Universal PFAS restriction proposal - Public consultation contribution regarding chemical substance packaging

CONFIDENTIALITY JUSTIFICATION

The confidential attachment to the public consultation provides additional context and details to support our public comments and attachment. The confidential information describes qualitatively or quantitatively the potential impacts regarding on production volume and on Merck operations (including employees) and customers, it also provides details around research and development and procurement activities. This information must remain confidential to prevent its use by competitors, suppliers or customers or investors to gain information regarding market share and potential strategy to gain market advantage or otherwise harm our commercial interests.

INTRODUCTION

This contribution to the public consultation on the universal PFAS restriction describes impacts of the proposed restriction on the packaging of chemical substances supplied by Merck to our customers in the Life Science sector (e.g., production of fine chemicals, pharmaceuticals, biochemicals, R&D and diagnostics).

Per- and polyfluoroalkyl substances (PFAS) are used in packaging materials for chemical substances based on their outstanding properties that help to assure safe containment during transport and storage. Through their inertness PFAS materials also assure the specified quality of the chemical which is crucial for applications ranging from drug development, food production (including food testing) to analytical lab applications and a myriad of other analytical or production purposes.

Merck Life Science KGaA has identified a crucial application of PFAS materials (fluoropolymers) in its chemical packaging, which is used in very large extent in the portfolio of chemical substances sold to customers in the European Union (EU) and globally. We use PFAS containing liner materials as essential part of closure caps used to close a variety of containers such as bottles which contain chemicals.

The Life Science division of Merck KGaA markets a product portfolio of more than 300,000 items which are offered to a wide range of customers globally. A significant part of this product portfolio consists of chemical substances and mixtures mostly in solid or liquid states

that are sold for applications including research, analytical testing, processing, and production of products in numerous industries. These chemical substances are packed into a variety of packaging materials, many of them being cap closed containers such as bottles shown in Figure 1. In addition, many other closures (such as septa) and bottles/containers use fluoropolymers as liners or otherwise in the material composition.

Figure 1: Illustrations of chemical container bottles with closure caps.

KEY FUNCTIONALITIES PROVIDED BY PFAS IN CHEMICAL PACKAGING

The most important part of the packaging system to assure containment and quality of the filled goods is the threaded closure cap on the container opening. To assure containment and seal the cap effectively onto the container opening, a liner disc is employed in the closure cap. This liner either is made of or coated with PFAS material (in most cases polytetrafluoroethylene (PTFE), ethylene tetrafluoroethylene (ETFE) and fluorocarbon-based fluoroelastomer (FKM) utilizing its **high chemical** and **thermal resistance** and **inertness**. The PFAS material functions as an inert barrier and performs the task of sealing and containing the chemical and avoiding interactions between the chemical and the plastic polymers of the cap body.

Figure 2 shows the detailed design of the cap system indicating the liner disc in green in the sectional view on the right.

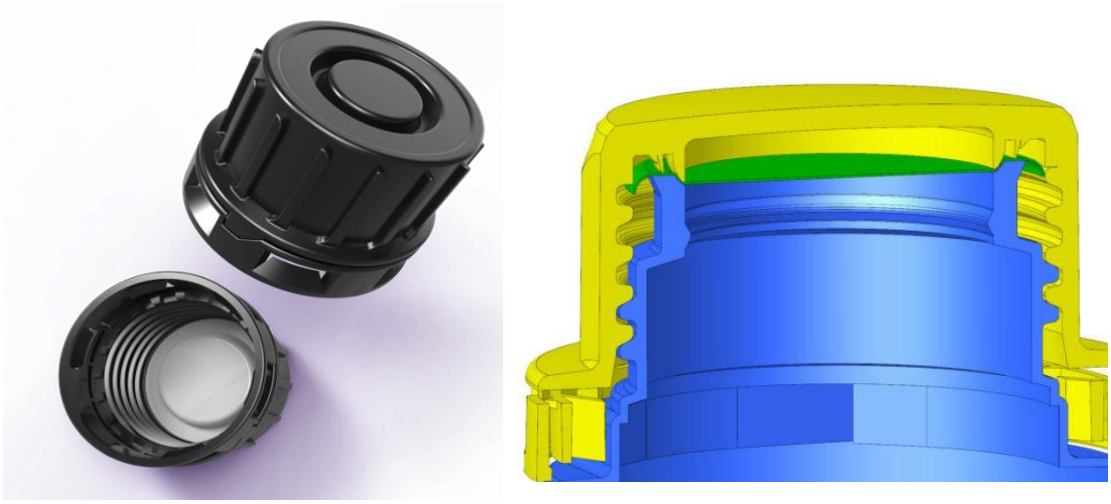

Figure 2: Design detail of an exemplary closure cap with PTFE liner insert. The liner is depicted as bright inlay on the left and marked in green on the sectional view on the right.

If the liner would not be present the safe sealing functionality of the closure would be impaired, resulting in potential leakage. In addition, the inert barrier protecting the cap material would be missing, enabling interaction between the filled goods and the cap material. These interactions can negatively impact the specified quality and purity of the product and thereby violate the requirements of pharmaceutical production (cGMP) and/or impact the safe containment of chemicals falling under Dangerous Goods Regulations for transport and storage.

Merck KGaA has contacted several packaging material suppliers in light of the EU PFAS restriction proposal and requested advice regarding possible options for substitution of the

PFAS containing liner materials. At the present time Merck has been informed that no suitable alternative material is available. According to these suppliers no material has been identified as a substitution option and no list of possible candidates for further evaluation exists.

Merck Life Science is continuing efforts to work with suppliers to further develop and implement the substitution plan as outlined in this document.

TONNAGE AND EMISSIONS ESTIMATES

To provide further data for assessment of the PFAS emission potential of the described application in chemical packaging material we have conducted the following model calculations to illustrate the extent of our use and provide context for the cost effectiveness of the proposed restriction:

From our list of the most important caps (& closures) globally utilizing fluoropolymer liner material we have chosen the widely used S40 cap which is a standard packaging material used at our sites in Europe. The cap has a pure PTFE liner inserted and can be used to calculate a worst-case scenario of the amount of fluoropolymers placed onto the market through the described packaging application.

The model calculation takes the weight of the pure PTFE liner from this model cap and multiplies it with the number of caps procured from suppliers based on the [redacted] most important caps globally (representing > 80 % of all used PFAS liner containing caps globally). The result is the total amount of fluoropolymers placed on the market. For this model calculation we used the sales data from 2022.

As not all liners are made of pure PFAS substances, and the figure also includes sales volumes outside the EU the resulting figure is likely to be higher than the PFAS actually placed on EU single market for this use. Nevertheless, we think this number gives orientation on the magnitude of worst-case emission potential through this application.

The calculation demonstrates that in a worst-case scenario (based on the data from 2022), approximately 1-10 ([redacted]) tonnes of fluoropolymer were placed on the global market. Considering the above-described generalized calculation, the figures for the EU should be significantly lower than this amount as global share of net sales for Merck Life Science in the European region was 33 % according to the 2022 annual report of the Merck Group. This share of global net sales for all products (not only packaged in bottle-cap systems) can be used as a proxy to estimate the amount of PFAS used in liner caps placed onto the EU single market for our use ([redacted]).

An analysis of the sales figures of products linked to the top [redacted] caps purchased in 2022 shows that about [redacted] belong to regulated products (e.g., GMP). The areas of application for these products are diverse and include, for example, use as pharmaceutical raw material or purification process material. A discontinuation would cause considerable problems for our customers, such as pharmaceutical manufacturers. These problems include potential reapprovals of their manufacturing processes or shortages of raw materials of the correct grade leading to reduced availability of pharmaceutical products.

Since our products are solely used in industrial (including GMP) and professional settings, waste is handled according to local regulations applicable to the setting, ensuring safe disposal. Hence, we consider environmental release potential as low.

FACTORS AFFECTING SUBSTITUTION

As one of the market leaders in specialty chemicals for research and analytical purposes, Merck's chemical substance portfolio features the whole spectrum of physicochemical properties, including strong acids, caustics, reactive and corrosive chemicals, organic solvents, and mixtures such as iodine containing formulations used in analytical applications. These chemicals can only be filled into packaging material with suitable performance proven by testing. The described packaging system utilizing the properties of PFAS chemicals such as PTFE or ETFE has been used for decades and proven to fulfill all needed requirements of Merck Life Sciences vast portfolio of chemicals.

In addition to meeting the requirements posed by the physico-chemical properties of the filled goods the packaging system that we have described has been designed specifically to fulfill legal and regulatory requirements that apply to a large part of the packed chemical portfolio. Intensive and complex chemical compatibility studies have been performed to create objective evidence of meeting various regulations stemming from pharmaceutical use of chemical products or the requirements of dangerous goods transportation and storage.

The two factors around this topic are material compatibility with regard to protecting the packaging material from chemical degradation and product compatibility with regard to protecting the filled goods from leachables and extractables out of the packaging material that compromise specified product quality.

Many chemical products that use the described packaging system relying on a PFAS material liner cap are sold into the healthcare market to pharmaceutical manufacturers and used as raw materials or process aids in drug manufacturing processes to produce medicines for the global market. These pharmaceutical raw materials, including active pharmaceutical ingredients and excipients, are highly regulated to protect patient safety. Relevant regulations impacting also the design and composition of primary packaging materials are e.g. EU GMP (good manufacturing practice) guidelines, German AMWHV (Arzneimittel- und Wirkstoffherstellungsverordnung), FDA cGMP guidelines.

Food and pharmaceutical regulations demand that evidence is provided to demonstrate that no critical substances migrate from the packaging into the product. These migrations studies are demanded by Regulation (EU) 10/2011, US 21 CFR §174-190 for food contact materials and / or by the European Pharmacopeia 3.1, 3.2, US Pharmacopeia USP 661.1, USP 1663 and USP 1164 for pharmaceutical applications.

Merck KGaA has performed studies on the current packaging system designed with the PFAS liner material to prove compliance with these regulations and has also provided these results to customers in the pharmaceutical industry. The composition and design of primary packaging materials for APIs is part of submission dossiers for market approval of medicines. Any change to such primary packaging material is subject to approval from authorities. Merck also contractually committed to change control commitments that need approval from customers from the pharmaceutical industry before changes in packaging can be implemented. This is an established industry regulatory standard and serves patient safety to avoid e.g., migration of toxic components from packaging materials into pharmaceutical raw materials.

Most of the chemicals classified as hazardous materials which fall under different regulations for the transport and storage of dangerous goods, such as the *UN Recommendations on the Transport of Dangerous Goods*, *ADR* (European Agreement concerning the International Carriage of Dangerous Goods by Road), *US DOT 49 CFR*, *IATA DGR* (Air transport of dangerous goods), *IMDG* (International Maritime Dangerous Goods Code) etc., have stringent requirements towards packaging material used for these chemicals including hydrostatic pressure testing of closed containers to demonstrate leak proofness. The obligation for compatibility studies of dangerous goods chemicals with plastic packaging is described in the ADR 4.1.1.2 in connection with ADR 6.1.5.

A change in liner material therefore creates requirements to study and prove any effect on the performance of the packaging material to achieve compliance to regulation and assure safe transport.

The above-described factors and obligations create severe consequences considering a possible ban of PFAS used in the described packaging design, as a change or elimination of the cap liner material would result in extensive change control activities including chemical compatibility studies to prove safety and effectiveness of the new closure design. Consequently, supply of crucial chemical products to many critical industries, including pharma and food sectors might be disrupted if the current packaging design and material cannot be used and efforts to find non-PFAS alternatives for the liner material are delayed or unsuccessful. With regard to the impact on the pharmaceutical industry we assume that our status as supplier in the EU single market can be described as critical based on volumes supplied into this industry.

LIST OF ACTIONS AND TIMETABLE WITH MILESTONES

The process of approving changes in packaging for 10's of thousands of chemical products (substances and mixtures) in multiple purity grades from technical laboratory reagent through to high-purity analytical references and GMP materials is highly challenging. Below, we provide timelines to find an alternative solution to the current liner. This assumes that a new "universal" solution is found but in reality, and particularly in the shorter term, a large range of different solutions will need to be employed to address different chemical incompatibilities and specifications. Maintaining a very wide range of caps is not sustainable in the long term because the resulting operational inefficiency and complexity will add to costs to Merck Life Science and customers. Lower performance materials with regard to leaching may also require reduced shelf-lives to compensate, increasing waste through the supply chain. Therefore, the timelines presented are realistic extremes for the vast majority of our products with some products falling outside of these timelines.

The timetables shown in Figure 3 and Figure 4 illustrate the planned systematic approach for the substitution of PFAS containing liners for products regulated under GMP with requirement to find a substitution candidate with very similar characteristics to PFAS material through an R&D project and another timeline for non-GMP products of simpler chemical complexity, which might be possible to investigate with potential liner material substitutes available on the market at time of project start. Separate timelines are displayed to indicate that a substitution for non-GMP products with lower chemical challenge would in an optimal scenario require less time because studies demanded by regulation and laws are fewer than for GMP products and one could hopefully mitigate an R&D project as needed for GMP and more demanding chemical profile. In addition, the change notification process of customers for non-GMP products is shorter as customers are expected to need less time for assessment of the impact on their application and no intense assessments or studies at the customer are demanded as in case of GMP products.

It must be noted that even the most optimistic project timeline described for non-GMP products and low chemical compatibility challenge, that would try to use of the market material solutions to cover this class of products takes 6 years and 9 months according to our estimate. Without a derogation for this use, the proposed restriction only provides an 18-month transition period. This would not be enough time for Merck to execute the substitution activity as described.

In exceptional cases for small parts of the portfolio that are non-GMP and non-dangerous-goods and in case that at time of project start, of-the-shelf alternatives for the liner caps are available from suppliers this timeline might be shortened through skipping the "Material manufacturing" phase ([redacted]) which includes new production tool equipment for liners, and the elimination of "Studies required by laws and regulations" ([redacted] month). This means that even in a best-case scenario for the part of portfolio with lowest change requirements the timeline would be 5 years and 3 months.

As part of the project initiation phase, Merck will assemble a project team that includes all relevant departments (e.g., regulatory, packaging engineering, sourcing). Furthermore, cooperation with the packaging material suppliers needs to be clarified in this phase in order

to start the search for alternative non-PFAS materials for cap liners. Similar processes will also need to be initiated for other fluoropolymer-containing packaging types (e.g., septa and containers), in some cases these may have even more specific and longer timeframes.

The start of the scouting phase is accompanied by intensive efforts to identify multiple candidates as possible substitute material. In our current plan, shown in Figure 3, this is estimated to take [redacted] months. At this point, it should be mentioned once again that this period can vary greatly. Since no possible substitutes are available at this time, the scouting and research may take [redacted] months or even more. The R&D scouting phase in close collaboration with the suppliers would consist of principle material component testing to investigate compatibility profiles of material samples with a range of requirements and the principal manufacturability of the material into the liner design. As these tests would also involve basic stability tests that require exposure over certain periods of time, we do not reasonably expect to shorten this phase significantly, even in best case scenarios.

When possible candidates have been identified, they will be used to produce liner samples. Depending on material type, suppliers will have to develop and built new tool equipment used in the manufacturing process which is reflected in the [redacted]-month time to manufacture samples for following studies. After receiving these samples, initial analyses must be completed. This analysis includes a feasibility study, in which the properties as well as the general suitability of the alternative materials in packaging systems are to be analyzed based on various laboratory tests at Merck. Furthermore, these investigations also include exploration studies to check the compatibility of the identified non-PFAS material with various chemicals.

At the end of this project phase, the most promising candidate must be defined which is then used for further detailed studies including product shelf life etc. The following phase for studies required by regulations and laws includes proof of effectiveness in containing hazardous substances (dangerous goods regulations) and the inertness required for packaging for pharmaceutical chemicals (GMP regulations) must be provided.

[FIGURE REDACTED]

Figure 3: PFAS liner substitution plan timeline for GMP products (figure confidential)

[FIGURE REDACTED]

Figure 4: PFAS liner substitution plan timeline for non-GMP products with potential substitution testing candidate (if available) for non-complex chemical requirement (figure confidential)

In order to introduce an alternative material, planning, initiation and execution of change must be in accordance with GMP practices. While meeting up on customer notification obligations and obtaining consent retrieval for GMP products, a global supply chain for the

non-PFAS liners needs to be established. At this point all global production sites of Merck Life Science KGaA need to be involved in this project.
According to our plan, the project would take a total of approximately 13 years and 9 months for GMP regulated end products and 6 years and 9 months for non-GMP regulated end products as shown in Figure 3 and Figure 4.

The approach described above focuses on a one-fits-all solution. Nevertheless, we understand the versatility of PTFE might not be able to be reproduced by only one solution but by multiple substitutes for the different materials that need to be filled in our packaging (e.g., acids, solvents, corrosive chemicals etc.). Should no suitable single substitution candidate be identified a project adjustment into assessment and introduction of different materials is needed to cover requirements from the different classes of chemicals. This would significantly increase the complexity of replacing PTFE, as separate R&D projects would have to be initiated for each of the candidates. Also in this case, the scouting phase of each solution can vary in length and differ greatly from one another.

Current assessments of potential liner solutions made of e.g., poly-vinyl, polyethylene, silicone and rubber show that no material of this type currently available can substitute e.g., PTFE performance due to underlying chemical characteristics of the carbon-fluorine bonds that result in the lack of chemical reactivity (hence compatibility with a wide range of substances), and extremely low leaching. A substitution with these materials might be possible for individual products or product groups but would need studies and testing on an enormous scale. These factors will result in a broad range of timelines for alternatives to be implemented across the portfolio of chemical products typically in the range of 6-13 years.

CONCLUSION

Merck Life Science KGaA has provided information on the described use of PFAS materials in its chemical packaging and outlined its projected plan to substitute this material in case of a PFAS ban. Based on the needed activities the complete substitution of the material is estimated to take at least 13 years. This estimate is affected by a degree of uncertainty, especially stemming from the R&D scouting phase for substitute material candidates that could also span considerably longer or fail completely in a worst-case scenario for some products/chemicals.

Based on intensive exchange with liner-cap suppliers there is no viable alternative currently available for the described applications. Also, the research in this area has not identified any possible candidates to be evaluated further for substitution that are able to meet all of the technical advantages of the fluoropolymers used. Instead, a complex range of alternatives need to be implemented and this requires extensive testing and qualification to meet regulatory needs (e.g., Dangerous Goods transport regulations, Food Contact Regulations and Pharmacopoeia requirements).

In case of a PFAS ban without derogations to allow substitution of PFAS in industrial and professional chemical packaging, severe damage to downstream supply chains at Merck Life

Science customers in the EU are to be expected, as a large part of the chemical portfolio would no longer be available to the market due to a lack of appropriate packaging.

The unavailability of the affected products is likely to cause severe consequences to society, most notably the unavailability of essential medicines or food stuff, as chemical raw materials or chemical reagents used for product release testing, which are registered through respective regulations, are missing or in reduced supply.