

**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:

- A horizon scanning for potential sandbox candidates including how sandboxes provide an additional tool to existing frameworks and identified examples to model the process.
- Analysis of how regulatory sandboxes can drive science and health technology innovation in an evolving environment.
- Recommendations for end-to-end operations of regulatory sandboxes to inform healthcare innovation developers, regulators, and other decision makers.

### **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 the 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 starting to transform the traditional methods used by regulatory agencies in the health sector to accompany the development of safe, efficacious, and high-quality health technologies<sup>1</sup>, which, due to their level of novelty, challenge the current regulatory framework. The mechanism enables breakthrough developments and the testing of alternative regulatory approaches for disruptive innovations for medicinal products, related platforms and their combinations, including where appropriate medical and digital technologies. Regulatory sandboxes are mentioned as important future-proofing elements in the legislative proposal<sup>2</sup> of the European Commission on the general pharmaceutical legislation. The European Commission's communication to boost biotechnology and biomanufacturing in the EU further promotes the establishment of regulatory sandboxes that allow the testing of novel solutions in a controlled environment for a limited amount of time under the supervision of regulators as a way of quickly bringing more of them to the market<sup>3</sup>. Regulatory sandboxes are not featured in the medical devices and *in vitro*

<sup>1</sup> '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

<sup>2</sup> 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 \(Articles 113-115\)](#)

<sup>3</sup> [https://research-and-innovation.ec.europa.eu/document/download/47554adc-dffc-411b-8cd6-b52417514cb3\\_en](https://research-and-innovation.ec.europa.eu/document/download/47554adc-dffc-411b-8cd6-b52417514cb3_en)

diagnostics regulations (MDR and IVDR)<sup>4</sup>, but the artificial intelligence (AI) Act<sup>5</sup> creates an opportunity for regulatory sandboxes focused on case studies for AI-enabled medical devices. 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 generation and minimises the risks of regulating ex-ante innovative and novel approaches prematurely or inappropriately. For the same reasons regulatory sandboxes also potentially facilitate the more efficient or rapid subsequent adaptation of the legislation either through translation into an adapted regulatory framework and/or through recommendations when the time comes for revising existing or developing new legislation.

Regulatory sandboxes should be able to experiment and draw on several relevant healthcare innovation related frameworks other than pharmaceutical products (i.e. medical devices, *in-vitro* diagnostics, AI, digital health technologies, and substances of human origin among others). Due to their anticipatory and adaptive nature, regulatory sandboxes are well placed to address gaps and complexity within and across regulatory frameworks. Indeed, as the number of drug and 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. To that end, when considering an innovation, it is important to consider all relevant legislative frameworks including MDR and IVDR, the Clinical Trials Regulation<sup>6</sup>, the General Product Safety Regulation<sup>7</sup> and AI ACT among others.

Although still new to the healthcare and pharmaceutical sector, there are a few examples of regulatory sandboxes such as the [Sante Canada sandbox for advanced therapeutic products](#) or the [Singapore sandbox to test telemedicine](#). More recently, the UK launched the [MHRA AI-airlock](#) 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 IHI topic is to contribute to the progression and successful implementation of regulatory sandboxes for healthcare innovations by developing a comprehensive and shared understanding of their value and process of implementation. The topic should also enable the development of a cross-sectoral community of stakeholders including pharma and medical device companies, regulators, and health technology assessment bodies (HTAs), among other stakeholders.

To fulfil this aim, the proposal should:

- 1. Scan the horizon for potential sandbox candidates including how sandboxes provide an additional tool to existing frameworks, and use the examples identified to model the process.**

To this end, a key objective is to identify a number of healthcare innovation case studies to better understand how a regulatory sandbox could be used to solve further-defined challenges at an existing regulation level and inform recommendations for end-to-end operations. These cases could draw from

<sup>4</sup> Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices and Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices.

<sup>5</sup> Regulation of the European Parliament and of the Council laying down harmonised rules on artificial intelligence (Artificial Intelligence Act)

<sup>6</sup> Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use

<sup>7</sup> Regulation (EU) 2023/988 of the European Parliament and of the Council of 10 May 2023 on general product safety

the past, present and from horizon scanning activities (the EMA's work in this area already provides a hint<sup>8</sup>) to anticipate future innovations, looking across their development value chain.

## **2. Analyse how regulatory sandboxes can drive science and health technology innovation in an evolving environment.**

The proposal should do this by:

- anticipating consequences for health technology development under a regulatory sandbox mechanism, acknowledging its time-limited scope and the consequences (considering the technical particularities of healthcare innovation) for other downstream activities e.g., standardisation, health technology assessment;
- proactively identifying any guardrails and mitigation measures.

## **3. Develop recommendations for end-to-end operations of regulatory sandboxes to inform healthcare innovation developers, regulators and downstream decision makers.**

The proposal should do this by:

- mapping out conceptual elements and operationalisation features of future sandbox mechanisms based on existing experiences in other fields such as governance, conditions fostering dialogue and collaboration, access to the right type of expertise, support, regulatory customisation, sharing/communicating lessons learned and their translation via the appropriate frameworks into new standards, among other elements to be further defined;
- modelling how to operationalise the sandbox(es) (including 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.

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

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

When developing a comprehensive and shared understanding of the value of regulatory sandboxes, applicants will have to explore key aspects across the life-cycle of healthcare innovations with the objective of accompanying their ultimate adoption, which could include as appropriate R&D, regulatory authorities, HTA bodies, payers, governments, clinicians and patients. Ethical considerations would also have to be considered as some innovations could trigger questions in this field. A shared objective should include to develop a regulatory strategy and interaction plan for generating appropriate evidence, enabling engagement across all the different decision makers in a timely manner (e.g. national competent authorities, EMA and the respective Innovation Task Force, qualification advice) and identifying aspects that can be leveraged by existing regulatory tools, as well as the limiting aspects and the flexibilities that would be required under a regulatory sandbox to achieve the timely development and access of healthcare innovations.

<sup>8</sup> Health horizons: Future trends and technologies from the European Medicines Agency's horizon scanning collaborations: <https://doi.org/10.3389/fmed.2022.1064003>

## 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 in the healthcare ecosystem.
- Support the future-proofing of the EU regulatory framework by design, enabling the efficient implementation of regulatory sandboxes where and when appropriate, and thus helping to make Europe more attractive as place of innovation.
- Enhancing and enabling the cooperation of key healthcare stakeholders, including patients, clinicians, small and medium-sized enterprises (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's Pharmaceutical Strategy for Europe](#), specifically the pillar on competitiveness, innovation and sustainability;
- related measures under the ongoing revision of the Pharmaceutical legislation;
- the [European Commission innovation agenda](#) (published in 2022) flagship initiative "*Enabling innovation through experimentation spaces and public procurement*" facilitating 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 these disciplines.

Engagement across sectors and multi-disciplinary collaboration are essential to support the deployment of regulatory sandboxes within different fields and across 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 devices, *in-vitro* diagnostics, AI, digital health technologies, and substances of human origin, among others.

Regulatory science and oversight are at the heart of regulatory sandboxes, 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 should also be involved. This diversity reflects the 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-sectorial 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 to ensure the adoption of the resulting mechanisms and future outputs.

## Pre-identified industry consortium

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

- Astellas
- Biogen
- CSL Behring
- EFPIA
- Eli Lilly
- F. Hoffman-La Roche (co-lead)
- Johnson & Johnson
- Merck KGA
- MSD (co-lead)
- Novo Nordisk
- Novartis
- Pfizer
- Sanofi
- Takeda
- Teva

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 5 200 000
- The indicative in-kind and financial contribution from industry beneficiaries is EUR 4 261 096

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.

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 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);
- contributions to 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 set-up 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 the fitness check evaluation of the regulatory framework against identified innovations to the development, simulation and design of the regulatory sandbox operating principles;

- healthcare professionals and patient perspectives, including a dimension on ethical considerations, would be beneficial;
- HTA and payer perspective;
- innovation, its management and foresight to inform horizon scanning activities and the identification of innovations susceptible to present challenges to their development and deployment;
- expertise in risk management to inform the anticipated consequences of the use of regulatory sandboxes (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