IHI JU Science & Innovation Panel (SIP)
6th Report to the IHI JU Governing Board

6th MEETING OF THE SIP
22 March 2023 (14:30 – 18:15 CET) & 23 March 2023 (09:30 – 14:00 CET) – Hybrid meeting

This report summarizes the SIP opinions related to:

- IHI Progress Report & Project highlights
- Preparing the next IHI Calls (single stage and two-stage))
- Collected ideas submitted to the SIP

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IHI Progress Report & Project highlights

The SIP welcomed the presentation of the progress report on the scientific and innovation activities of IHI and in particular,

- the comprehensive roadmap for launching the IHI calls,
- IMI project results with significant impacts on regulatory processes [1]
- sustainability of project outputs, namely through the establishment of legacy organisations [2] and outputs developed in further projects [3]
- results on respiratory diseases which impacted European hospitals in the winter [4]
- results showing potential of full cross-sector partnerships [5]

[1] E.g. PREFER, NECESSITY, MACUSTAR, EHDEN
[2] E.g. INNODIA vzw, EQIPD association, PharmaLedger association
[3] E.g. ENABLE (IMI1) to GNA-NOW (IMI2), TRIC-TB (IMI2) to EDCTP2 project, European Lead Factory (IMI2) to Horizon Europe project
[4] E.g. RESCEU, FLUCOP, DRIVE, various projects on COVID-19
[5] E.g. BigData@Heart framework, BIGPICTURE, c4c & CDISC user guide, EHDEN data network, FAIRplus 'cookbook', MELLODDY federated machine learning

The SIP wishes to congratulate the IHI Programme Office on the continuously impressive amount of work and outputs, including the demonstration of its excellence in administration.

The SIP welcomed the detailed updates on contributing partners, on mechanisms in place within IHI for synergies, future calls, as well as close out meetings for different IMI projects.

The SIP appreciated the presentation of two project highlights and made the following comments:

- eTRANSAFE: The SIP saluted the important and significant achievements delivered by the consortium, aiming at the sharing of legacy drug safety data. The SIP noticed the challenge of combining donated industry data and data from public sources, in terms of interoperability when dealing with integration of information from different databases.
- PREMIER: The SIP acknowledged that the project's vision is compelling and addresses the need for science-based prioritization when dealing with the environmental risks of medicines. The SIP welcomed the synergy with the EU-funded TransPharm project.

Preparing the next single-stage Call

The IHI Scientific Project Officers presented four early draft topic texts. The SIP opinion is as follows:

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

The SIP welcomes this proposed topic, since addressing the reduction of animals used in research is a very important topic in the development of health technologies. Envisaging the involvement of regulators from outside the EU is a good idea. In addition, the industry partners, as global players, have a good understanding of the regulatory landscape worldwide in this area. The SIP is of the opinion that it is important to clarify the sequence between developing a new technology and the acceleration of its implementation, for instance, by mentioning that performance evaluation and validation would need to be done before the acceleration phase. Moreover, the terminology regarding the use of animals should focus on the 3Rs and make sure the wording is consistent with these principles across the call text.

1.2 Development and proof of principle of new clinical applications of theranostic solutions

The proposed topic is ambitious, timely and scientifically sound. However, it should not be limited to the development of new diagnostics. The combination of new technologies with existing modalities could deliver innovation, for instance, by combining state of the art diagnostics and state of the art treatment with the aim of improving implementation in the clinic. In addition, when developing new clinical applications, it is important to include a proof-of-concept element to demonstrate the benefit for the patient versus existing approaches.

1.3 Improved prediction, detection and treatment approaches for comprehensive stroke management

The proposed topic is very ambitious and addresses a high-unmet medical need. The SIP has identified a few challenges, which are related to the heterogeneity of health systems across the 27 EU member states, the logistics of bringing patients to the hospital and the potential eligibility of the health structures (cf. stroke units accreditation). The text should emphasize the place of primary and secondary prevention and how they could be combined, and clarify the expected innovation (e.g. prediction, detection and management of risk, detection at early stage, improved logistics of organizing access to treatment). An additional challenge is related to the aim of addressing a large patient pool. Therefore, the SIP would advise to focus on specific patient groups or including stratification of patients at risk.

1.4 Maximising the potential of synthetic data generation in healthcare applications

The SIP finds the proposed topic ambitious and timely. Several questions were raised and which are related to:

- the need to emphasize in the text the application side and how this would build on existing data from other initiatives (e.g. EHDEN, link with EHDS).
- the need to connect with the regulators and address how would this generate capacity to have approval for different treatments.
- the interest of having sufficient data to build predictive models and how validation will be done and, in particular, the place and value of synthetic data versus augmentation of datasets or other existing validation methods. For instance, in some cases, synthetic data do not always need to be validated (cf. synthetic voice pathology samples). In this case, the text could explicitly state that, whenever applicable, validation should be addressed.
- the challenge of having access to EU patient data vs GDPR.

Finally, the potential links with EHDS being challenged by the fact that the legislation is not yet finalized, it is recommended to add a standard sentence in the call text to have alignment with EHDS.

Preparing the next two-stage Call

The industry-founding members presented a series of early draft topic texts. The SIP's opinion is as follows:

1.1 Inclusive clinical studies for equitable access to clinical research in Europe

The SIP supports the proposed topic text overall and made a series of comments aiming to improve the readability and clarity of the call scope and expected outcomes and impacts:

- The scope of the topic should be clearer, whether it aims at the same time at health services, clinical trials, and a platform; how a platform would increase inclusiveness, how it would be

interconnected with other platforms and how the ownership issues will be dealt and it would be governed for sustainability.
- The topic text should be clearer regarding the difference between access to health services and access to clinical trials.
- The definition of vulnerable population and related criteria would need to be completed with additional criteria to increase inclusiveness in clinical trials (e.g. difference between "underserved" vs "under represented" patients). The SIP recommends reviewing it with patient societies to shape it further and eventually engaging with less educated patients to identify gaps in reaching less informed patients.
- Elements of social determinants of health should also be included.
- Finally, the proposed topic should not only focus on recruitment but also insist on patient retention, especially among difficult to reach populations that would be advocates for further inclusion of additional patients in clinical trials.

1.2 Establishing novel methodological approaches to enable designing and executing novel clinical trial designs for medicines in rare and ultra-rare diseases

The proposed topic addresses a huge unmet need for clinical trials in patients affected by rare and ultra-rare diseases. The SIP welcomes the fact that it builds on existing initiatives and that it appropriately highlights the potential synergies. Consortium representation across the EU is needed but might be challenging for member states with less developed healthcare systems. The aiming at higher probability to assign patients to active treatments could carefully be highlighted as an added value, including the types of clinical trial designs that would be appropriate for establishing novel treatments while achieving this for patients. Finally, the SIP recommends more explicit wording in relation with regulatory objectives.

1.3 Safe & Sustainable by Design (SSbD) packaging and single use device solutions for healthcare products

The SIP finds this topic highly important. However, the four Rs (Rethink, Reuse, Reduce, Recycle) elements are missing and the topic should not focus on plastics only. The proposed topic should include new other materials and new approaches for logistics and supply chains and address additional pathways of waste related to hospitals, ambulatory structures and nursing homes. It would be useful to add an education dimension and consider a pilot to test the pathway from factory to patient, which would also include regulatory questions related to green goals. Finally, the text could benefit from building on existing initiatives and frameworks (e.g. The Netherlands Integral Circular Economy).

1.4 Sustainable circular development and manufacturing of healthcare products and their quantitative environmental impact

The proposed topic is clearly complementary to the previous one (1.3) and to the presented IMI project PREMIER. The SIP asked for the reasons to focus on active pharmaceutical ingredients

(APIs) and suggested to explore the opportunity to include medical device combination products, as they represent an increasing share in the environmental impact of healthcare products.

Collected ideas submitted to the SIP

The SIP found the presentation of the state of play of the ideas that have been submitted so far, including the countries and disease areas representation, very informative.

One SIP member suggested an idea that would address the use of data from developments of health interventions (medicines and devices) that were not brought to the patient or market. The SIP discussed the challenge of compiling data that are heterogeneous and the need to consider validity and reliability of the data, how to structure it and which models could be applied to this data. A potential call could address the mapping and understanding of the data. The SIP is of the opinion that the way forward would be exploring the idea and eventually consider including this dimension in already proposed topics (e.g. in the areas of stroke, ischemia…). The SIP also mentioned the need to look at earlier projects that have focused on patient stratification, patient responder subgroups, pharmacogenomics, and projects including medical devices and diagnostics. The IHI office could prepare and present a condensed set of previous projects to build on the idea.