IHI JU Science & Innovation Panel (SIP)

11th Report to the IHI JU Governing Board

11th MEETING OF THE SIP

27.02.2025 (09:30 – 18:00 CET) - 28.02.2025 (09:00 – 13:00 CET) – Hybrid meeting

This report summarizes the SIP opinions related to the following agenda items:

- IHI Progress Report
- Preparation of the 2025 two-stage Call
- Review of the latest ideas submitted by the wider health and research community
- Exploring areas for future IHI activities

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1. IHI Progress Report

Report from last meetings of the IHI JU governance bodies and IHI multi-annual science plan.

The SIP welcomed the report presented by the IHI Executive Director. The focus on innovations and how the IHI Science Plan aligns with members' priority actions were very clearly articulated. The way IHI Call topics and ideas align with priority actions provides a good basis for including horizontal themes. In this regard, it would be worthwhile considering the EU life sciences and biotechnology strategies, as well as the developments in relation with the European Biotech Act, the Critical Medicines Act, and the Critical Raw Material Act, including AI and cybersecurity regulatory requirements (at organizational level and on product specific level). The impact of all of these legal and regulatory developments will require a strategic reflection towards workforce development and continuity of support over time [1]. This includes tools and solutions addressing healthcare services efficiency and their impact on patients. Moreover, seeing the current geopolitical developments, the SIP would question how the dual use of innovations will be addressed, including how project reviews would, for instance, exclude high risk suppliers (countries or entities?). This includes optimizing workforce mobilization by considering learnings from the defense sector or from contexts of chronic healthcare personnel shortage (e.g., LMICs).

[1] E.g., ongoing THCS initiative; policy papers addressing training of healthcare workforce.

Portfolio and project highlights

The SIP had previously highlighted the importance of increasing the visibility of the biotechnology and ATMPs investments in the IHI portfolio of activities. The SIP acknowledged the presentation of the IMI/IHI funded projects to date which have addressed the following four major areas in biotechnology-based treatments:

- Innovation for Biotechnology Manufacturing Process development, Biotechnology Tools [2]
- Safety, Metabolism, Distribution of Biotechnology treatments [3]
- Regulatory aspects and clinical trial networks of Biotechnology development [4]
- Funding for product development in Ebola and Covid-19 related technologies [5]

The SIP congratulated the IHI office on the delivery of this vast portfolio with already 30 projects launched and appreciated the constellation of projects around the strategic objectives of IHI, including the IMI legacy and projections of IHI into the mid 2030's. Supporting excellent science, and the biotechnology sector is key in driving innovation. Improving uptake and implementation of innovation for high impact results should capitalize on the unique positioning of European healthcare systems' coverage. The availability of almost complete healthcare data represents a competitive advantage for Europe. Identifying areas where Europe is a forerunner and areas where it is not, but with higher potential for patients, should be strategically considered when planning the development of future IHI activities.

Synergies with other initiatives

The SIP recognized the numerous IHI activities, namely in oncology, supporting EU priorities such as Europe's Beating Cancer Plan, the SAMIRA action plan and Cancer Mission, as well as vaccines and preparedness discussions with CEPI, GH EDCTP3 JU and EC (HERA, RTD, INTPA, SANTE). The SIP encourages IHI to continue exploring the EU ecosystem in order to increase potential synergies and partnerships with ongoing initiatives even further (potential for projects in the areas of post-market surveillance and regulatory science).

The SIP recommends continuing exchanges with currently identified initiatives for potential synergies for specific themes or topic ideas under discussion (e.g., THCS for healthcare delivery optimization, and EP PerMed for pharmacogenomics).

The SIP also recommends seeking interactions with the European Partnership for Brain Health, which is being prepared by the Coordination and Support Action (CSA) BrainHealth and with the European partnership on One Health Antimicrobial Resistance, which is starting its activities in 2025.

[2] EBISC2, Inno4Vac, iConsensus, Chem21
[3] ARDAT, RealHope, COMPACT, ImSAVAR
[4] T2Evolve, EDENT1FI, Innodia/Innodia Harvest, C4C, Aims2trial
[5] Covid red, Decision, DRAGON, Impentri, KRONO, MAD-CoV 2, RAPID-COVID, EbolaMoDRAD, FILODIAG, Mofina

The SIP recognizes the challenge of developing and maintaining such network in the current research and innovation ecosystem, considering potential conflicts of interest as some of the other partnerships could be IHI applicants, and would therefore advise to identify priorities within a forward-looking exercise on 2025-2027 potential synergies based on partnerships or themes (e.g., EIC Accelerator, PerMed, implementation science…).

Engagement with contributing partners (CPs), and in-kind contributions to additional activities (IKAA)

The SIP welcomed the presentation of the IHI total amount of CPs' contributions as approved by the Governing Board. The presentation of the breakdown of CPs in IHI Calls 1-7 and of the total IKOP as declared in the applications letters and in the Call 8 topics text was very informative. Charities and foundations are present. However, the SIP finds that IHI could be more visible to healthcare/hospital organizations and to NGOs. Overall, the SIP would recommend keeping attention on the structure of the organizations involved (i.e., check EU versus non-EU funding through origine of expertise that is made available in IKOP setting). The planned IKAA are well within the regulation envelope.

Bibliometrics analysis

The SIP welcomed the very comprehensive presentation of the bibliometrics analysis made by the IHI scientific officer. The SIP would like to see the impact report per domain under preparation by the IHI office and would recommend to further link this analysis with the deliverables of IMI/IHI projects, such as annexes of publications that could for instance be easily accessible (e.g., dedicated repository) and serve for advice to developers (e.g. tools, programs used by the researchers...).

Although publications represent an important KPI (among the many other relevant IHI KPIs) and an external validation of the quality of the research of IHI, it is important to consider ways to maximize the utilization and the long-term viability of the published tools and related databases. The results of these publications could also be disseminated more widely and meaningfully to the general public by adapted communication as being part of the "research journey story" with the aim to improve patients' lives.

Seeing the vast number of publications produced from IMI/IHI projects, the SIP would suggest urging future proposals to consider the long-term viability of their deliverables at a much earlier stage, including ways to sustain funding (i.e., innovation scaling strategies, operationalization and continuation of activities, IP strategy and governance for the dissemination/sharing of data).

2. Preparation of the 2025 two-stage Call

The industry leaders presented 9 early draft topic texts to the SIP. The first 4 early draft topic texts were presented under the common theme "Care beyond the Hospital Walls Flagship". The opinion of the SIP is summarized as follows:

Theme "Care beyond the Hospital Walls Flagship"

1) "Hospital at Home and Home Care"

The proposed draft text addresses an important issue, and the expected impacts make sense. However, the SIP would like to see where the innovation would occur beyond the management and procedural research questions. It could be worthwhile looking at examples of successful public-private partnerships such as the operating model of the CleverHealth Network [6] in Finland and clarify objectives of research versus implementation.

Considering the challenges related to differences in healthcare coverage and reimbursement systems across the EU, the question of equity of future access to the technologies needs to be considered. This includes considering adapted educational tracks for staff providing such home care services and operation management outcomes.

The currently drafted objectives are not fully aligned with identified challenges, and it is important to highlight what the envisaged project would aim to offer beyond what is already available. The SIP would suggest considering emphasizing the healthcare workforce dimension within this topic.

2) "Chronic Disease Management"

The proposed topic is overall in line with the IHI strategic objectives, but from the draft text as it stands it seems that the objectives are more about implementation rather than science. The proposal from the presenters to merge the draft texts 1, 2 and 3 in one would make more sense but it is recommended to clarify the aims (healthcare delivery vs policy transformation) and to better align them with the identified challenges.

The SIP would recommend exploring existing partnerships involving other sectors such as insurance companies and primary care networks (e.g., Care-Connect[7], Control DTx[8], that are publishing outcomes for chronic disease management) and envisage the development of HTA tools with new criteria for payers and decision makers to make the innovation accessible to more patients.

3) "Digital Infrastructure"

The SIP understands the relevance of the proposed draft text within the theme of care beyond the hospital walls and sees this as an objective of the 3 texts that would be merged, because digital infrastructures are prerequisites for enabling implementation. The SIP recommends illustrating how this would differentiate from EHDS and other initiatives. Moreover, it would be important to highlight which gaps would be addressed by such infrastructure towards existing standards (e.g., HL7 [9])

[6] https://www.cleverhealth.fi/en/home
[7] https://care-connect.ie/
[8] https://controldtx.com/
[9] https://www.hl7.org/

considering the challenges of varying technical standards in EU, silos of care and diverse reimbursement systems.

From the proposed draft text, it is not yet clear how technology would overcome these hurdles and if criteria would be developed to choose between ambulatory setting and hospital. If the proposal is to feed decision making in real time, the SIP advises to formulate the research questions for collecting the data and clarify the objectives around harmonization for data sharing.

4) "Ambulatory Surgical Centers"

The SIP questioned the feasibility of the proposed topic as it stands due to the safety requirements around general anesthesia (i.e., need for ICU) and the implications in terms of workforce training. It is important to clarify how the proposal will consider anesthesiology guidelines and how this would address staffing issues and cost-effectiveness.

The SIP would recommend verifying the state of play in EU (check figures of how many surgeries are day surgeries) and clarify how separate ambulatory surgery centers would bring innovation.

The safety and effectiveness dimensions need to be further developed, and the types of stakeholders that would be involved need to be identified. The proposed text could address the safety, efficiency and cost-effectiveness of colocalized settings, where day surgery occurs in hospital premises requiring lean management to move patients through the system. This would also need identifying existing evidence to make sure the topic addresses identified gaps.

Finally, the SIP is of the opinion that the cost-effectiveness and HTA objectives should be more prominent.

Other themes

Regarding the early draft texts 5 and 6, the SIP has completed their opinion based on additional information received after the SIP meeting.

5) "AI-Powered Signal Detection in Pharmacovigilance"

The proposed topic is very relevant for public health and regulatory science. It should focus on signal detection and on (spontaneously reported) ICSRs, because this area will remain having a high public health impact (safe medicines; much more than 50% of all signals come from this source) and will remain representing a high workload for all stakeholders (pharmaceutical industry, regulators, health professionals and others). EMA's Regulatory science research needs (draft 2024 update) include the priority RP11 on AI in pharmacovigilance processes, for improving signal management, a well-established pharmacovigilance activity, and for exploring complementary data sources.

Relevant stakeholders should be involved which my have different utilities (e.g., ethics boards, DPOs) and costs related to false positives and false positives should be considered when it comes to personalized risk prediction.

The ambitions ("Expected impacts") would need to cover:

a) earlier signal detection
b) faster and more precise signal evaluation
c) new tools that are demonstrated as robust (working across different scenarios)
d) improved data quality across pharmacovigilance data management (incl. duplicate detection)
e) improved risk mitigation, including communication

To enable significant change for all actors in the EU pharmacovigilance system, the deliverables ("Expected outcomes" or "Scope") should be very practical, beyond an 'aligned AI position':

a) It should be stated that a suite of tools / algorithms will be developed and piloted
b) and tested against different business scenarios by different stakeholders, including EudraVigilance, FDA published data, UMC datasets, company datasets
c) subsequently made available timely and publicly as open source so that stakeholders can implement and continue to collaborate; particularly if EMA is involved in the testing of tools, there is a high probability of implementing the tools and algorithms in EudraVigilance
d) user guides and training materials should accompany the validated tools

Furthermore, sources other than ICSRs mentioned in the draft are less of a priority and the call text should emphasize that trustworthiness and transparency should be central to the development, testing and availability of the tools and methods.

The SIP also raised questions regarding education and training dimensions, regarding the fact that some therapeutic areas would be prioritized by the proposers, if and how pharmacogenomics would be dealt with, and about the applicability of such approach to medical devices.

6) "REACH – Real-world Evidence Acceleration through Continuous Harmonization"

The SIP finds it relevant to capitalize on the EHDEN deliverables, which would entail to be "disease agnostic" based on use cases in specific diseases, which would provide insights on how to further improve the system. The text needs more clarity regarding objectives and expected outcomes within the governance of EHDS. It is unclear if EHDS is referenced only to say that terminologies can be applied through the EHDS. It is therefore important to include studies / use cases with EHDS data.

Besides facilitating the conversion of an increasing number data sources into the common data model (OMOP), in a continual fashion, the proposal should also include that for each data source, the number of variables (data) that are translated are expanded, based on the experience that, at the time a study needs to be executed, it was found that relevant variables available in source data had not been converted.

The expected outcomes need to be clearer on what general type of physical and / or logical organisation is targeted for the project and its self-sustained structure that is expected to be targeted (loose network unlikely sufficient). The concepts of “platform”, “dynamic network” are unclear. The expected outcomes should include a structured representation of study protocols, of the scientific research approach, including the phenotype(s) definition and operationalization; the project should also include how phenotypes are identified, evaluated, and validated.

The call should express that the project needs to develop a global international strategy to ensure driving the field, in addition to the clear focus and applicability for EU and EHDS.

Regarding the expected outcome “sustainable processes for standardized vocabularies and mappings,” it should include a concept phrase that expresses the necessary high level of ambition such as EU or international ‘Vocabulary Services’. For example, high needs exist for automated mapping of terms between vocabularies, as many as possible (e.g., a MedDRA code automatically finds the corresponding ICD code[s]). The call text should be clear where the expected developments concern the mapping and application, and / or where they concern the content improvement of vocabularies – both needed. Thus, the call should include the need to develop systematic strategies for feeding improvement proposals to the bodies responsible for vocabularies (ontologies, terminologies), which are often owned and curated at international level and outside the EU (by bodies such as WHO [ICD], ICH [MedDRA] or national [MeSH]). Specialty vocabularies should be explicitly mentioned in “Scope”, e.g. ICD-O, mCODE, CTCAE, Orpha codes, bioinformatics terminologies.

The expected outcomes should include publishing source-specific mappings as open source and to enable broad and practical re-use with lowest possible hurdle. The “certification of data partners”: should be somewhat clearer on the expected scope, e.g. standardization of conversion into OMOP, of standard analyses feasibility or beyond. The draft refers to “advanced methods”, but these are not regularly needed; simple and basic methods are often enough to address the research questions and study design.

Finally, it is important to mention a training (system) in the expected outcomes as it was a byproduct in EHDEN, and which will benefit from being brought into the focus of project planning.

7) *“From empiric to evidence-based medicine in Mental Health – European Factory to identify new symptomatic stratification and efficacy markers of CNS function and mechanisms”*

The SIP understands that the proposal is about mapping symptoms to the biology and change diagnostic criteria from disease as specified in DSM5 or ICD10 to biology-driven diagnosis. Shifting from solely relying on symptoms/environmental circumstances for diagnosis to including biological patterns in order to treat the underlying biological cause in the brain dysfunction would be relevant.

However, the currently described objectives lack clarity about the specific measures that would be considered and their potential impact on the feasibility within the envisaged project timelines.

For instance, it is not clear what type of data and markers would be considered (change in diagnostic criteria classification, endpoint or biomarker validation), and which stakeholders would be involved (psychologists and psychiatrists?). The SIP also questioned how subjective measures of mental health based on questionnaires would be dealt with and how would they be linked with wearable data? Would the data/evidence collected through questionnaires and the biological features to inform biological circuit, include imaging, assessments of mood etc.? The targeted population of such project could include young people suffering from mental health issues.

The need to improve assessments beyond the qualitative approaches could for instance be addressed in the validation for the proposed platform which also needs clarity regarding its scope (one big platform or disease specific?). The SIP also questions the platform as a main deliverable of such project and recommends quality gates and validation studies to be included along the setting up of the platform, which would generate further hypotheses. For instance, it is not clear if the envisaged evidence would help inform reimbursement and what the long-term goals would be. It would therefore be relevant to anticipate HTA parameters.

The destiny of the platform beyond the project needs to be addressed based on experience from previous IMI projects foreseeing future funding to maintain databases and platforms.

Finally, it will need to be open source and when aiming at driving standards, it should consider EHDS to leverage the platform.

8) "The interception between infectious and chronic diseases"

The objectives of the proposal are strategically aligned and organized around three pillars of action. However, the proposed sequence may be reviewed in light of the challenges related to the access to preclinical models and to the collection of new tissues from patients.

The proposal needs more framing and scoping to generate refined hypotheses and refined methods because associations have been reported. Before application to such call, work should be carried out to explore causality of developed methodologies to ascertain the association. Therefore, the proposed 3 pillars need to be reviewed and address what happens after the mining and how will hypotheses be ascertained. Moreover, it is not clear how that would generate RWE from anonymized data and how they would be connected with prospective collected tissues. If the same patients would be identifiable/identified it would be necessary to anticipate the regulatory implications.

Some of the objectives need to be more precise and consider the challenge of lag time between an infection and the presentation of NCD, including individual susceptibility factors, e.g. COVID is difficult to detect after the viral infection. Could managing this timeline within the project, be achieved by interrogating an existing cohort retrospectively?

Because of the complexity linked with the discovery of potential new pathogens and new associations the SIP recommends focusing on specific diseases and suggested deep immuno-

profiling as part of the exposome to be considered. This could be considered for auto-immune diseases as an interface between infection and NCD and potentially when following up transplant patients NCD outcomes.

The SIP also recommends exploring learnings and evidence from other sources such as health insurance entities and from previous projects within HORIZON EU, which would help identify consortia with relevant expertise.

9) "Cell therapy for Diabetes"

The proposal identifies critical challenges to overcome for making cell therapy available to patients, which is an interesting and ambitious opportunity. The SIP sees the importance of addressing quality of manufacturing and evidence collection for further regulatory approval and recommends considering an EMA consultation for regulatory scientific advice.

The proposal should more explicitly address costs and reimbursement by including payers and HTA early on, as well as patients. For this, it would be important to highlight the need to work with professional societies to define a clinical pathway that would demonstrate appropriate evidence for reimbursement and subsequent criteria for patient access based on success rate of the procedure, types of patients more likely to benefit from it (i.e., age range, hypoglycemic unaware patients, young people in 30s with CVD complications, retinopathy, …).

Finally, the SIP also questioned the idea of adding immune monitoring and continuous glucose monitoring, through biosensors and AI, because there is a big gap in the monitoring. Therefore, it could be worthwhile exploring how to leverage learnings from immune monitoring strategies within the oncology space.

3. Review of the latest ideas submitted by the wider health and research community

The SIP further discussed the latest 4 ideas submitted by the wider health and research community and agreed on how to finalize the SIP outcomes.

4. Exploring areas for future IHI activities

The SIP further discussed the areas which have been previously identified areas for future IHI activities in the form of the horizontal themes.

Mental health

The recent developments within the EU policy arena have further highlighted the need to consider mental health as a transversal theme when preparing future calls.

The SIP agreed to recommend mental health of children as a priority and would recommend to already include children in the currently drafted text addressing mental health in the 2025 two-stage call.

Based on its latest discussions, the SIP has finalized its recommendation paper[10] listing the knowledge gaps in mental health that they have currently identified, and which could potentially be addressed within IHI.

Healthcare delivery optimisation

The SIP acknowledged and appreciated the fact that some of its previous recommendations had already been taken on board in current calls.

Given the transversal dimension of this theme, the SIP has finalized a revised version of the recommendation paper[11] that aims to convey key questions that could be included in the template for applicants, and which could eventually be shared with potential contributing partners.

Annexes to the report:

IHI JU Science & Innovation Panel (SIP) - Recommendations to the Governing Board

I. MENTAL HEALTH
II. HEALTHCARE DELIVERY OPTIMISATION

[10] As annex I to this SIP report.
[11] As annex II to this SIP report