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 1: Digital label: one source of comprehensive information for medical technology products

Expected outcomes

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

1. A consensus-based digital label concept/framework for medical devices and *in vitro* diagnostic medical devices (IVDs) is available to be used by manufacturers that meets end users' requirements and addresses regulators' demands.
2. Multiple valid and scalable digital label solutions based on a standardised approach are available and they:
    a. all work with the same enabler (label reader) for all medical technology product labels (all medical devices and IVDs, all types, all classes). This topic does not cover pharmaceutical products as such. Combination products that fall into the scope of regulations on medical devices and *in vitro* diagnostic medical devices (MDR/IVDR) are, therefore, regulated as devices and are considered to be part of this topic;
    b. serve as an up-to-date single point of access to all information about the specific device;
    c. are interoperable with other EU legislations (such as digital passport);
    d. consider accepted international standards for data carriers;
    e. are acceptable after verification via user testing.
3. Evidence-based recommendations are available that may inform European Commission and National Competent Authorities policy recommendations.
4. Training materials on digital labels are available to the end users (healthcare professionals (HCPs) and patients), regulators (National Competent Authorities) and Notified Bodies in the EU Member States.
5. Basis towards future international acceptance is created via:
    - documentation gathered that would be needed to launch under the International Organisation for Standardisation/International Electrotechnical Commission (ISO/IEC) a proposal for a new digital label standard or adaptation of an existing standard[1] (development of a standard itself is not planned during the lifetime of the project);
    - awareness raising with other international jurisdictions that consider digital label initiatives.

Scope

A digital label is a form of e-labelling provided as an array of elements supporting a medical technology product, which is additional to critical information on the printed label (identification & traceability of the device, warnings and precautions, handling and use information). Access to the digital label is achieved,

[1] e.g ISO 20417 already offers a segway for digital label. This standard is also foreseen for harmonisation with MDR.

for example in the form of barcodes, 2D data matrix, QR codes, etc., which provides a scannable link to curated digital landing pages (websites) where the additional information will be displayed.

Under the current Regulations on medical devices and *in vitro* diagnostic medical devices (MDR/IVDR: 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) both critical information as well as additional information have to be included on the product's printed label.

While many medical technology products are decreasing in physical size, mandatory requirements for additional product compliance information are growing, which leads to various problems. Users might find it difficult to locate the desired information on the label due to the extensive text and small print. Manufacturers have to update their entire physical label if they change an economic operator. Such label changes have an impact on the environment, product availability and inventory and they cause inefficiencies and ultimately raise costs. Local requirements for the label regarding device disposal are increasing and lead to increased amounts of packaging (and therefore later increased amounts of waste). In case of new environmental legislation, the physical label needs also to be updated during the device's lifetime.

The overall aim of this topic is to establish a consensus-based digital label concept applicable to all types and classes of medical devices and IVDs, making use of existing technologies that will be further improved to suit medical technology products specifically.

Note that this topic does not cover medicinal products, except combination products that fall into the scope of MDR/IVDR Regulations and are, therefore, regulated as devices. Furthermore, this topic does not directly address the electronic provision of IFU (instructions for use) as this is already allowed for certain medical devices and IVDs in the EU. Access to eIFU through the digital label is only an additional benefit to facilitate access to all relevant information in one place (on top of the means of delivery allowed currently by MDR/IVDR). Finally, the scope of this topic does not address post market surveillance aspects.

To fulfil the overall aim, the action funded under this topic must:

- deliver a framework for:
    - mapping of data elements that must be physically present on the label and those that the manufacturer can provide digitally. The framework will consider the requirements of EU Regulations (MDR General Safety and Performance Requirement (GSPR) 23.1, IVDR GSPR 20.1; the Packaging and Packaging Waste (PPWD) Directive; Digital Product passport, waste & packaging, battery, etc.) and is meant to also support future EU legislation (or transposition thereof in Member States).
    - a standardised concept in providing digital content and structure for the medtech manufacturers.
- define and make publicly available key performance indicators (KPIs) (e.g. trends of access and digital content type) or other measures to assess the acceptability and workability of the potential digital label solution(s), provided by manufacturers, and to be tested with end users (HCPs & patients).
- generate evidence on the acceptability and usability of digital label solutions through testing in a variety of use environments that will be defined by the full consortium. This will include user feedback on behaviour changes in a variety of use environments. The action should also make the results of testing, analysis and conclusions public.
- engage with all relevant stakeholders (e.g. HCPs, patients, National Competent Authorities, Notified Bodies) throughout the project lifetime to get robust input through consultations, surveys, workshops and testing in order to:

- maximise end user adoption (and understanding) of digital labels
- ensure that concerns and demands of end users and regulators are met

- based on the results of testing and body of evidence gathered, develop recommendations on digital labels to inform relevant stakeholders, regulators, policy makers, and the relevant ISO/IEC bodies for the possible development of IEC/ISO standard for digital label for medical devices and IVDs (or for the update of an existing standard) (the standard itself will NOT be developed during the lifetime of the project).
- ensure appropriate knowledge dissemination via:
  - developing training materials
  - subsequently finetuning training material for deployment to the public at large in all EU national languages: end users (HCPs, patients)/regulators (National Competent Authorities)/Notified Bodies in the EU Member States and any other relevant stakeholders
  - facilitating awareness and communication with other global jurisdictions' digital label initiatives

Applicants should develop a strategy and plan for generating appropriate evidence as well as for engaging and formally consulting with regulators (e.g. national competent authorities).

Expected impacts

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

1. Streamlined and 'green' delivery of information
   a. Key information as well as additional information is easily (and more) visible, accessible and identifiable to users (HCPs, patients) and health authorities equipped with a simple smart phone;
   b. Significant reduction of carbon footprint and avoidance of over-labelling, hereby contributing to the European Green Deal.
2. Improved accessibility of information for users (HCPs and patients) and regulators. All the information that users might need is available in one place in their language of choice, thus increasing equal access of users to medical technologies.
   a. Targeted information based on user location: in the EU, summary of safety and clinical performance (SSCP), the European database for medical devices (EUDAMED) modules when available[2]; globally, electronic instructions for use (eIFU));
   b. Crucial information from the printed label is additionally visible upon scanning (e.g. expiry date);
   c. Connection to technical support in case of problems;
   d. Reducing risk of use errors;
   e. Real time updates;
   f. Avoidance of cluttered labels.
3. Increased alignment between MDR and other EU legislation & streamlined compliance for all. The one digital carrier will directly link the user with the up-to-date information required by the Digital

[2] https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=OJ:L_202401860

Product passport in multiple languages (EU Packaging and Packaging Waste Regulation EU Battery regulation, information on spare parts, etc.), hereby contributing to the European Green Deal.

4. Increased competitiveness in the EU market thanks to improved supply management and streamlined packaging and labelling operations.
5. Driving acceptance through (voluntary) adoption of digital labels by medical devices manufacturers and their use by end users, Notified Bodies, National Competent Authorities in the European market, supported by the developed training material. Digital label is considered an additional tool to requirements in current legislation (MDR, IVDR).

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

The digital label is an innovative concept offering benefits to all healthcare stakeholders and society at large. Currently, for the medical technology industry no regulatory basis exists anywhere in the world. There is therefore a need to test this concept with users, gather evidence for regulatory decision making and build regulators' as well as users' trust as a basis for a common standard and policy recommendations.

This new approach of providing information on the label digitally will therefore need all stakeholders (industry, health institutions, healthcare professionals, patients, researchers, including researchers in health literacy, regulators (National Competent Authorities) and Notified bodies to work together in a neutral framework to lay the groundwork for a sustainable and user centred healthcare information delivery in the EU and ensure its regulatory acceptance.

An aligned multistakeholder approach to the digital label will ensure the speedy success of this concept.

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 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 3 960 000. ***NB: this amount is indicative and subject to change, pending approval by the IHI Governing Board.***
- The indicative in-kind contribution from industry beneficiaries is EUR 6 156 800. ***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 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:

- IT infrastructure provision and IT expertise;
- Expertise in labelling; regulatory affairs & intelligence; clinical research, marketing and communications, global supply chain management, project management etc.;
- Usability engineering.

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 experience in running multi-stakeholder, cross-sectoral projects;
- digital labels for medical devices;
- healthcare, medical device engineering and design, as well as medical device regulation and compliance;
- demonstrated experience in interacting with regulators, citizens and/or patient representatives, health care professionals;
- data standards and interoperability;
- software and digital health;
- legal, patient literacy, health literacy, ethical, social science.

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.

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 2: Safeguarding innovation in secondary use of health data in the European Health Data Space (EHDS)

Expected outcomes

The European Health Data Space (EHDS) is a key initiative under the European Strategy for Data and the European Health Union that enables the secondary use of health data for various purposes, including research and innovation. The outcomes of this topic will lead to the identification of paths for innovation through the EHDS while safeguarding intellectual property and trade secrets in health data.

This topic must contribute to all of the following outcomes:

- comprehensive frameworks, processes, policies and guidelines are available to support the procedural and operational aspects of the EHDS from an innovator's perspective;
- recommendations to inform EHDS governance are available to address the needs of a broad set of stakeholders, including citizens, hospitals, public institutions and the healthcare industry. The right balance must be struck between the need for an EHDS that enables efficient data sharing to promote research and innovation in healthcare, and the need for maintaining a strong Intellectual Property (IP) system and preserving confidential information within health research data;
- Recommendations are available for enabling dialogues between health data holders (HDHs), health data users (HDUs) and health data access bodies (HDABs) to address issues around innovation utilising the EHDS and the operationalisation of the EHDS; and
- Materials, guidance, recommendations, training and other support tools are available to educate interested parties about innovation and data sharing under the EHDS.

The target groups for all the outcomes are:

- those establishing the EHDS and the federated data network, through which data will flow and be used for secondary purposes;
- member state agencies involved with the establishment and functioning of HDABs;
- HDHs making sensitive and confidential data available through the EHDS for secondary use; and
- HDUs intending to access sensitive and confidential data for secondary use.

Scope

The background to this topic arises from the EU regulation for an EHDS. This topic focuses on the secondary use aspects of the regulation establishing the EHDS and recognises that to be successful there is a need to consider both the societal benefits of data-driven advancements in healthcare and the legitimate interests of public and private sector innovators for a strong IP system and an efficient means of supporting the secondary use aspect of the EHDS.

The specific challenges/problems addressed by the topic include:

- Balancing the societal benefits of data-driven innovation in healthcare against the legitimate interests of public and private sector innovators to safeguard relevant legal and regulatory rights related to their data (e.g., (*sui generis*) database rights, CCI (Confidential Commercial Information), trade secrets, RDP (Regulatory Data Protection)**,** patents, etc.);
- Empowering HDHs and users to engage with and use the EHDS for data-driven healthcare innovation by providing them with knowledge and tools to operationalise secondary data sharing and to safeguard intellectual property rights, trade secrets and regulatory data protections;
- Developing robust frameworks and guidelines to support the implementation of the EHDS to enable harmonised and efficient data sharing (including in the context of data anonymisation considerations) across all member states and safeguarding IP and trade secrets in support of innovation; and
- Exploring concerns regarding commercial and competition-sensitive data and risk of unauthorised disclosures.

The topic objectives are:

- Build trust and confidence in the EHDS: respecting and keeping proprietary information confidential, creating trust and confidence among stakeholders and promoting their active participation in the EHDS to enable responsible and timely data sharing;
- Propose implementation practices that will support the efficient inclusion of health data in the EHDS for secondary research purposes and support the procedural and operational aspects of the EHDS;
- Support innovators' competitiveness by safeguarding valuable IP and trade secrets data whilst fostering further research and innovation;
- Advancing data governance and confidentiality practices within the EHDS to ensure appropriate protection of IP and trade secrets;
- Ensuring data governance throughout the whole product life cycle, from development to post market monitoring and update;
- Minimising administrative burden for HDABs, HDHs and HDUs impacted by the EHDS;
- Ensuring that relevant legal and regulatory rights of innovators are respected and timely preserved to minimise uncertainty and maximise opportunities for innovation under the EHDS;
- Supporting an EHDS implementation that facilitates data sharing, innovation, and research to advance healthcare for EU citizens, and uses processes that take advantage of existing practices in industry and health authorities and are resource efficient.

Applicants should envisage the following activities as part of their proposal:

<u>With regards to the outcome supporting the procedural and operational aspects of the EHDS</u>

- Conduct research into data strategy, management and governance;
- Conduct comparative reviews of existing data exchanges and the needs for transparency, interoperability and standardisation of data;
- Through elaborate use cases, explore the procedural and operational aspects of the EHDS from various perspectives, including:

    - Assessing data sharing platforms and technologies, such as data security measures like encryption technologies, access control mechanisms, black boxes, federated learning, and their implications on the data sharing and IP system;
    - Investigate the sharing of different types of data covered by the EHDS, including trade secret and sensitive data, for secondary use. This will help to address different scenarios regarding purpose, time of sharing, and territorial scope, potentially leveraging test environments to evaluate operational and practical aspects of data sharing and data usability under the EHDS.

- Identify best practices, guidelines, standards, and tools for intellectual property, trade secret, and opt-in/out management that can be used and advanced within the EHDS frameworks;
- Develop proposals for comprehensive frameworks, processes, policies and guidelines balancing the needs of HDHs to safeguard the IP system and minimising administrative burden while facilitating data sharing and collaboration;
- Develop mechanisms and technologies for IPR-aware data anonymisation/ pseudonymisation and synthetic data generation, with the goal of facilitating the reuse of electronic health data that is subject to IP protection;
- Prepare recommendations for technical standards for access controls, data minimisation, secure data storage, and anonymisation techniques, handling of evolving data sets, etc., which might benefit innovation related to trade secrets and IP protected data covered by the EHDS.

<u>With regards to the outcome striking the appropriate balance</u>

- Evaluation and comparative study of laws, including trade secret laws and other laws of the EU Strategy for Data and of the EU member states, to identify common and differentiating features and legal bases in order to propose recommendations for member state implementation of HDABs and to develop guidance for IP and data protection covering areas such as dataset descriptions, data sharing policies and agreements, access controls, and governance practices and data use;
- Comprehensive research into the interplay between IP, transparency, data protection, state aid, competition laws, international treaties, the need for openness, and the potential risk for misuse of data under the EHDS;
- Conduct research exploring compatibility and gaps of the EHDS versus existing laws around data and data sharing, IP, including protection of confidential information and trade secrets, and related laws, such as privacy, the EU data governance act, the EU data act, the EU AI act and regulatory data protection;
- Propose guidelines and frameworks regarding data sharing and data use to support the balance of the societal benefits of data-driven healthcare research and innovation under the EHDS against the legitimate interests of public and private sector innovators for a strong IP system, including, for example, a classification of data into categories depending on IP sensitivity;
- Develop guidance on responsible use and mechanisms to hold irresponsible / misusing users accountable and prevent misuse;
- Develop clear rules for data ownership and IP ownership determination for all kinds of newly generated data using EHDS;
- Propose a harmonisation framework including standard agreements for IP ownership to enable secondary use of data provided via the EHDS for research purposes;

- Analyse and provide recommendations on exploitation and publication of results by HDU and impact on HDHs with IP and trade secret protected data.

With regards to the outcome establishing frameworks for dialogues

- Engagement of public and private innovators in the European Health Data Space 2 (EHDS2) Stakeholder Engagement initiative to shape the definition of responsible secondary use of data for research and innovative purposes under the EHDS, including territorial considerations;
- Preparing recommendations to develop a framework for dialogues between innovators and health data access bodies (HDABs) to address issues around innovation and operationalisation under the EHDS, balancing all the relevant stakeholders' legitimate interests.

With regards to the outcome educational aspects

- Development of training packages, including educational materials, guidance, recommendations, and other support tools to educate stakeholders about innovation, data sharing and the IP system under the EHDS;
- Educating stakeholders about using the EHDS for innovative purposes.

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 relevant regulators in a timely manner.

Expected impacts

The action contributes to all the general objectives of IHI JU and particularly to specific objective 4 "exploit the full potential of digitalisation and data exchange in health care".

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

- Fostering data-driven research and innovation advancing healthcare in the EU;
- A world-leading approach to IP protection of data;
- Improved balance between data utilisation and access control rights;
- Best practices for data sharing, data security and prevention of unauthorised disclosure;
- Recommendations for legal and ethical standards; and
- Increased industry confidence in the EHDS.

The action will also contribute to several European policies/ initiatives, which include:

- The European Health Data Space;
- 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 Trade Secret Directive;
- The European Strategy for Data, incl. GDPR, Data Act, Data Governance Act, AI Act;
- The Digital Strategy; and
- The Digital Single Market Strategy.

Overall, these expected impacts aim to create a secure, collaborative, and innovative ecosystem within the EHDS, which will increase trust and confidence among stakeholders, optimise data utilisation,

enhance protection of intellectual property, and facilitate advancements in healthcare research and innovation.

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

The Intellectual Property ("IP") system exists to support innovation and is a key driver for all healthcare industries operating in EU. Thus, understanding how the EHDS interacts with, and might impact, the IP system will be key to its success and that of the European innovation landscape.

Public and private partners will be Health Data Holders (HDHs) and Health Data Users (HDUs) who may simultaneously be innovators. Thus, combining the strengths and expertise of private and public partners is essential to develop holistic solutions balancing the protection of IP (including trade secrets) with an EHDS that facilitates data sharing and utilisation for research and innovation.

Industry partners bring expertise in secondary use of health data, IP and trade secret management, which can be leveraged to develop effective strategies for protecting innovation whilst also facilitating health data sharing. They also understand the concerns of industry in protecting innovation with IP.

Public partners bring their knowledge of and insights into the healthcare sector, and expertise in health data management as well as technology transfer. Public partners will provide insights into the needs of the healthcare system and societal considerations for sharing health data for secondary use.

The proposed public-private collaboration is essential to develop robust frameworks, policies, and processes addressing the complex challenges posed by the EHDS. A close collaboration is necessary for the implementation of an EHDS that facilitates secondary use of data whilst also respecting the needs of innovators for a strong IP system. The collaboration will enable the EHDS to exploit the full potential of digitalisation and data exchange in health care.

The relevant stakeholders for this topic are those involved with the establishment of the EHDS for secondary use purposes and those who will provide and access data utilising the EHDS, which includes:

- HDHs and HDUs, including healthcare providers, pharmaceutical companies, and medical technology companies;
- Patient organisations and other Non-Governmental Organisations in the health research space;
- Universities and institutions or other organisations with an interest in health data;
- EU and Member State authorities responsible under the EHDS to handle and protect data of HDHs; and
- EU and Member State authorities who will establish federated data networks, HDABs and secure processing environments under the regulation for the EHDS.

Pre-identified industry consortium and contributing partners

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, it is envisaged that IHI JU proposals and actions may allocate a leading role within the consortium to a constituent or affiliated entity of a private member.

Indicative budget

- The maximum financial contribution from the IHI JU is up to EUR 5 200 000. ***NB: this amount is indicative and subject to change, pending approval by the IHI Governing Board.***

- The indicative in-kind contribution from industry beneficiaries is EUR 4 929 500. ***NB: this amount is indicative and subject to change, pending approval by the IHI Governing Board.***

- The indicative in-kind contribution from IHI JU contributing partners is EUR 70 500. ***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 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 and contributing partner(s) 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 partner(s) expect to contribute to the IHI JU project by providing the following expertise and assets:

- Legal, paralegal experts and advisors/consultants specialised in IP & trade secrets protection in the digital and medical environments;
- Governmental Affairs and Policy experts;
- ISRM (Information Security & Risk Management) experts;
- Data strategy and governance experts;
- Communication expertise for webinars & workshops;
- Data privacy experts;
- Public affairs experts.

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(s).

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

- Academic and/or research organisations involved in innovation and competition with particular expertise in legal and IP;
- ISRM (Information Security & Risk Management) experts;
- Hospital networks/health data holders/ health data users (clinical research units);
- Implementers of large digital healthcare infrastructures for primary and secondary data use (i.e., which make use of the EU policies mentioned in the expected impact section) from across the EU;

- Project management expertise related to qualitative market research and public relations;
- Project management organisations with project management expertise of large multi-stakeholder European public-private partnerships;
- Legal expertise and, in particular, privacy and data protection expertise;
- Experts from, or with connections to country ministries, involved with implementing and operating Health Data Access Bodies;
- Publicly accessible datasets.

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.

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: Per- and Poly-fluoroalkyl substance (PFAS) exposure, emissions, and end of life management in the healthcare sector

Expected outcomes

Per- and Poly-fluoroalkyl substances (PFAS) are a broad range of materials which have many uses within the scope of healthcare products, including as components of medicines, vaccines, medical devices, and diagnostics. These substances are currently critical to product quality, safety, and efficacy and essential to their manufacture and safe storage. PFAS make up a large group of persistent anthropogenic chemicals which are difficult to degrade and/or dispose of in an environmentally respectful manner. This IHI topic prioritizes phasing-out PFAS of concern *(specified below)* as much as possible by using alternatives that maintain at least the same level of patient safety and product performance. Additionally, where it is not feasible to replace the use of PFAS, e.g. for technical or toxicological reasons, applicants should investigate how their use can be minimized / adequately controlled with respect to environmental exposure. The current knowledge needed to address these challenges is fragmented and incomplete.

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

- Replace PFAS: New environmentally sustainable materials as alternatives to PFAS that maintain patient safety are developed for the benefit of the healthcare industry and the citizens;
- Reduce / re-use PFAS: Improved usage of PFAS materials and minimized exposure is achieved for the benefit of the environment and therefore citizens and society;
- A mapping of the types and applications of PFAS throughout the supply chain is available for healthcare technologies and products, including collaborating with upstream suppliers;
- A database of alternatives to PFAS is available;
- New disposal processes of PFAS are available for the benefit of the environment and therefore citizens and society.

Scope

To replace PFAS in medical technologies without risking human health, input from supply chain actors, scientists, and engineers is crucial. This includes assessing material availability, feasibility, and testing. Where current technology falls short, understanding PFAS environmental exposure and mitigation must improve. Standardized testing protocols and quantification methodologies are needed to measure exposure accurately. Effective mitigation requires knowledge of exposure routes and environmentally sensitive disposal methods. A scientific, data-driven approach that aligns with the safe and sustainable by design (SSbD[1]) framework is essential for lifecycle exposure management and ensuring alternative materials are safe and effective. Collaboration among scientists, policymakers, regulators, healthcare providers, chemical manufacturers, patient groups and trade associations and waste managers is vital

[1] https://publications.jrc.ec.europa.eu/repository/handle/JRC128591

to address technical, legal, and practical considerations. Proper scientific assessment of alternatives is necessary to maintain safety and quality.

The key challenges in the field include:

- Obtaining information on PFAS uses in healthcare due to a complex global supply chain and limited data sharing;
- Many specific use requirements and potential exposure routes due to the ubiquitous nature of PFAS use in the healthcare sector, including in production equipment, consumables, packaging, delivery devices, medical devices, complex machinery and cleaning agents;
- Identifying alternatives for high-performing PFAS like polytetrafluoroethylene (PTFE) while ensuring product quality and safety;
- End-of-life management of healthcare products is underdeveloped, with inconsistent approaches to multicomponent waste management;
- Current wastewater treatment technologies struggle to eliminate complex PFAS;
- A globally accepted definition of PFAS is needed to avoid regional policy disparities.

The overall aim of this IHI topic is to provide world leading, fully integrated and globally applicable solutions to address PFAS emission and exposure concerns, for example by substitution.

To fulfil the IHI topic aim, the applicant should address the following objectives:

Objective 1: Cross-Sector Solutions to Develop PFAS Alternatives

- **Activities:**
    - Establish public-private collaboration to increase knowledge about PFAS applications and alternatives with a focus on prioritised PFAS chemicals listed in Tables 1 and 2;
    - Document key performance characteristics for PFAS used in healthcare products, manufacture, and testing;
    - Exploit industry, academic and manufacture collaborations, incorporating skills such as chemical synthesis, material sciences and analytics to develop PFAS alternatives;
    - Test and validate PFAS alternatives generated by this project and, in addition, PFAS alternatives developed through research external to this project against performance characteristics and applications.
- **Outputs:**
    - Reporting system to label PFAS-containing raw materials or medical device components;
    - Technology on optimized materials capable of replacing PFAS in specific applications;
    - Data on alternative materials that could replace PFAS and corresponding design and performance characteristics;
    - Technology for replacing PFAS chemicals in chemical synthesis or excipients in drug manufacturing;
    - Replacements for Trifluoroacetic acid (TFA) in chromatography and other analytical methods;
    - Development of PFAS-free process aids (tubing, gaskets, fittings);
    - Searchable database of validated PFAS alternatives.

Objective 2: Understanding PFAS in the medtech sector

- **Activities:**
    - Identify and map PFAS types and applications in the medtech sector and align with those already identified in previous mappings of PFAS in the pharmaceutical industry;
    - Develop a methodology for risk-benefit analysis of PFAS use;
    - Establish public-private collaboration to gain knowledge about PFAS applications, alternatives, risks, and risk management options;
    - Identify suppliers to raise awareness of PFAS alternatives and secure continuous supplies of raw materials and parts;
    - Collect data on PFAS materials used in the supply chain, emissions, and mitigation options.
- **Outputs:**
    - Increased knowledge of PFAS types and applications throughout the medtech and diagnostic process supply chain;
    - Robust evaluation of PFAS alternatives;
    - Enhanced stakeholder information sharing.

Objective 3: Sector-Specific Solutions to Reduce and Reuse PFAS Materials

- **Activities:**
    - Map and calculate PFAS exposure from different categories of applications;
    - Develop end-of-life management options across the sector in line with the SSbD framework;
    - Evaluate and leverage PFAS removal technologies;
    - Evaluation of sector specific circular economy principles for applications where removal is not yet possible;
    - Evaluate sector-specific solutions to minimize PFAS exposure in partnership with healthcare facilities and waste management companies.
- **Outputs:**
    - End-of-life management guidelines for PFAS components/chemicals, including circularity aspects and waste treatment;
    - PFAS-specific removal, decontamination or environmentally responsible disposal technologies for TFA from wastewaters.

PFAS Application	PFAS Materials
Films/plastics (primary contact material) for final drug product sterile packaging: • cap or stopper coatings/liners • Vial stoppers • Syringe stoppers • Seal linings • Blister packs	ETFE (cap or stopper coatings/liners) Other coatings (proprietary) eg OmniFex stopper coatings PTFE (coating for vial and syringe stoppers and seal linings)
Films/plastics (primary contact material) in manufacture and containment of drug intermediates (drug substance). • Containers/films/bottles • Single use processing bags • Single Use bioreactors • Probes/inserts	PVDF PTFE bottles FEP bags/bottles
Films/plastics (primary contact material) for final drug product non-sterile packaging- blister packs	PCTFE
Devices	PTFE
Intermediate, raw material or ancillary material used in manufacture or Purification of protein-based drugs	TFA
Analytical	HPLC methods use TFA in the mobile phase PTFE filters PTFE seals
ETFE: Ethylene tetrafluoroethylene; PTFE: Polytetrafluoroethylene; PVDF: Polyvinylidene fluoride; FEP: Fluorinated ethylene propylene; PCTFE: Polychlorotrifluoroethylene; TFA: Trifluoroacetic acid	

Table 1 - Types of PFAS in use in healthcare. The project scope includes exploring alternatives to the PFAS materials listed here. (Table adapted from EFPIA response to the ECHA consultation on the proposal for a universal ban on PFAS, Annex 3: ISPE_Industrial Use of Fluoropolymers & Fluoro-Elastomers in Pharmaceutical Manufacturing Facilities).

PFAS Application	PFAS material
Sterile Liquid filtration membranes	PVDF, PTFE
Liquid filtration - virus clearance	PVDF
Vent and/or Gas Filtration (of bioreactors/carboys) - filter membranes	PVDF, PTFE
Biopharma drug cryostorage bags and Cell culture cryostorage bags	PTFE, FEP, custom fluoropolymer
Tubing & tube fittings (manufacturing engineering systems and transfer of drug material intermediates and final product) incl gaskets & O-rings	PVDF (tubings and fittings), PTFE, FKM (tubing/O-rings/gaskets), FEP, PFA
Support filters (e.g. HEPA/ HVAC air purification	PTFE, other materials with hydrophobic or non hydrophobic coating
Hardware systems (lined pipes, TFF cassette seals/components/solvent exchange systems/lined valves/gaskets). Pumps & components (diaphragm)	PVDF, PTFE, FKM
Heat and/or chemical resistant components, nonreactive coatings / insulation / lubricants / Refrigerants	Additive of ABS Additive in polycarbonates
PTFE thread sealing tape in engineering systems	PTFE
ETFE: Ethylene tetrafluoroethylene; PTFE: Polytetrafluoroethylene; PVDF: Polyvinylidene fluoride; FEP: Fluorinated ethylene propylene; PCTFE: Polychlorotrifluoroethylene; TFA: Trifluoroacetic acid; FKM: Fluorine Kautschuk Material; PFA: perfluoroalkoxy; ABS: Acrylonitrile butadiene styrene	

Table 2 - Types of PFAS in use in healthcare: consumables. The project scope includes exploring alternatives to the PFAS materials listed here. (Table adapted from EFPIA response to the ECHA consultation on the proposal for a universal ban on PFAS, Annex 3: ISPE_Industrial Use of Fluoropolymers & Fluoro-Elastomers in Pharmaceutical Manufacturing Facilities).

In addition to the critical uses in Tables 1 and 2, the following high-priority PFAS use cases in the healthcare sector are core to this project's scope:

- Production equipment and consumables (filters, tubing, seals/gaskets);
- Primary and secondary packaging;
- Medical devices (with and without patient contact) e.g. catheters, implants, needles, contact lenses; in-vitro diagnostics (IVD), device handles;
- Medical technology processing aids;
- Complex machinery (diagnostic, imaging, research equipment);
- Healthcare cleaning agents;

- Healthcare consumables (surgical drapes, gowns, packaging, tapes, sutures, wound dressings, personal protective equipment (PPE));
- Wastewater treatment.

The proposal should aim to collaborate with the following actors and initiatives:

- Industry associations and task forces with PFAS focus, such as EFPIA PFAS task force, Biophorum PFAS response team, Innovative Quality (Pharma) Consortium, American Chemical Society ACS) Green Chemistry Institute Pharmaceutical Roundtable, Pharmaceutical Supply Chain Initiative (PSCI), Animal Health Europe (AhE);
- IMI and IHI consortia (past and ongoing), including Prioritisation and Risk Evaluation of Medicines in the EnviRonment (PREMIER) and Intelligent Assessment of Pharmaceuticals in the Environment (iPiE) (on waste treatment), and ENKORE (on primary packaging);
- Ongoing Horizon 2020 projects and future Horizon Europe calls comprising a PFAS focus;
- The Partnership for the Assessment of Risk from Chemicals (PARC);
- Regulators (to inform, align expectations, assess impact on regulatory pathways and ensure data and results produced will be fit-for-purpose); for the pharmaceutical and medical device industries including the European Medicines Agency (EMA), European Directorate for the Quality of Medicines & HealthCare (EDQM) & Official Medicines Control Laboratory (OMCL) network as well as additional national competent authorities. In the scope of this specific topic, engagement with the European Chemicals Agency (ECHA) should also be included.

Expected impacts

This IHI topic will enable and directly contribute to EU health priorities, initiatives, and policies. Healthcare products containing PFAS are often essential for the health of citizens in Europe and worldwide. The proposed IHI topic would strengthen collaboration between healthcare system stakeholders to reduce emissions of, and exposure to PFAS, evaluate alternatives and therefore, contribute to the EU Chemicals Strategy for Sustainability of the EU Green Deal.

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. Contribute to the objectives of the Industrial Strategy for Europe and Pharmaceutical Strategy for Europe;
2. Understanding human health and environmental risks from PFAS in healthcare from a life cycle perspective;
3. Manage PFAS risks with novel mitigation measures, including safe disposal, reuse, and recycling;
4. Develop methodologies and solutions for PFAS replacement that meet regulatory requirements without compromising efficacy, quality, safety, or environmental performance;
5. Position the EU as a leader in safe, sustainable PFAS alternatives through industry-academia collaboration;
6. Strengthen stakeholder collaboration to reduce emissions and exposure until alternatives are found;
7. Share industry knowledge and best practices to inform future PFAS policy;

8. Improve business planning certainty for medical technology manufacturers, ensuring long-term sustainability and patient access.

Possible target groups: medical technology and medicines manufacturers and their supply chains, stakeholders involved in regulatory approval process (i.e., notified bodies, policy makers); waste management companies; hospitals and other healthcare settings and providers.

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

Addressing widespread PFAS use in medical technologies, medicinal products and vaccines requires cross-sector collaboration, involving industry (the pharmaceutical and vaccines development and manufacturing industry, as well as the medical technology development and manufacturing industry (medical devices, in vitro diagnostic devices (IVDs), imaging devices, drug-device combination products, etc.)), plus academia, healthcare professionals, patients, health authorities, manufacturers, and IHI partners. Mapping, risk assessments, and understanding performance characteristics need expertise from chemistry, environmental science, healthcare, and engineering. Resource sharing through a public-private partnership is essential for funding, research facilities, and data. Engaging diverse stakeholders ensures comprehensive and accepted solutions.

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 several 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 24 000 000. ***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 23 500 000. ***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 567 500 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).

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 will provide the following expertise:

- chemical synthesis and active pharmaceutical ingredient (AP)I/drug product manufacturing;
- medical device manufacturing and assembly, packaging, distribution, medical supply chain management and quality control;
- regulatory affairs topics, occupational safety;
- standardized analytical methods and in process controls;
- use of process aids, their procurement and quality assurance aspects (e.g. qualification);
- management of chemical/biotechnology waste and decontamination of waste water;
- circular economy expertise;
- safe and Sustainable by Design methodologies;
- activities, results and insights from existing pilots and studies (these may include historical data generated outside of the project timelines that will not constitute part of the in-kind contribution);
- publication support and data dissemination.

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:

- Academic Centres and Research Organizations:
  - Expertise in PFAS analytics, chemical synthesis, material sciences, coatings, and biodegradation;
  - Researchers working on PFAS alternatives and optimizing existing materials.
- Manufacturers:
  - PFAS materials (e.g., films, spare parts, equipment, implants, foils);
  - Medical manufacturing, critical technologies, medicinal products, and vaccines;
  - Drug substance manufacturing/vaccines targeting PFAS excipient replacements/reductions.
- Analytical Methods Experts: Replace TFA in chromatography and other technologies;
- Standards Organizations: Develop and update analytical standards/testing methodologies;

- Process Aids Development experts: Replace process aids (tubing, gaskets, fittings) with alternative materials;
- Circular Economy Experts: Establish PFAS-specific collection and recycling systems;
- Safe and Sustainable by Design Experts;
- Healthcare Waste Management Organizations;
- Urban Wastewater Treatment Management Organizations;
- Healthcare Sector Consultants: Provide input and test solutions;
- Project Management:
    - Coordinate communication, meetings, and risk management;
    - Grant administration, financial management, and reporting;
    - Digital/IT develop and implement support for data governance and management;
    - Coordinate internal and external networking and stakeholder engagement.

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.