PFAS Public Consultation BD Input

Becton, Dickinson and Company (BD) wants to highlight and fully support the public consultation input submitted by MedTech Europe regarding the proposed EU REACH restriction of per- and polyfluoroalkyl substances (PFAS), as published in March 2023. BD entirely echoes the industry-wide commitment to the objective of the EU Chemicals Strategy for Sustainability to encourage innovation for chemicals that are safe and fully sustainable. BD is committed to assessing uses of PFAS and possible alternatives where this is technically feasible. These processes are being performed while ensuring continued availability of life-saving and life-sustaining technologies to satisfy patients' health needs worldwide.

Apart from the uses raised in the MedTech Europe submission, BD would like to raise three additional uses falling outside Regulation (EU) 2017/745 on medical devices (MDs) and Regulation (EU) 2017/746 on *in vitro* diagnostic medical devices (IVDs), which are each equally vital for the overall medical technology innovation ecosystem and the delivery of safe and efficient medical devices critical for patients and healthcare professionals. In the following paragraphs, technical information, and irreplaceable functionality of three uses is being provided in order to request derogations from the PFAS restriction proposal: (1) Research Use Only (RUO) and Laboratory Use Only (LUO) products, (2) Automated medication dispensing systems, and (3) Medicinal product packaging.

It is key to highlight that this is a non-exhaustive list due to the time it takes to identify uses of PFAS in the entire manufacturing life cycle of medical devices and technology. Apart from considering the above mentioned three novel uses of PFAS, BD calls upon the legislators to consider including increased flexibility in terms of the ongoing discoveries of new uses of PFAS and establish a mechanism by which these uses will be able to be included in the derogations within the proposed PFAS restriction. Given the multifaceted functionality and wide characteristics of PFAS, companies performing thorough checks are forced to move within time pressure thus increasing the probability of not identifying all uses of PFAS within the timeframe given. The following is the description of three uses of PFAS not covered within MedTech Europe's submission.

(1) Research Use Only (RUO) and Laboratory Use Only (LUO) products

Scope or restriction option analysis

In the healthcare industry, research and laboratory instruments play a pivotal role in innovation and discovery of new possibilities of providing better care and treatment for patients globally. These instruments assist researchers in their daily work of identifying new medicines, vaccines, diseases, or lifesaving devices and diagnostics that ensure that patients are provided quick, efficient, and suitable care. Some of these 'research use only' and 'laboratory use only' products rely on PFAS in their manufacturing process solely due to the specific and irreplaceable characteristics of these substances, for which there are currently no known alternatives on the market.

Therefore, our submission strongly advocates for the exemption of Research Use Only (RUO) and Laboratory Use Only (LUO) products from the PFAS restriction and the blanket ban which it envisages, underscoring their pivotal role in scientific research, laboratory operations, and healthcare.

1. Fundamental to Scientific Discovery:
RUO and LUO products are fundamental to scientific discovery and innovation. They form the backbone of wet research, enabling researchers to explore new frontiers in fields such as medicine, life sciences, environmental sciences, and material sciences.

2. Research Instruments vs. Clinical Instruments:
Research instruments, such as those used with RUO and LUO products, offer a level of flexibility and investigating features that are unparalleled. They allow researchers to investigate multiple parameters, fostering innovation and the development of new methodologies. This flexibility is vital for understanding complex biological systems and advancing scientific knowledge.

3. Unavailability of Alternatives:
It is essential to acknowledge that suitable alternatives for many RUO and LUO products are currently lacking in the market. Attempting to replace these products with CE marked *in vitro* diagnostic medical devices (IVDs) devices is not a viable solution, as RUO and LUO products are designed for research, offering a unique set of characteristics crucial for experimentation.

4. Wide Research Applications:
RUO products find applications across a broad spectrum of research areas related to organism's health, diseases, and general laboratory use. They play an instrumental role in cancer biology, stem cell research, immunology, infectious diseases, virology, toxicology, forensics, and beyond.

5. Potential for In-House Diagnostic Development:
RUO and LUO products are invaluable for the development of in-house diagnostic devices in cases where commercially available CE IVD devices cannot fulfill unmet clinical needs. Their adaptability and versatility make them essential tools for advancing diagnostics and healthcare.

6. Advancing Scientific Understanding:
RUO and LUO instruments empower researchers to delve deeper into the intricate details of biological systems, enhancing our understanding of organism's health and diseases. They enable the analysis of a broader range of parameters, contributing to groundbreaking discoveries.

7. Indirect Benefits to Healthcare:
While RUO and LUO products are not intended for direct clinical diagnosis, they indirectly benefit healthcare by supporting research that underpins clinical practice. They contribute to the development of safer and more effective diagnostics and therapies, ultimately improving patient care.

RUO and LUO products are very similar to *in vitro* diagnostic medical devices regulated under Regulation (EU) 2017/746 on *in vitro* diagnostic medical devices (IVDs). Therefore, BD requests the same derogations for RUO/LUO as MedTech Europe has requested for regulated *in vitro* diagnostic medical devices in their submission dated 14 July 2023. This includes but is not limited to:

- Add to proposed derogation 5(n) 'Research use only and laboratory use only testing and Research use only and laboratory use only equipment (e.g. for cell analysis related to organisms' health and diseases)'.

Please note that BD supports MedTech Europe's request to reword proposed derogation 5(n) as 'diagnostic laboratory testing and diagnostic equipment'. In addition, BD requests that research use only and laboratory use only products are included in the proposed derogation 5(n).

- Expand MedTech Europe's additional derogation requests for sterile and non-sterile packaging applications (for devices and supplies) of medical devices and of *in vitro* diagnostics medical devices, including similar products such as the device part of a drug-device combination product to include research use only and laboratory use only products.
- Expand MedTech Europe's additional derogation request for accessories and spare/replacement parts for medical devices and *in vitro* diagnostic medical devices to include research use only and laboratory use only products.
- Expand MedTech Europe's additional derogation request for Electrical and electronic equipment in medical devices and *in vitro* diagnostics medical devices, including investigational and the device part of drug device combination products, to include research use only and laboratory use only products.
- Expand MedTech Europe's additional derogation request for manufacturing and processing aid for devices, components and in the supply chain to support the manufacturing of research use only and laboratory use only products.

For RUO/LUO equipment ('instruments') it should be noted that the components are mostly the same or similar as in diagnostic equipment. As such, components containing PFAS are mostly the same or similar. This includes but is not limited to ducting and tubing, filters, fittings, valves, tape, O-ring, plugs, seals, lubricants, chemical, heat and moisture resistant coatings, PTFE coating of moving mechanical parts (e.g. sliding guides), and sterile and non-sterile packaging.

PFAS materials are chosen to provide friction free, chemical resistant, durable and hydrophobic compatible surfaces for the fluid (patient sample) contact components such as containment parts, tubing, ducting and sample dispensing tips that allow the sample to be contained within or dispensed from one compartment to another to be read accurately within the device. Non PTFE tubing can cause cavitation leading to bubble formation, negatively impacting accuracy of the test result.

Electrical and electronic equipment in RUO/LUO may contain PFAS components. PTFE material is used as a protective barrier that provides mechanical flexibility and durability properties, moisture protection and the dielectric strength to prevent electrical current leakage needed to achieve essential electrical safety requirements for users throughout the useful life of the product. FEP is used as a dielectric barrier that enables critical design requirements for durability and performance such as flexibility, optically clear for light transmission, low light absorption, high dielectric strength, high electrically insulative, free of voids, and biocompatibility.

Hazard or exposure

The only identified potential route of exposure is through dermal contact, which may be possible when handling during assembly and maintenance (including service using spare parts) but would not detrimentally affect human health (Fluoropolymer). During use of the RUO/LUO product, direct contact does not happen or is considered low, as PFAS materials are contained internally within components. The use is subject to strict control measures and external certification requirements.

Environmental emissions

Overall, the risk to the Environment is considered low during the service life of an RUO/LUO product as PFAS materials are contained internally within components. There are no specialized disposal instructions related to PFAS. The disposal of such instruments at the end of life follows the requirements of the European Union's WEEE Directive (2012/19/EU on Waste Electrical and Electronic Equipment).

Information on alternatives

There are no known alternatives materials meeting current technical or sustainability standards:

Given the broad range of PFAS materials and uses and the variations in technical function, there is no single drop-in replacement that could be considered for a single instrument/device that could provide the same technical function. Several solutions will need to be identified.

There are no known alternative materials that can perform to the same standard in the majority of these applications without negatively impacting the quality of the test results. Previous research into alternative materials for cost and performance has not yielded success. In fact, PFAS substances have been selected where other (non-PFAS) substances fail to deliver the required performance.

Examples demonstrating the difficulties in finding PFAS alternatives:

PFAS provides high hydrophobic and friction-free surfaces, reduces the surface tension, and provides a critical function in the fluid pathways of sample dispensing/containment RUO/LUO instruments. PFAS improves the sample transfer and reading performance, reducing the risk of inaccurate results and/or repeat testing being necessary. Non PTFE tubing can cause cavitation leading to bubble formation impact accuracy of test result.

Chemical compatibility: Performance of O- Rings, tubing, fittings, valves, plugs, and seals improves when higher PFAS grades are used in harsh environments.

Dry, self-lubricating slide guides provide minimal friction, longevity, and avoids use of grease that, otherwise, can drip and contaminate liquid samples. Finding non-PFAS alternatives that are of the wet-type lubrication would introduce contamination risk instead.

PFAS provides high hydrophobicity, friction-free surfaces and provides a critical function in the fluid pathways, and sample dispensing/containment of RUO/LUO instruments. Some materials are not compatible with components which are known to cause sample reading errors in the device, due to incomplete transfer from internal extraction tips to reaction vessels.

In electrical and electronic equipment, potential alternatives to PTFE have been found to reduce cable flexibility impacting durability and ergonomic usability issue. Potential alternatives to FEP have been evaluated but failed to meet required properties and technical specifications for safe and effective use, including IEC60601 electrical insulation requirement.

Information on costs

A single RUO/LUO instrument includes multiple components containing PFAS materials. Efforts must be made to engage many diverse suppliers. There may be alternate plastics and electrical components available that do not use PFAS. However, there is a need to test for compatibility within any instrument specific applications, and manufacturers are required to work with suppliers to alter their design and customize components that are not suitable to existing applications. Re-design, substitution, customization, and revalidation costs would reach millions of Euros.

Other SEA issues

Disruption in the sale and service of RUO and LUO until PFAS alternatives were validated and integrated into the instruments would leave a critical gap in the research community. If RUO and LUO products could no longer be placed on the market, it would result in major disruption to life science research activities.

For example, researchers rely on the unparalleled efficiency and accuracy of flow cytometer in their work of cell analysis, single cell studies, and cell sorting, suspending the use of flow cytometers will exponentially set back the research capabilities. Similar to clinical laboratory technicians, researchers rely on instrument automation to achieve high throughput with less risk of errors, and would otherwise, have to perform extensive manual activities with reduced productivity.

Scientists and researchers will lose access to tried-and-true instruments assisting their work.

The restriction of this entire class of substances risks halting continuous innovation around human health and that of other organisms.

Transitional period/deferred entry into force

Timelines are not compatible as each instrument has numerous components containing PFAS and each requires individual design and validation. Even if suitable alternatives were found, long validation and verification processes would still be required before complete substitution is realized. It could be feasible to find some PFAS alternatives, but it would be extremely challenging to find PFAS alternatives for all components across multiple diverse suppliers within a complex RUO/LUO instrument. In such a scenario, removal of PFAS from all components of complex RUO/LUO instruments could take in excess of 12 years.

(2) Automated medication dispensing systems

Scope or restriction option analysis

A derogation is missing for automated medication dispensing systems (‘dispensing systems’). Dispensing systems help hospitals & health systems ensure medication availability to dispense the right medications safely and efficiently for the right patients at the right time. This prevents the risk of potential harmful medication errors and the risk of diversion. The systems also give the pharmacy visibility into medication inventory and utilization.

1. Precision and Accuracy in Medication Delivery:
Dispensing systems enable precise and controlled medication administration.

2. Enhanced Patient Safety and Quality of Care:
Dispensing systems contribute significantly to patient safety by minimizing dosing errors and maintaining necessary visibility of available stocks thus preventing medicine shortages that directly impact patient health and safety.

3. Lack of Equally Effective Alternatives:
Restricting the use of PFAS in dispensing systems may hinder healthcare providers' ability to administer medications accurately and efficiently.

4. Intrinsic to Healthcare Operations:
Dispensing systems form an essential part of modern healthcare systems. They facilitate the smooth functioning of medical procedures and processes, ultimately benefiting both healthcare providers and patients.

5. Preserving High Healthcare Standards:
Dispensing systems are vital to uphold the highest standards of precision, accuracy, and patient safety in healthcare. Any compromise on this front could negatively impact patient care and outcomes.

While acknowledging the environmental and health concerns associated with PFAS, it is crucial to recognize the important role PFAS play in dispensing systems within the healthcare sector. Balancing environmental considerations with the critical need for precise medication administration and patient safety is of paramount importance.

In dispensing systems, PFAS is being used as an additive in plastic molded components for its wear and lubricative properties. PFAS helps ensure that moving components, such as latch mechanisms and cable guides, stay functional during the life span of the dispensing system. In some components PTFE is embedded within the polymer matrix; in others PTFE has been applied as a coating.

Dispensing system components are often manufactured and supplied in multi-tier supply chains. As for most PFAS there is currently no obligation for disclosure in the supply chain, manufacturers of dispensing systems are unlikely to be aware of all PFAS in the components or their upstream manufacturing processes.

- Therefore an additional derogation is requested for automated medication dispensing systems, including spare parts and processing aids used in manufacturing.

Hazard or exposure

PFAS-containing components are behind enclosures within the dispensing system, so there is no end user contact during its service life. The service life is approximately 5 to 10 years.

During servicing of the systems there generally is no contact with PFAS containing components, unless the PFAS containing components themselves are being replaced. Repairs of PFAS containing components

may happen 1 or 2 times per year. Servicing is undertaken at customer sites. The technician goes to the customer site, works approximately 1 hour on the dispensing system during which they could come into contact with the PFAS containing components. Exposure is limited because PFAS is embedded in plastics or present as a solid coating. Personal protective equipment can be used while servicing the systems, further limiting exposure to PFAS.

Environmental emissions

Treatment of dispensing systems at the end of life is subject to the European Union's WEEE Directive (Directive 2012/19/EU on Waste Electrical and Electronic Equipment).

For the moving components that have been identified to contain PTFE, the estimated annual amount of PFAS placed on the market as part of our dispensing systems is <100 kg. Considering the 5-10 years' service life, PTFE emissions are expected to be limited.

Information on alternatives

There may be alternate plastics and electrical components available that do not use PFAS, however, manufacturers are required to work with suppliers to redesign the components and verify their suitability before making replacements.

Risks to reliability of equipment and premature failed components could lead to patient care issues.

High level substitution project flow:

- Design (6 months)
- Engineering verification testing (6 months)
- Plastic injection tooling design, and first article component procurement (9 months)
- Design verification testing, including cycle testing (9 months). For moving components, there are typically requirements around reliability, this is typically documented as cycling the moving components hundreds of thousands of times across a statistically significant sample size
- Process validation (3 months)
- Design transfer to manufacturing (2 months)

Design and testing must be undertaken for each component containing PFAS.

Information on costs

The impact will be diminished patient care as manufacturers would be unable to ship systems to the EU (European Union) until design changes for the replacement materials are complete.

Other SEA issues

Design change requires careful expert work that takes time, and such specialized resources are limited. All excess material and spare parts would need to be scrapped. Disruption in the sale and service of the automated medication dispensing systems until PFAS alternatives were validated and integrated into the systems would leave a critical gap in the ability for hospitals and health systems to provide medication to their patients in a precise and safe manner.

Transitional period/deferred entry into force

Timelines are not compatible as one dispensing system has multiple components containing PFAS that each require a design change. The systems have >10 known custom components that contain PFAS. Each component change can take up to 3 years to complete based on the complexity of the component and industry regulations and directives, e.g. Low Voltage Directive (LVD) (2014/35/EU), Radio Equipment Directive (RED) (2014/53/EU) & Electromagnetic Compatibility Directive (EMC) (2014/30/EU). Some of these individual components are linked together in a subsystem which can be tested and implemented at the same time. There are 4 discreet subsystems that will need to be tested. This amounts to approximately 12 years to remove PFAS from all the subsystems.

(3) Medicinal product packaging

Scope or restriction option analysis

Medicinal product packaging plays a vital role within the overall healthcare provision due to its positive impact on preservation, integrity, safety, and medication traceability. Medicinal product packaging should be granted a derogation from the PFAS restriction due to the following reasons:

1. Preservation and Integrity:
Packaging provides a protective barrier, safeguarding medicinal products from external elements like air, light, moisture, and contamination. This preservation ensures the integrity and efficacy of the medicinal product throughout its shelf life.

2. Safety and Security:
Proper packaging ensures the safety of both healthcare professionals and patients. It prevents unauthorized access, tampering, and misuse, particularly crucial for sensitive or controlled substances.

3. Compliance and Adherence:
Packaging often includes instructions and information regarding correct usage, helping healthcare providers understand and adhere to prescribed dosages. Clear packaging facilitates compliance with prescribed regimens, promoting successful treatment outcomes.

4. Identification and Traceability:
Packaging provides a platform for labeling, enabling easy identification of the medicinal product, its manufacturer, expiry date, and batch number. This is essential for traceability, recall processes, and managing product recalls effectively.

5. Regulatory Compliance:
Packaging must meet regulatory requirements and standards set by health authorities. Compliance with these regulations ensures the safety, quality, and efficacy of medicinal products, aligning with public health priorities.

6. Hygiene and Infection Control:
Sealed packaging maintains the sterility and cleanliness of medicinal products, critical for preventing infections and maintaining hygiene standards, especially in healthcare settings.

In summary, medicinal product packaging is an essential component of healthcare, ensuring the safety, efficacy, and proper usage of medicinal products, ultimately promoting better patient outcomes, and supporting effective healthcare delivery. An example of a medicinal product is preoperative skin antiseptics and their single-use applicators.

Proposed derogation 6(l) covers PCTFE-based packaging for medicinal preparations, medical devices and medical molecular diagnostics. Benefits of PFAS in production, packaging and devices include thermal and chemical stability, smooth hard surfaces that are easily cleaned and disinfected, and outstanding barrier properties protecting products from air, moisture, impurities, extractables and particles. These safeguard the safety and quality of products throughout their shelf life. The derogation is currently marked for 'reconsideration' and only covers PCTFE-based packaging. It does not include packaging made from other fluoropolymers or packaging made with processing aids containing PFAS.

- Therefore it is requested to expand derogation 6(l) to: packaging for medicinal products, medical devices and medical molecular diagnostics containing PFAS, including processing aids used in manufacturing.

Hazard or exposure

Medicinal products, and therefore the packaging, are typically handled by healthcare professionals wearing gloves in a sterile environment prior to a surgery or veinous procedure. As such there would be no or limited exposure to the healthcare professional.

Environmental emissions

No specific instructions on how to dispose of the packaging are provided. The packaging may get disposed of together with the medicinal product as medical waste or end up separately in the normal waste bin. Emissions depend on local waste management requirements.

Information on alternatives

Alternatives for PFAS in production and packaging may exist in some cases. However, the sought-after properties of outstanding resistance against heat, light, chemicals, time and abrasion, are naturally linked to persistence. This means that alternatives are most likely persistent, too.

There may be alternate packaging available that does not use PFAS, however BD will need to work with suppliers to redesign the packaging and verify their suitability before making replacements. Due to extended feasibility and lengthy regulatory approval process, the estimated timeline for replacement is between 9 and 12.5 years:

- Find an alternative (if possible) (3-5 years)
- Validation (1-1½ years)
- Shelf-life testing of the sterile barrier (3 years)
- Regulatory approval process (1½-2 years)
- Implementation (½–1 year)

Information on costs

Antiseptic skin preparation applicators are widely used globally in surgical and vascular procedures in order to reduce bacteria on the skin which may cause infection. An analysis from the latest NICE[1] guidelines to prevent surgical site infections (SSIs) demonstrates the cost-effectiveness of using single-use alcoholic chlorhexidine gluconate (CHG) or alcoholic povidone iodine (PVI) over bulk antiseptics. Further, the WHO recommends alcohol-based antiseptic solutions based on CHG for surgical site skin preparation be used in patients undergoing surgical procedures. An inability to obtain appropriate skin antiseptic products in the EU could have a deleterious impact on the health and safety of patients undergoing surgical and venous procedures. Further, there are benefits to healthcare providers in utilizing standardized skin prep across different care settings, which include reduced errors and waste and increased compliance with guidelines for usage.

Removing single-use applicators from the European market will impact standardized skin preparation costs across care settings as the products offer a wide range of coverage areas fitting clinical needs.

Other SEA issues

Until suitable alternatives are found for packaging and processing aids, BD would be unable to place medicinal products such as preoperative skin antiseptics and their single-use applicators on the European market therefore impacting healthcare. There are many benefits to using single-use antiseptic applicators for surgical or veinous site preparation and prevention of infections. “A single-use skin antisepsis applicator has the potential to control the antiseptic volume, reduce drug errors, save time, and reduce waste.”[2]

Transitional period/deferred entry into force

The established substitution timelines (5 or 12 years) are tailored to technical substitution. They do not factor in regulatory timelines such as mandatory stability testing or re-submission of market authorizations for regulated products. The estimated timeline for replacement is 9-12.5 years (see substitution timeline above).

Conclusion

In conclusion, BD welcomes the opportunity to provide comments on the PFAS restriction proposal. BD entirely echoes the industry-wide commitment to the objective of the EU Chemicals Strategy for Sustainability to encourage innovation for chemicals that are safe and fully sustainable. However, such actions should not be performed to the detriment of patient safety and the overall quality of healthcare provision.

[1] NICE guideline [NG125]. Surgical site infections: prevention and treatment, https://www.nice.org.uk/guidance/ng125/evidence

[2] Casey AL, Badia JM, Higgins A, et al. Skin antisepsis: it’s not only what you use, it’s the way that you use it. J Hosp Infect. 2017;96(3):221-222. doi:10.1016/j.jhin.2017.04.019

As explained above, BD requests derogations from the PFAS restriction proposal for the following uses, in addition to those submitted by MedTech Europe in their submission dated 14 July 2023: (1) Research Use Only (RUO) and Laboratory Use Only (LUO) products, (2) automated medication dispensing systems, and (3) Medicinal product packaging. Given the extensive timelines required to find suitable and safe alternatives, BD asks for derogations of at least 12 years.

Furthermore, BD recognizes that the derogations requested by MedTech Europe and our own submission are likely non-exhaustive given the ongoing processes identifying uses of PFAS.