig model, the Vanguard-project[39], the Islet-project[40], JOIN4ATMP[41], and relevant Horizon 2020/Europe projects. Furthermore, the project should explore synergies with the European Pancreas and Islet Transplantation Registry (EPITR)[42], an initiative led by the European Pancreas and Islet Transplant Association (EPITA) to establish a pan-European registry collecting data on individuals who have received pancreas or islet transplants. By leveraging their insights and networks, the project aims to strengthen the impact of beta-cell therapy development, ensuring that these collaborations contribute to a more comprehensive and effective approach to tackling T1D through cell-based therapies.

Expected impacts

The action under this topic is expected to achieve the following impacts:

- to support the widespread adoption of beta-cell therapy, ensuring long-term efficacy, accessibility, and integration into healthcare systems;
- to accelerate the development of stem cell-based therapies through advancements in manufacturing, preclinical models, regulatory alignment, and predictive tools;
- to strengthen Europe's position as a leader in beta-cell therapy by fostering innovation hubs and clinical networks;
- scientific and regulatory progress will advance regenerative medicine for other metabolic and autoimmune disorders beyond T1D;
- patients, healthcare providers, regulators, policymakers, and industry stakeholders will all benefit from improved treatments, clearer guidelines, and increased investment;
- boosting European industrial competitiveness by driving innovation in cell-based therapies, fostering cross-sector collaboration, and enhancing Europe's global leadership in regenerative medicine.

These impacts are expected to advance IHI JU's objectives of improving healthcare quality, accessibility, and sustainability while contributing to European health policies and initiatives.

The action under this topic is expected to contribute to the following EU policies/initiatives:

[38] https://www.nhpig.eu/
[39] https://vanguard-project.eu/
[40] https://isletproject.eu/
[41] https://www.join4atmp.eu/
[42] https://esot.org/epita/epita-epitr/

- The European Health Union: addressing the chronic disease (diabetes) burden; accelerating groundbreaking therapies while drawing on the potential of digital and AI solutions; contributing to modern and innovative health policies (by working on models, tools and pathways enabling the adoption of innovative/breakthrough therapies by European healthcare systems);
- The Pharmaceutical Strategy for Europe: Advancing innovative cell therapies and improving patient access to cutting-edge treatments;
- The EU political priority to boost European competitiveness: establishing Europe as a hub for cutting-edge scientific and research innovation; contributing to the announced EU Biotech Act as a forward-looking framework to leverage the potential that biotechnologies can bring to our economy;
- UN Sustainable Development Goals (SDG 3: Good Health & Well-being): reducing the impact of non-communicable diseases (NCDs) like type 1 diabetes.

The action will also contribute to a number of European policies/initiatives, which include the European Commission's European Health Data Space Regulation (EHDS)[43] and the EU Artificial Intelligence Act[44].

Why the expected outcomes can only be achieved by an IHI JU action

The outcomes outlined can only be achieved through a cross-sectoral, multidisciplinary public-private partnership (PPP) like the IHI JU action, given the complexity of the challenges involved. The development of innovative immune-modulating strategies, scalable manufacturing processes, and advanced preclinical models requires collaboration across multiple sectors, including pharmaceuticals, academia, medical devices, health ICT, clinical societies and patient organisations. Europe's strong academic expertise in islet transplantation is critical for advancing beta-cell therapies, and academic institutions can provide the foundational research necessary to drive progress in this field. Collaboration with pharmaceutical companies, healthcare practitioners, and regulators ensures that beta-cell therapies are scientifically sound, clinically effective, and aligned with patient needs.

In addition to academic and industry expertise, patient organisations, payers, and HTA bodies play a pivotal role in making these therapies accessible and sustainable. Patient organisations provide valuable insights into real-world patient needs, helping shape therapies that focus on improving quality of life. Payers and HTA bodies ensure that beta-cell therapies are financially viable and can be integrated into healthcare systems across Europe. Their involvement helps secure reimbursement and fosters the widespread adoption of these therapies.

This public-private collaboration facilitates the efficient use of resources, combining scientific research, innovation, clinical expertise, regulatory guidance, and patient input. It enables the creation of therapies that are scalable, cost-effective, and accessible to diverse patient populations. By leveraging Europe's collective expertise, this model accelerates the development and integration of beta-cell therapies, making them a sustainable and viable solution for patients with type 1 diabetes across Europe.

Pre-identified industry consortium and contributing partners

The pre-identified industry consortium that will contribute to this cross-sectoral IHI JU project is composed of the following medical technology industry beneficiaries ('constituent or affiliated entities of IHI JU private members'):

- Eli Lilly

[43] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:L_202500327
[44] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32024R1689

- Novo Nordisk

In addition, the following contributing partners will participate in the IHI JU action:

- Breakthrough T1D (Lead)
- Fundación DiabetesCERO
- Fondazione Italiana Diabete

In the spirit of partnership, and to reflect how IHI JU two-stage call topics are built upon identified scientific priorities agreed together with a number of proposing industry beneficiaries (i.e. beneficiaries who are constituent or affiliated entities of a private member of IHI JU), it is envisaged that IHI JU proposals and actions may allocate a leading role within the consortium to an industry beneficiary. Within an applicant consortium discussing the full proposal to be submitted for stage 2, it is expected that one of the industry beneficiaries may become the project leader. Therefore, to facilitate the formation of the final consortium, all beneficiaries, affiliated entities, and associated partners are encouraged to discuss the weighting of responsibilities and priorities regarding such leadership roles. Until the role is formalised by execution of the Grant Agreement, one of the proposing industry beneficiaries shall, as project leader, facilitate an efficient drafting and negotiation of project content and required agreements.

Indicative budget

- The maximum financial contribution from the IHI JU is up to EUR 8 825 000.
- The indicative in-kind contribution from industry beneficiaries is EUR 2 300 000.
- The indicative in-kind and financial contribution from IHI JU contributing partners is EUR 7 340 000.

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 (IKOP) from those countries that are neither part of the EU nor associated to the Horizon Europe programme.

The allocation of the EUR 6 550 000 financial contribution (FC) from IHI JU contributing partner(s) will be decided by the full consortium at the second stage when preparing the full proposal.

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

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 predefined industry consortium may jointly agree on a different duration when submitting the full proposal.

Contribution of the pre-identified industry consortium and contributing partners

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

- provision of training materials for healthcare professionals on cell therapy;
- regulatory, R&D, and clinical expertise;
- specialised knowledge in clinical protocol design and the development and regulatory alignment of clinically meaningful endpoints;
- expertise in defining clinically meaningful endpoints;
- engagement with payers, policymakers, and regulatory agencies to support value-based healthcare adoption;

- dissemination and communication efforts, including the open sharing of all relevant learnings, tools, and materials to maximise their accessibility and uptake across the healthcare ecosystem.

Applicant consortium

The first stage applicant consortium is expected, in the 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.

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

1) **Scientific expertise**
    - *Beta-cell biology & immune modulation*: Deep knowledge of immune tolerance, beta-cell biology, and strategies to prevent graft rejection and enhance long-term cell survival;
    - *Stem cell technology*: Proficiency in generating and assessing stem cell-derived beta cells in preclinical and clinical settings;
    - *Gene editing and advanced therapies*: Expertise in gene-editing technologies (e.g., CRISPR) to improve cell compatibility and function, alongside immune-modulating therapies.
2) **Manufacturing and quality control expertise**
    - *Cell therapy production*: Experience in scalable cell therapy manufacturing, cryopreservation, and adherence to Good Manufacturing Practices (GMP);
    - *Process development*: Capability to design cost-effective, reproducible manufacturing systems with batch consistency.
3) **Regulatory expertise**
    - *Regulatory affairs*: Strong background in regulatory engagement with bodies like the EMA to facilitate beta-cell therapy approval;
    - *Clinical trial design*: Expertise in preclinical and clinical trial development, particularly for different age groups.
4) **Preclinical and clinical development resources**
    - *Preclinical models*: Access to predictive models that accurately simulate human T1D for assessing safety and efficacy;
    - *Clinical trial networks*: Established networks to support the transition from research to human trials, including patient recruitment;
    - *Retrospective and prospective data analyses*: The applicants are expected to bring data from both retrospective and prospective analyses, including clinical, biomarker, and health outcomes data from cadaveric islet transplantation cohorts. This data should include samples from islet transplants that have successfully provided full insulin independence, as well as those that have not, to support the development of models and biomarkers to assess engraftment success, metabolic function, and immune responses;
    - *Access to islet transplantation datasets*: Availability of and experience working with comprehensive datasets from islet transplantation registries, including long-term clinical outcomes, graft function, metabolic control, and immune response data. These datasets will be instrumental in developing predictive models and biomarkers for therapy success.
5) **Advanced monitoring technologies**
    - *Monitoring systems development*: Ability to create real-time tracking tools such as continuous glucose monitoring (CGM) and biosensors;
    - *AI and machine Learning*: Expertise in predictive models for personalised treatment and immunosuppression optimisation;

- *Imaging technologies*: Access to non-invasive imaging (e.g., MRI, PET) for monitoring graft health and immune responses.

6) **Patient-centred research**
   - *Patient engagement*: Integration of patient perspectives and real-world data to define meaningful clinical endpoints;
   - *Post-transplant care*: Development of protocols to minimise immunosuppression side effects and ensure long-term therapy sustainability.
7) **Economic and policy expertise**
   - *Health economics*: Ability to assess cost-effectiveness and long-term viability of beta-cell therapies;
   - *Health technology assessment (HTA)*: Experience engaging with HTA bodies to secure reimbursement pathways.
8) **Multidisciplinary collaboration**
   - *Healthcare training*: Development of training programmes for clinicians in cell therapy management;
   - *Collaborative networks*: Existing partnerships with academic institutions, industry, regulators, and patient organisations.
9) **Engagement with regional healthcare systems and health authorities**
   - Early and active involvement of regional healthcare systems and health authorities in discussions to ensure alignment with local healthcare priorities, regulatory requirements, and reimbursement pathways. This will facilitate smoother integration of innovations into healthcare practice and enhance the broader societal impact of the project.
10) **Infrastructure for knowledge sharing**
    - *Knowledge exchange platforms*: Capacity to organise workshops, webinars, and conferences for knowledge dissemination;
    - *European networks*: Ability to participate in or establish innovation hubs dedicated to beta-cell therapy.
11) **Technological capabilities**
    - *Advanced technologies*: Access to gene editing platforms, real-time monitoring systems, and imaging tools;
    - *Data sharing infrastructure*: Capability for secure, multi-institutional data collaboration.
12) **Patient advocacy and public engagement**
    - *Engagement with patient groups*: Active collaboration with advocacy organisations to improve access, awareness, and policy influence.

These combined resources and expertise are essential for applicants to effectively contribute to achieving the objectives of advancing beta-cell therapies for T1D, ensuring successful clinical translation and adoption across Europe. Applicants must also document that these resources are shareable with the full public-private partnership from the beginning of the action to ensure broad impact across the European research and healthcare landscape.

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

Legal entities established in the UK

According to the conditions of the calls and call management rules under ‘Entities eligible for funding’, legal entities participating in this topic and established in UK are not eligible to receive funding.

Legal entities established in Canada

According to the conditions of the calls and call management rules under ‘Entities eligible for funding’, legal entities participating in this topic and established in Canda are not eligible to receive funding.

Topic 5: Establishing ortho and cardiology ambulatory surgical centres in Europe

Expected outcomes

With advances in clinical and surgical techniques, medical technology, pain management as well as pre- and post-surgical care, more procedures that have been traditionally performed in hospital settings can now be performed in facilities outside hospitals with no overnight stays required, easing the demand on overstretched hospitals and reducing hospital acquired infections. These facilities are referred to as ambulatory surgical centres (ASCs).

The actions under this topic contribute to all the following outcomes:

1. consensus-based understanding on the hurdles, needs and requirements to establish ASCs within a European healthcare setting with a regional/national expert committee driving the community involved and acting as reference opinion leaders;
2. comprehensive framework and 'know how' for establishing ASC facilities with details on infrastructure, medical technology, protocols and healthcare resources required for establishing new facilities;
3. training schemes and programmes including care pathways and enhanced recovery protocols for all health care providers (HCPs) involved in ASCs in orthopaedics and cardiology, operating safe scalable models that achieve high quality results;
4. creation of a clinical database and generation of economical evidence forming a basis towards European acceptance, standardisation and funding allowing establishment of ASC services as an integrated part of healthcare services provided;
5. the availability of an interoperable IT technology solution required to integrate clinical data from multiple stages of the patient journey and the related digital health solutions for patient preparation, post-discharge management and home monitoring.

Target group for the outcomes are:

- hospital managers, healthcare system providers, medical technologies and digital companies seeking solutions in European, national and regional healthcare services, to address capacity and efficiency hurdles in hospitals in the fields of orthopaedics and cardiology;
- HCPs establishing ASCs in orthopaedics and cardiology to further provide and advance healthcare services and efficiency;
- patient groups and carer associations working towards patient access to more convenient locations, shorter waiting times and easier scheduling (relative to hospital inpatient and outpatient procedures). This will improve patient experience, satisfaction and outcomes from pre-procedure to recovery at home;
- HCPs and researchers working on incorporating advanced medical technology in and out of hospital settings for improved patient outcomes and healthcare efficiency;
- reimbursement bodies as well as HTA bodies providing guidelines and innovative payment schemes.

Scope

The EU's ageing population and a rising burden of diseases and disorders, in particular noncommunicable diseases (such as cardiometabolic diseases, cancers, neurodegenerative or musculoskeletal disorders), have resulted in increasing health care costs and limited procedural capacity in operating rooms and cath labs (catheterisation laboratory). Lack of specialists is also an issue. This delays patient access to health care and increases the need for alternative and more cost-effective forms of care [5]. The shift of inpatient

surgeries and treatments to ambulatory surgical centres (ASCs) could potentially provide a solution to the hospital capacity problem as well as reducing hospital acquired complications and providing improved access to healthcare services for patients in rural areas. ASCs are healthcare facilities focused on providing same-day surgical care, including diagnostic and preventative procedures for patients who do not require overnight stays. It is believed that ASCs can transform the outpatient experience for patients by providing them with a more convenient alternative to hospital-based outpatient procedures. ASCs can be operated by private or public healthcare services.

Numerous factors influence whether surgical procedures can be carried out within ambulatory surgical centres. The key drivers are changes and further development in clinical practice and medical technology. The action funded under this topic will be focused on ASCs specialised in orthopaedics for knee and hip joint replacement surgery as well as ASCs specialised in cardiology for cardiac ablation procedures and elective rhythmology. All of these procedures are elective and will increase in the next years due to the ageing population, improved diagnostics and extension of medical guidelines. Based on patient selection, these procedures have been proven suitable for ambulatory settings. This is reinforced by the downward trend in length of stay in hospitals for these procedures in recent years. This also reflects developments in medical technology in these procedures over the last years, that have led to more precise, faster, easier, gentler and more patient-specific interventions. Shifting those procedures from hospitals into ASCs can help to relieve inpatient capacities, enabling faster patient access to those surgeries and in the end reducing overall health care costs. It is important to stress that treatment in ASCs requires good patient selection prior to the surgery based on medical classifications – like the American Society of Anaesthesiologists' risk classification for estimating the perioperative risk – and social factors, such as the individual domestic situation of the patient, to make the intervention in ASC successful. Severe and complicated cases will still have to be treated in hospitals.

ASCs offer a lot of benefits to the health care system and can address some problems associated with inpatient treatments in hospitals. Studies show that outpatient procedures are safe and can achieve similar or superior functional outcomes compared to inpatient procedures and, for example, the early mobilisation facilitated by outpatient pathway in hip and knee replacement surgeries contributes to faster recovery timelines [1] [2].

Due to the fact that the costly infrastructure of the hospital is not needed, and patients go home the same day after an outpatient procedure, the shift of procedures into the outpatient setting results in significant cost savings (an outpatient total shoulder arthroplasty (TSA) results in a 40% decrease in charges [3] and unicompartmental knee replacement (UKR) saving up to roughly EUR 18 000 [USD 20 500] per patient [4]). Enhanced healthcare resource utilisation and reduced patient waiting times are additional benefits. Additionally, there are also some patient-related benefits of outpatient procedures. It is proven that patients benefit from recovering in familiar home setting, with various technologies to help monitor their recovery and provide them with access to HCPs. This reduces anxiety [1] and leads to earlier mobility, thus a faster recovery time and a quicker return to daily activities. Overall, this enhances patient satisfaction [1] [2]. On top of that, ASCs decrease the risk of nosocomial infections with the reduced exposure to hospitals environment.

Effective implementation of ASCs faces multiple hurdles including:

1. reimbursement models: lack of reimbursement and funding procedures, limiting financial incentives to move procedures from in-hospital to ASCs;
2. stakeholder acceptance: non-clinical decision-makers are not fully comfortable with ASC as a part of the solution to the capacity and demand problem;
3. evidence: lack/limitation of safety and quality data measuring performance and outcomes;
4. human resource readiness: HCPs are not trained to perform in ASCs and run them efficiently;
5. digital infrastructure: data privacy hurdles, interoperability, digital exclusions;

6. protocols: lack of standardised care models across different therapies. Limited implementation of patient-centred evidence-based approaches for quicker and improved recoveries – enhanced recovery programmes;
7. patient readiness: patient expectations and previous experiences making them unwilling to accept procedures in ASCs;
8. home recovery and care system: lack of integration of ASCs with the broader healthcare systems.

Applicants should envisage the following activities as part of the action funded under this topic:

- Establish a multistakeholder advisory board leading and advocating for change in national and regional healthcare services. The advisory board will quantify the requirements for establishing ASCs in orthopaedics and cardiology including different financial and resource models, training modules, reimbursement pathways, digital health solutions for patient preparation and post-discharge management, registry databases as well as clinical and economical end points required for studies and reimbursement pathways;
- Demonstrate the safety of targeted procedures for patients performed in ASC facilities through the conduct of two medical cohort studies: one in orthopaedic joint replacement and another in cardiology cardiac ablation. These studies will assess the risks, patient medical eligibility complications, and patient outcomes of ASCs in comparison to hospital-based procedures;
- Generate and share protocols and best practices across multiple centres in same country and beyond borders, including a strategy for contextual adaptation for ASC scalability across Europe;
- Create a network of selected ASCs, with successful ASCs leading in sharing best practice, protocols, trainings, and efficiency models;
- Collect real world evidence (RWE) to demonstrate and model the cost-effectiveness of ASCs vs hospital-based procedures. The study should be multicentre and will establish a registry database answering proposed research questions;
- Develop a shared framework for clinical data interoperability, and combine an interoperable IT technology solution to integrate clinical data collected at multiple stages of the patient journey with the related digital health solutions that are used for patient preparation, post-discharge management and home monitoring. Adequate consideration should be given to relevant ethical and privacy aspects.
- Provide a sustainability strategy for the maintenance, update, and validation of the project's results beyond the project duration.

Applicants should consider learnings and synergies with relevant initiatives at national and European level to maximise the potential impact of the future project.

Expected impacts

The action under this topic is expected to achieve the following impacts:

1. Contribute to IHI JU SRIA objectives, driving cross-sectoral health innovation for a competitive European health industry;
2. Infrastructure funding initiatives establishing ASCs in orthopaedics and cardiology;
3. New long term healthcare strategy, planning and funding in HCP recruitment and training as well as digital solutions and medical technology for efficient ASC services;
4. Implementing new payment systems (coding and reimbursement) allowing for patient referral to ASC based on medical and clinical decisions and provider capacity, rather than on payment system;

5. Establishment of a sustainable network of ASCs followed by the creation of national and regional ASCs associations;
6. Regulation and accreditation of ASC facilities;
7. Comprehensive and interoperable digital solutions supporting people-centred care, disclosing entire patient treatment pathways and experiences including points of access for patients;
8. Treatment database/registry as a source of evidence enabling research, decision making, further development and improvement of ASCs.

The action will also support the EU political priority to boost European competitiveness and contribute to a number of European policies/initiatives, which include the European Commission's European Health Data Space Regulation (EHDS)[45] and the EU Artificial Intelligence Act[46].

Why the expected outcomes can only be achieved by an IHI JU action

Changing trajectory and practice from in-hospital procedures to ambulatory surgical centres will depend on the involvement of a range of stakeholders: hospital management, healthcare providers, technology developers, academics, health insurance companies, reimbursement agencies, patient organisations as well as medical technology companies. IHI facilitates this collaboration by fostering cross-sector cooperation which is unique and a pivotal requirement for initiatives of complex scale.

Pre-identified industry consortium

The pre-identified industry consortium that will contribute to this cross-sectoral IHI JU project is composed of the following medical technology industry beneficiaries ('constituent or affiliated entities of private members'):

- Medacta
- Medtronic
- Johnson & Johnson
- Smith & Nephew
- Stryker
- Zimmer Biomet (Lead)

In the spirit of partnership, and to reflect how IHI JU two-stage call topics are built upon identified scientific priorities agreed together with a number of proposing industry beneficiaries (i.e. beneficiaries who are constituent or affiliated entities of a private member of IHI JU), it is envisaged that IHI JU proposals and actions may allocate a leading role within the consortium to an industry beneficiary. Within an applicant consortium discussing the full proposal to be submitted for stage 2, it is expected that one of the industry beneficiaries may become the project leader. Therefore, to facilitate the formation of the final consortium, all beneficiaries, affiliated entities, and associated partners are encouraged to discuss the weighting of responsibilities and priorities regarding such leadership roles. Until the role is formalised by execution of the Grant Agreement, one of the proposing industry beneficiaries shall, as project leader, facilitate an efficient drafting and negotiation of project content and required agreements.

Indicative budget

- The maximum financial contribution from the IHI JU is up to EUR 12 351 000.

[45] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:L_202500327
[46] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32024R1689

- The indicative in-kind contribution from industry beneficiaries is EUR 12 351 000.

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 (IKOP) from those countries that are neither part of the EU nor associated to the Horizon Europe programme.

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

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 predefined industry consortium may jointly agree on a different duration when submitting the full proposal.

Contribution of the pre-identified industry consortium

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

- Facilitate logistics and communication for advisory board establishment and ASC network;
- Access to the latest medical technologies and equipment, ensuring that ASCs can offer high-quality care;
- Assistance with training medical and administrative staff, ensuring that ASCs have skilled personnel to deliver excellent patient care;
- Facilitate partnerships with other healthcare providers, organisations and established ASCs, which can conduct training, share best practices in enhancing service offerings and patient care
- Research and regulatory expertise and guidance in conducting studies, setting databases and real world evidence generation;
- Health economics modelling;
- Digital solutions for tracking patient pathways to streamline and enhance patient experience;
- Project management.

Applicant consortium

The first stage applicant consortium is expected, in the 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.

The consortium must demonstrate the ability to jointly deliver innovation, evidence generation, and implementation across various healthcare systems in Europe.

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

1) Hospitals and healthcare providers - required expertise:
    - Experience in performing orthopaedic and cardiac procedures, including joint replacement and ablation;
    - Involvement in outpatient care models or previous piloting of ASCs;
    - Capacity to lead and contribute to clinical studies comparing inpatient and ASC-based interventions;

- Insight into patient pathways, clinical protocols, and integration with home recovery services.

2) Academia and research and technology institutions - required expertise:
   - Design and conduct of health services research and clinical studies, including RWE (real world evidence) and health economics;
   - Capability to lead evidence generation on safety, efficacy, and cost-effectiveness of ASCs;
   - Methodological support for patient selection criteria, Patient Reported Outcomes Measures (PROMs) collection, and statistical evaluation.
3) Medical technology companies - required expertise:
   - Developers and providers of surgical devices, diagnostics, and digital tools used in orthopaedics and cardiology;
   - Capacity to adapt or develop technology suited for ASC environments;
   - Expertise in digital health solutions including remote monitoring, electronic health records integration, and telemedicine platforms.
4) Digital health and IT Providers - required expertise:
   - Deployment of interoperable health information systems across care settings;
   - Data security and privacy compliance (e.g. General Data Protection Regulation, 2016 'GDPR') and digital infrastructure support;
   - Tools for patient management, telehealth, and care navigation;
   - Development of ASC registries and clinical databases.
5) Patient organisations - required expertise:
   - Insight into patient expectations, preferences, and concerns regarding surgical care in ASCs;
   - Contribution to communication strategies and patient-centred design of care pathways;
   - Support in recruitment for surveys and qualitative research.
6) Payers and reimbursement bodies - required expertise:
   - Understanding of current reimbursement frameworks and their gaps;
   - Co-development of innovative payment models adapted to ASCs;
   - Guidance on defining clinical and economic endpoints relevant for reimbursement acceptance.
7) Policy and regulatory experts - required expertise:
   - Knowledge of national healthcare policies and regulations affecting outpatient and ASC settings;
   - Development of recommendations for ASC recognition, quality assurance, and standardisation;.
   - Engagement with health technology assessment bodies and regulators to support project sustainability.
8) Professional medical societies and networks - required expertise:
   - Support in standardisation of care protocols and guidelines for ASC procedures;
   - Dissemination of training materials and best practices;
   - Endorsement and outreach to accelerate uptake across member organisations.

At the second stage, the applicant consortium selected at the first stage and the pre-identified industry consortium will form the full consortium. The full consortium will develop the full proposal in partnership,

including the overall structure of the work plan and the work packages, based upon the short proposal selected 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.

Legal entities established in the UK

According to the conditions of the calls and call management rules under ‘Entities eligible for funding’, legal entities participating in this topic and established in UK are not eligible to receive funding.

Legal entities established in Canada

According to the conditions of the calls and call management rules under ‘Entities eligible for funding’, legal entities participating in this topic and established in Canda are not eligible to receive funding.

References

[1] Daher, M., Cobvarrubias, O., Boufadel, P., Fares, M. Y., Goltz, D. E., Khan, A. Z., Hornef, J. G., & Abboud, J. A. (2024). Outpatient versus inpatient total shoulder arthroplasty: A meta-analysis of clinical outcomes and adverse events. Journal of Shoulder Surgery. Int Orthop. 2025 Jan;49(1):151-165. doi: 10.1007/s00264-024-06364-5. Epub 2024 Nov 5. PMID: 39499293

[2] Bemelmans, Y. F. L., Keulen, M. H. F., Heymans, M., van Haaren, E. H., Boonen, B., & Schotanus, M. G. M. (2021). Safety and efficacy of outpatient hip and knee arthroplasty: a systematic review with meta-analysis. Arch Orthop Trauma Surg. 2022 Aug;142(8):1775-1791. doi: 10.1007/s00402-021-03811-5. Epub 2021 Feb 15. PMID: 33587170.

[3] Ahmed, A. F., Hantouly, A., Toubasi, A., Alzobi, O., Mahmoud, S., Qaimkhani, S., Ahmed, G.O., & Al Ateeq Al Dosari, M. (2021). The safety of outpatient total shoulder arthroplasty: A systematic review and meta-analysis. Int Orthop. 2021 Mar;45(3):697-710. doi: 10.1007/s00264-021-04940-7. Epub 2021 Jan 23. PMID: 33486581; PMCID: PMC7892728.

[4] French JMR, Woods A, Sayers A, Deere K, Whitehouse MR. Day-case knee and hip replacement. Bone Joint J. 2024 Dec 1;106-B(12):1385-1392. doi: 10.1302/0301-620X.106B12.BJJ-2024-0021.R1. PMID: 39615519.

[5] Messerle R, Hoogestraat F, Wild EM. Which factors influence the decision of hospitals to provide procedures on an outpatient basis? –Mixed-methods evidence from Germany, Health Policy, Volume 150, 2024, 105193

Glossary

Acronym	Meaning
AD	Alzheimer’s disease
AI	Artificial Intelligence
ASCs	Ambulatory Surgical Centres
CGM	Continuous glucose monitoring
CMV	CytoMegaloVirus
CNS	Central nervous system
EBV	Eibstein Barr Virus
EEG	Electroencephalography
EHDS	European Health Data Space
EHRs	Electronic Health Records
EMA	European Medicines Agency
EPITA	European Pancreas and Islet Transplant Association
EPITR	European Pancreas and Islet Transplantation Registry
EPND	European Platform for Neurodegenerative Diseases
FAERS	FDA Adverse Event Reporting System
FC	Financial contribution
FDA	Food and Drug Administration
fMRI	Functional magnetic resonance imaging
GDI	Genomic Data Infrastructure
GDPR	General Data Protection Regulation
HCP	Healthcare professional
HCPs	Healthcare professionals
HERA	European Health Emergency Preparedness and Response Authority
HITL	Human in the Loop

HSV	Herpes Simple Viruses
HTA	Health Technology Assessment
IA	Infectious agent
ICT	Information and Communication Technologies
IHI	Innovative Health Initiative
IHI JU	Innovative Health Initiative Joint Undertaking
IKKA	In-kind contributions to additional activities
IKOP	In-kind contributions to operational activities
IP	Intellectual Property
LE	Lived experience
LLM	Large Language Model
MDD	Major depressive disorder
MEG	Magnetoencephalography
MoA	Mechanism of action
MRI	Magnetic Resonance Imaging
NCD	Non-communicable disease
NCDs	Non-communicable diseases
NLP	Natural language processing
PET	Positron emission tomography
PoS	Probability of Success
PPP	Public-private partnership
PROMs	Patient reported outcomes measeures
PV	Pharmacovigilance
RM&I	Reward/motivation and impulsivity
RWE	Real World Evidence
SDG	Sustainable Development Goals

SOPs	Standard Operating Procedures
SRIA	Strategic Research and Innovation Agenda
SRSs	Spontaneous reporting systems
T1D	Type 1 Diabetes
TIR	Time in Range
TiTR	Time in Tight Range
TSA	T shoulder arthroplasty
VZV	Varicella Zoster Virus
WHO	World Health Organisation