All information regarding future IHI Call topics is indicative and subject to change. Final information about future IHI Calls will be communicated after approval by the IHI Governing Board.

Topic 3 : Modelling regulatory sandbox mechanisms and enabling their deployment to support breakthrough innovation

Expected outcomes

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

- Recommendations for end-to-end operations of regulatory sandboxes to inform health care innovation developers, regulators, and other decision makers.
- Roadmap for innovation regulatory support pathways to guide emerging health technologies identified through horizon scanning to the most suitable mechanism.
- Alignment on the understanding of how regulatory sandboxes can drive science and health technology innovation in an evolving environment, and how uncertainties can be addressed.

Scope

While there is no concrete definition, regulatory sandboxes generally refer to regulatory frameworks that provide a structure for healthcare innovation developers to test and experiment with new and innovative products, services, or approaches under oversight of a regulator for a limited period of time. These adaptive tools are meant to address challenges arising from the acceleration of technological / scientific advances and the mechanisms intended to regulate them. It offers customisation in terms of how a regulatory framework can be applied, combined with appropriate safeguards.

Regulatory sandboxes, first tested in the fintech sector (2015), are making their way towards transforming the traditional methods used by regulatory agencies in the health sector to accompany the development of safe, efficacious, and high-quality health technologies[1] which novelty challenge the current regulatory framework. The mechanism enables breakthrough developments and the test of alternative regulatory approaches for disruptive innovations for medicinal products, related technologies and their combinations. Regulatory sandboxes are mentioned as important future-proofing elements in the legislative proposal[2] of the European Commission on the general pharmaceutical legislation, this concept does not yet exist in the field of medical devices and in vitro diagnostics Regulations.

Regulatory sandboxes entail a shared learning objective for innovators (finding a pathway and getting regulatory predictability) and regulators (understanding the technology and defining how best to regulate it). The mechanism helps to inform future regulation through experimentation and evidence

[1] 'health technology' means a medicinal product, a medical device or medical and surgical procedures as well as measures for disease prevention, diagnosis or treatment used in healthcare

[2] Proposal for a Regulation of the European Parliament and of the Council laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency, amending Regulation (EC) No 1394/2007 and Regulation (EU) No 536/2014 and repealing Regulation (EC) No 726/2004, Regulation (EC) No 141/2000 and Regulation (EC) No 1901/2006 Chapter IX Regulatory Sandbox (Articles 113-115)

generation and minimises risks of regulating ex-ante innovative and novel approaches prematurely or inappropriately. For the same reasons, it also potentially facilitates more efficient or rapid subsequent adaptation of the legislation either through the translation into an adapted regulatory framework and / or by making recommendations when the time comes for revising an existing legislation or developing a new one.

Regulatory sandboxes should be able to experiment and draw on several relevant healthcare innovation related frameworks other than pharmaceutical products [i.e. medical device, in-vitro diagnostics, artificial intelligence (AI), digital, and substance of human origin among others]. Its anticipatory and adaptive nature positions the sandbox to address gaps and complexity within / across regulatory frameworks. Indeed, as the number of drug-device combinations increases, and technology integration becomes the norm rather than an exception in healthcare innovation R&D, manufacturing and healthcare delivery, the current siloed technology specific frameworks may not provide a clear path forward.

Although still new to the healthcare and pharmaceutical sector, there are a few examples such as the Sante Canada sandbox for advanced therapeutic products or Singapore sandbox to test telemedicine. More recently, in the UK MHRA AI-airlock was announced to assist in the development and deployment of software and AI medical devices, safely providing patients with earlier access to cutting edge innovations that improve care.

The overall aim of this topic is to contribute to the progression and successful implementation of regulatory sandboxes for healthcare innovations through developing a comprehensive and shared understanding of their value and process of implementation.

To fulfil this aim, the proposal should:

Develop recommendations for end-to-end operations of regulatory sandboxes to inform healthcare innovation developers, regulators and downstream decision makers by:

- mapping out conceptual elements and operationalisation features of future sandbox mechanisms based on existing experiences in other fields; for example governance, conditions fostering dialogue and collaboration, access to right type of expertise, support, regulatory customisation, sharing/communicating lessons and their translation via the appropriate frameworks into new standards, among other elements to be further defined.
- identifying a number of healthcare innovation case studies to better understand how a regulatory sandbox could apply in solving further-defined challenges at an existing regulation level and defining recommendations for end-to-end operations. Those cases could draw from the past, present and from horizon scanning activities (EMA's one already provides a hint[3]) to anticipate future innovations, looking across their development value chain.
- modelling how to operationalise the sandbox(es) (incl. governance, operations, principles) and how they could be used in healthcare innovation development and evaluation in conjunction with existing regulatory mechanisms to advance innovation at European and national levels.

Build a roadmap for innovation regulatory support pathways to guide emerging healthcare innovations (identified through horizon scanning) towards the most suitable innovation support mechanism by:

[3] Health horizons: Future trends and technologies from the European Medicines Agency's horizon scanning collaborations: https://doi.org/10.3389/fmed.2022.1064003

- identifying areas of innovation in healthcare technologies suitable for consideration in a regulatory sandbox that we could identify today and anticipate for the future.
- mapping limitations and opportunities of the existing regulatory science support tools to support potentially transformative healthcare innovations (products, technologies or platforms); evaluating regulations or policies that may impede a beneficial healthcare innovation.
- align understanding of how regulatory sandboxes can drive innovation in an evolving environment, and how uncertainties can be addressed by anticipating consequences for health technology development under a regulatory sandbox mechanism, acknowledging its time-limited scope and the consequences (considering the technical particulars of the healthcare innovation) for other downstream activities e.g., standardisation, Health Technology Assessment and proactively identifying any guardrails and mitigation measures.

Part of the topic implies modelling a regulatory sandbox. To that end the proposal should consider good practices for designing and evaluating the necessary operating models to ensure robustness and future applicability of the output of the project.

The project outcomes could also offer directions for translation of the resulting recommendations into digital tools and systems deemed necessary for the functioning of regulatory sandboxes (e.g. ensure collaboration between different health authorities triage mechanisms, horizon scanning, fitness check evaluation), as relevant.

When developing a comprehensive and shared understanding of the value of regulatory sandboxes, applicants will have to ensure that the understanding must encompass the entire healthcare innovation life-cycle including R&D, regulatory authorities, Health Technology Assessment (HTA) bodies, payers, governments, clinicians and, most importantly, patients.
Applicants are therefore expected to develop a regulatory strategy and interaction plan for generating appropriate evidence, for engaging with regulators and other decision makers in a timely manner (e.g. national competent authorities, EMA and the respective Innovation Task Forces, qualification advice) and clearly identify aspects that can be leveraged by the existing regulatory tools, what are the limiting aspects and what flexibilities would be required under a regulatory sandbox to achieve timely development and access of healthcare innovations.

Expected impacts

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

- meaningful contributions to the successful implementation of regulatory sandboxes through developing a comprehensive and shared understanding of their use and value among key stakeholders of the healthcare ecosystem.
- support future-proofing of the EU regulatory framework by design, enabling the efficient implementation of regulatory sandboxes where and when appropriate, and thus contribute to increasing attractiveness of Europe as place of innovation.
- enhancing and enabling the cooperation of key healthcare stakeholders, including patients, clinicians, SMEs and academics, with regulators in developing a competitive and innovation-friendly landscape.
- fostering interaction with regulators to develop healthcare solutions when it is not possible to develop them within the current framework.

The action will also contribute to a number of European policies/initiatives, which include:

- The European Commission Pharmaceutical Strategy pillar on competitiveness, innovation and sustainability
- Related measures under the ongoing revision of the General Pharmaceutical Legislation
- The European Commission innovation agenda (published in 2022) flagship initiative "*Enabling innovation through experimentation spaces and public procurement*" facilitate innovation through improved framework conditions including experimental approaches to regulation (e.g. regulatory sandboxes).
- The EU biotech strategy
- The Green and Sustainability agenda

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

As health innovation happens at the interface of disciplines and will be increasingly driven by technology, regulatory challenges will arise at the interface of the regulatory frameworks that govern those disciplines.

Engagement across sectors and multi-disciplinary collaboration are essential to support the deployment of regulatory sandboxes within different fields and across respective regulatory frameworks.

Therefore, a wider cross-sectorial community of stakeholders is needed to achieve the topic objectives. Innovators from the academic sector and from the various developer organisations (including biotech and start-ups) are increasingly coming together in areas such as medical device, in-vitro diagnostics, artificial intelligence (AI), digital, and substance of human origin among others.

Regulatory science and oversight are at the heart of regulatory sandbox so regulatory authorities and the wider regulatory science community including notified bodies are at the centre of the project. Downstream decisions makers such as HTA bodies and payers as well as solution recipients like patients and healthcare professionals shall also be involved. An ethical perspective could be useful as some innovations could trigger questions in this field. This diversity reflects actors of the ecosystem and is essential to ensure the uptake of innovation in a holistic manner.

A public-private partnership is the ideal framework for such a multi-sectoral and disciplinary endeavour and the diversity of representation in a neutral collaborative platform like an IHI consortium would help to build trust which is essential aspect to ensure the adoption of the resulting mechanisms and further future outputs.

Pre-identified industry consortium

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 with regard to 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 5 300 000. ***NB: this amount is indicative and subject to change, pending approval by the IHI Governing Board.***
- The indicative in-kind and financial contribution from industry beneficiaries is EUR 3 700 000 (including EUR 100 000 financial contribution). ***NB: this amount is indicative and subject to change, pending approval by the IHI Governing Board.***

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 100 000 financial contribution (FC) from industry beneficiaries will be decided by the full consortium at the second stage when preparing the full proposal. ***NB: this amount is indicative and subject to change, pending approval by the IHI Governing Board.***

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

Note that contributions to be provided by the full consortium to this action funded by IHI JU shall amount to at least 40% of the action's eligible costs and costs of its related additional activities (for more information, see the "Standard eligibility conditions" of section 4.2.3 (b) "Conditions of the calls and call management rules").

Indicative duration of the action

The indicative duration of the action is 36 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:

- expertise in manufacturing/CMC (chemistry, manufacturing, and controls) in healthcare innovation development R&D, clinical development, clinical trials, benefit/risk assessment
- expertise in regulatory, HTA/pricing and reimbursement, legal and intellectual property, medical and health affairs and communication
- expertise and input on impact on decision-making
- risk assessment and risk management expertise
- expertise in organisational design (design thinking)
- contribution in case simulation.

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.

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

- project management expertise in running cross-sectorial projects
- broad expertise in R&D of healthcare innovation
- expertise in simulation setup to design appropriate conditions to run the simulation exercises
- expertise in organisational design (e.g. design thinking) to inform the architecture of the regulatory sandbox mechanism
- regulatory and legal expertise are core to a number of activities ranging from fitness check evaluation of the regulatory framework against identified innovations to development simulation and design of the regulatory sandbox operating principles
- healthcare professionals and patient perspective, including a dimension on ethical consideration would be beneficial
- HTA and payer perspective
- innovation, its management and foresight to inform horizon scanning activities and identification of innovations susceptible to present challenges to their development and deployment.
- expertise in risk management to inform anticipated consequence of use of regulatory sandbox (e.g. via scenario design) and contribute to defining mitigation solutions
- IT and digital expertise.

Applicants are also expected to propose case studies in their short proposals. The pre-identified industry consortium would also propose case studies, to be aligned and decided by the full consortium at the second stage when preparing the full proposal.

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.

Glossary

Acronym	Meaning
CMC	chemistry, manufacturing, and controls
EMA	European Medicine Agency
EU	European Union
FC	Financial contribution

IHI JU	Innovative Health Initiative Joint Undertaking
HTA	Health Technology Assessment
IKAA	in-kind contributions to additional activities
IKOP	in-kind contributions to operational activities
R&D	Research and development
SMEs	Small and Medium sized enterprises