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.