David Jansson

Who is commenting? *(choose the best fit)*
Representative of a product manufacturer(s)

If you are commenting as a representative, what is the name of the entity you are commenting on behalf of?
Cytiva

If you represent a product manufacturer or industry group, what industry(ies) do you represent?
Product manufacturer, Life Sciences Supplier

If you represent a product manufacturer, what types of components, products, or product categories do you manufacture that you will be requesting a CUU determination for?
Products (including equipment and consumables) used in the research, development and manufacturing of biopharmaceuticals, therapies and Life Sciences at large. These include filters, gaskets, O-rings, tubing, bags, hardware (including HPLC system, mixers, bioreactors) and more.

Do you have any recommended changes or other considerations that you think the MPCA should take into account when defining the term "essential for health, safety, or the functioning of society"? *(Please review the proposed definitions in the rule concept document prior to answering)*
All products used in the research, development and manufacturing of FDA regulated products should automatically be placed out of scope and considered as CUU to reduce risks to disruptions in life saving pharmaceuticals and therapies. Similar exemptions have been successfully included in other US state legislative proposals, including Maine and New Mexico.

Do you have any recommended changes or other considerations that you think the MPCA should take into account when defining the term "alternative"? *(Please review the proposed definitions in the rule concept document prior to answering)*
Replacing materials used in FDA regulated processes has to show like-for-like properties to their fluoropolymer counterparts. This includes the minimum performance requirements of the material (e.g. remove pathogens, maintain integrity, volume throughput for filters, binding or adsorption of drug ingredients, temperature and caustic stability, etc.) as well as properties related to how the material may impact the drug manufacturing process stream (e.g. leachables, free radicals that interact with the drug or excipient, etc). In many cases the properties of the drug manufacturing process and fluid also influence these performance

properties, leading to a healthcare authority regulated requirement for all critical applications with the materials be validated (a time consuming and costly process for each pharmaceutical process and fluid). Even in cases where PFAS free version of components like a filter exists, these materials do not generally have like-for-like properties and changes would result in costly and time-consuming revalidations that may impact the quality of the final product.

Do you have any recommended changes or other considerations that you think the MPCA should take into account when defining the term "reasonably available"? (*Please review the proposed definitions in the rule concept document prior to answering*)
Replacing materials used in FDA regulated processes has to show like for like properties to their fluoropolymer counterparts. Even in cases where PFAS free version of material like a filter exists, these materials do not have like-for-like properties and changes would result in costly and time-consuming revalidations that may impact the quality of the final product.

When considering the proposed definition of “product category”, how broadly should the agency group product categories? *(Examples: “vehicles” versus “sedans, SUV’s, vans, trucks, RV’s” or "printers" versus "receipt printers, thermal printers, label printers, residential printers, commercial printers, etc.")*
Categories should be as broad as possible (ideally on the level of “products used in FDA regulated processes”) to ensure no uses are restricted to the gaps in input or assessments by the authorities.

Should each request for a CUU determination be limited to a single product category, or should applicants be allowed to submit a request for a CUU determination for multiple product categories?
Requests should be grouped as much as possible if products are used in the research, development and manufacturing of FDA regulated products, or otherwise consider these applications entirely out of scope. These products are used in all parts of the biopharma manufacturing process; considering some of them as CUU and some not would not make sense as any changes would result in the same re-validation requirements at the end-user. This would also reduce the administrative burden placed on suppliers.

What safety or other standards require the use of PFAS in a product? *(Please include the specific citation)*
PFAS containing products, in particular fluoropolymers, are widely used in biopharma manufacturing and related research industries. The materials are used for the chemical stability, chemical compatibility with solvents, low leaching potential, oleophobic properties, thermal resistance and mechanical properties of the polymers. These materials currently have to meet Good Manufacturing Practices (GMP) standards and US Pharmacopeia (USP) requirements including extractable and leachable data to ensure that these materials cause no adverse effect as a part of their use in the manufacturing process.

The agency is seeking feedback on the potential that the initial positive CUU determination duration for existing products will expire eight years from the date of issuance regardless of product category. This is intended to stagger renewal deadlines and ease the administrative burden of processing renewals.

- Do you have any concerns about unintended consequences with this proposal?
- Do you have any alternative recommendations to stagger renewal deadlines?

The administrative burden to reapply will be massive for small volume industries such as the Life Sciences industry which places a large number of niche products on the market compared to other industries which sell large volumes some bulk products. In cases where there are not sufficient administrative resources to meet the submission requirements, and it may require companies to stop shipments to Minnesota rather than risk regulatory non-compliance.

All products used in the research, development and manufacturing of FDA regulated products should automatically be considered as CUU to reduce risks to disruptions in the supply chain for life saving pharmaceuticals and therapies. Similar exemptions have been made in other US states such as Maine and New Mexico.

For manufacturers: Administrative cost of requesting a CUU determination (Part 1 of 2). *Please provide your best estimates or rough orders of magnitude (for example "approx. 200 hours"). Precise accounting data is not necessary to answer this question.*

If your company currently possesses information regarding intentionally added PFAS (to the CAS number level) for all components in your product lines, please estimate the number of technical staff hours that were required to establish this baseline.
More than 500 hours

For manufacturers: Administrative cost of requesting a CUU determination (Part 2 of 2). *Please provide your best estimates or rough orders of magnitude (for example "approx. 200 hours"). Precise accounting data is not necessary to answer this question.*

If your company does not possess information regarding intentionally added PFAS (to the CAS number level) for all components in your product lines, please estimate the number of technical staff hours needed to obtain this data from your Tier 2 or 3 suppliers for a single product line.
More than 500 hours

For manufacturers: Expenditure considerations when seeking non-PFAS alternatives (Part 1 of 2). *Please provide your best estimates or rough orders of magnitude (for example "primary cost is CapEx"). Precise accounting data is not necessary to answer this question.*

If you have identified a technically viable non-PFAS alternative for one of your products that contains intentionally added PFAS, does implementing this alternative require Capital Expenditure (such as purchasing new molds, retooling machinery) or primarily Operational Expenditure (such as purchasing more expensive raw materials)?

- Please estimate the ratio of Capital Expenditure to Operational Expenditure (or indicate which category is the dominant cost driver).

PFAS free alternatives currently exist for some but not all fluoropolymer containing products used in biopharmaceutical manufacturing; however these have properties that do not make them suitable for every use case in the pharmaceutical manufacturing process, and replacing a fluoropolymer with a non-fluoropolymer material will impact the drug manufacturing process and drug in which it is used, requiring re-validations subject to health authority approvals.

For manufacturers: Expenditure considerations when seeking non-PFAS alternatives (Part 2 of 2).

If you <u>have not</u> identified a technically viable non-PFAS alternative for one of your products that contains intentionally added PFAS, have you conducted a Research & Development (R&D) feasibility study?

- If so, what was the cost of that study?

Finding alternative polymers to replace PTFE and PVDF will require massive R&D investments for both the Life Sciences industry and their resin suppliers, this work is in the early phases and the timeline for finding fully functioning alternatives for all uses at is expected to be at least 15+ years, we cannot today fully assess the long term CapEx for these activities given the scope of the work, and the implementation of any potential alternatives in the future will require massive re-validations for biopharma manufacturers, resulting in costly and time-consuming revalidations that may impact the quality of the final product.

For manufacturers: Research and development safety validation cycles.

What is the typical duration of the R&D and safety validation cycle for a reformulated product in your sector (from concept to market entry)?

Does this cycle align with the 5-year renewal period typically associated with regulatory exemptions?

- If not, please explain the specific technical barriers that would require a longer validation period.

No, the regulatory barriers for replacing materials used in FDA registered processes would be longer then 5 years, in particular if a large number of companies would have to re-validate their processes at the same time, creating backlogs at the competent authorities.

Please provide any additional information or documentation needed to support your answers to any of the questions posed.
Note - This comment has been uploaded by the MPCA on behalf of the commenter. Commenters located outside of the United States are unable to access the comment portal website due to network security. Accommodations were made to accept these comments in an alternative format and upload them on behalf of the commenters.

1. Who is commenting? (*choose the best fit*)

• Member of the general public

• Representative of an environmental group

• **Representative of a product manufacturer(s)**

• Representative of another unit of government

• Representative of a public health group

• Academic or research organization

• Other (please specify)

2. If you are commenting as a representative, what is the name of the entity you are commenting on behalf of?

Cytiva

3. If you represent a product manufacturer or industry group, what industry(ies) do you represent?

Product manufacturer, Life Sciences Supplier

4. If you represent a product manufacturer, what types of components, products, or product categories do you manufacture that you will be requesting a CUU determination for?

Products (including equipment and consumables) used in the research, development and manufacturing of biopharmaceuticals, therapies and Life Sciences at large. These include filters, gaskets, O-rings, tubing, bags, hardware (including HPLC system, mixers, bioreactors) and more.

5. Do you have any recommended changes or other considerations that you think the MPCA should take into account when defining the term "essential for health, safety, or the functioning of society" (*Please review the proposed definitions prior to answering*)

All products used in the research, development and manufacturing of FDA regulated products should automatically be placed out of scope and considered as CUU to reduce risks to disruptions in life saving pharmaceuticals and therapies. Similar exemptions have been successfully included in other US state legislative proposals, including Maine and New Mexico.

6. Do you have any recommended changes or other considerations that you think the MPCA should take into account when defining the term "alternative"? *(Please review the proposed definitions prior to answering)*

Replacing materials used in FDA regulated processes has to show like-for-like properties to their fluoropolymer counterparts. This includes the minimum performance requirements of the material (e.g. remove pathogens, maintain integrity, volume throughput for filters, binding or adsorption of drug ingredients, temperature and caustic stability, etc.) as well as properties related to how the material may impact the drug manufacturing process stream (e.g. leachables, free radicals that interact with the drug or excipient, etc). In many cases the properties of the drug manufacturing process and fluid also influence these performance properties, leading to a healthcare authority regulated requirement for all critical applications with the materials be validated (a time consuming and costly process for each pharmaceutical

process and fluid). Even in cases where PFAS free version of components like a filter exists, these materials do not generally have like-for-like properties and changes would result in costly and time-consuming revalidations that may impact the quality of the final product.

7. Do you have any recommended changes or other considerations that you think the MPCA should take into account when defining the term "reasonably available"? (*Please review the proposed definitions prior to answering*)

Replacing materials used in FDA regulated processes has to show like for like properties to their fluoropolymer counterparts. Even in cases where PFAS free version of material like a filter exists, these materials do not have like-for-like properties and changes would result in costly and time-consuming revalidations that may impact the quality of the final product.

8. When considering the proposed definition of “product category”, how broadly should the agency group product categories? (Examples: “vehicles” versus “sedans, SUV’s, vans, trucks, RV’s” or "printers" versus "receipt printers, thermal printers, label printers, residential printers, commercial printers, etc.")

Categories should be as broad as possible (ideally on the level of “products used in FDA regulated processes”) to ensure no uses are restricted to the gaps in input or assessments by the authorities.

9. Should each request for a CUU determination be limited to a single product category, or should applicants be allowed to submit a request for a CUU determination for multiple product categories?

Requests should be grouped as much as possible if products are used in the research, development and manufacturing of FDA regulated products, or otherwise consider these applications entirely out of scope. These products are used in all parts of the biopharma manufacturing process; considering some of them as CUU and some not would not make sense as any changes would result in the same re-validation requirements at the end-user. This would also reduce the administrative burden placed on suppliers.

10. What safety or other standards require the use of PFAS in a product? (*Please include the specific citation)*

PFAS containing products, in particular fluoropolymers, are widely used in biopharma manufacturing and related research industries. The materials are used for the chemical stability, chemical compatibility with solvents, low leaching potential, oleophobic properties, thermal resistance and mechanical properties of the polymers. These materials currently have to meet Good Manufacturing Practices (GMP) standards and US Pharmacopeia (USP) requirements including extractable and leachable data to ensure that these materials cause no adverse effect as a part of their use in the manufacturing process.

11. The agency is seeking feedback on the potential that the initial positive CUU determination duration for existing products will expire eight years from the date of issuance regardless of product category. This is intended to stagger renewal deadlines and ease the administrative burden of processing renewals.

• Do you have any concerns about unintended consequences with this proposal?

The administrative burden to reapply will be massive for small volume industries such as the Life Sciences industry which places a large number of niche products on the market compared to other industries which sell large volumes some bulk products. In cases where there are not sufficient administrative resources to meet the submission requirements, and it may require companies to stop shipments to Minnesota rather than risk regulatory non-compliance.

• Do you have any alternative recommendations to stagger renewal deadlines?

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12. The MPCA has developed a preliminary list of potentially eligible data categories that may be considered for trade secret requests. (*Please review the list of potentially eligible data prior to answering*)

• Do you have any concerns about unintended consequences with this proposal?

• Do you have any alternative recommendations for data that should or should not be eligible for trade secret requests?

13. What are the potential ongoing costs to society if the commissioner issues a positive currently unavoidable use determination for the continued use of PFAS within a product or product category? *(For example: environmental, human health, or remediation costs)*

14. For manufacturers: Administrative cost of requesting a CUU determination (Part 1 of 2). *Please provide your best estimates or rough orders of magnitude (for example "approx. 200 hours"). Precise accounting data is not necessary to answer this question.*

If your company currently possesses information regarding intentionally added PFAS (to the CAS number level) for all components in your product lines, please estimate the number of technical staff hours that were required to establish this baseline.

• Not applicable

• Less than 40 hours

• 40 to 100 hours

• 101 to 500 hours

• **More than 500 hours**

• Other (please specify)

15. For manufacturers: Administrative cost of requesting a CUU determination (Part 2 of 2). Please provide your best estimates or rough orders of magnitude (for example "approx. 200 hours"). Precise accounting data is not necessary to answer this question.

If your company does not possess information regarding intentionally added PFAS (to the CAS number level) for all components in your product lines, please estimate the number of technical staff hours needed to obtain this data from your Tier 2 or 3 suppliers for a single product line.

Not applicable

• Less than 40 hours

• 40 to 100 hours

• 101 to 500 hours

• More than 500 hours

• Other (please specify)

16. For manufacturers: Expenditure considerations when seeking non-PFAS alternatives (Part 1 of 2). Please provide your best estimates or rough orders of magnitude (for example "primary cost is CapEx"). Precise accounting data is not necessary to answer this question.

If you have identified a technically viable non-PFAS alternative for one of your products that contains intentionally added PFAS, does implementing this alternative require Capital Expenditure (such as purchasing new molds, retooling machinery) or primarily Operational Expenditure (such as purchasing more expensive raw materials)?

PFAS free alternatives currently exist for some but not all fluoropolymer containing products used in biopharmaceutical manufacturing; however these have properties that do not make them suitable for every use case in the pharmaceutical manufacturing process, and replacing a fluoropolymer with a non-fluoropolymer material will impact the drug manufacturing process and drug in which it is used, requiring re-validations subject to health authority approvals.

• Please estimate the ratio of Capital Expenditure to Operational Expenditure (or indicate which category is the dominant cost driver).

17. For manufacturers: Expenditure considerations when seeking non-PFAS alternatives (Part 2 of 2).

If you have not identified a technically viable non-PFAS alternative for one of your products that contains intentionally added PFAS, have you conducted a Research & Development (R&D) feasibility study?

• If so, what was the cost of that study?

Finding alternative polymers to replace PTFE and PVDF will require massive R&D investments for both the Life Sciences industry and their resin suppliers, this work is in the early phases and the timeline for finding fully functioning alternatives for all uses at is expected to be at least 15+ years, we cannot today fully assess the long term CapEx for these activities given the scope of the work, and the implementation of any potential alternatives in the future will require massive re-validations for biopharma manufacturers, resulting in costly and time-consuming revalidations that may impact the quality of the final product.

18. For manufacturers: Research and development safety validation cycles.

• What is the typical duration of the R&D and safety validation cycle for a reformulated product in your sector (from concept to market entry)?

• Does this cycle align with the 5-year renewal period typically associated with regulatory exemptions?

• If not, please explain the specific technical barriers that would require a longer validation period.

No, the regulatory barriers for replacing materials used in FDA registered processes would be longer then 5 years, in particular if a large number of companies would have to re-validate their processes at the same time, creating backlogs at the competent authorities.

19. Please provide any additional information or documentation needed to support your answers to any of the questions posed.

20. Do you have any additional questions or comments regarding the PFAS in products: Currently unavoidable use rule? *(Please note that we may be unable to respond to specific questions regarding rule content in this phase of the rulemaking process).*