27 March 2026

Minnesota Pollution Control Agency (MPCA)

Minnesota, USA

Re: Submission of consultation feedback – PFAS currently unavoidable use (CUU) rule

To whom it may concern,

I am writing on behalf of BioPhorum to formally submit our consolidated feedback regarding the Proposed PFAS Currently Unavoidable Use (CUU) Rule. We appreciate the opportunity to provide input as part of this consultation process and to contribute the perspective of the global biopharmaceutical manufacturing community.

BioPhorum represents over 150 biopharmaceutical manufacturers and suppliers worldwide, encompassing the vast majority of global biopharmaceutical output. Given the essential role that PFAS-containing materials play across drug development, production, testing, storage, and delivery, it is critically important that the CUU framework recognises the scientific, regulatory, and supply-chain realities unique to this sector. The enclosed document provides detailed responses to each of the consultation questions, including clarification notes, interpretation of provided definitions, and necessary contextual explanations drawn from the February 2026 Draft Rule Concept Summary.

Where the information supplied by the agency did not allow a question to be fully addressed, this has been clearly indicated, with additional commentary provided in a dedicated section. Our aim is to support MPCA's understanding of the highly regulated environment in which biopharmaceutical manufacturers operate and to ensure that any future policy recognises patient safety and public-health imperatives.

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PFAS Currently Unavoidable Use (CUU) Rule – Feedback Questions with Embedded Requirements

This document lists each of the Minnesota Pollution Control Agency (MPCA) feedback questions with the required background information, definitions, and constraints placed directly underneath each question, taken from the February 2026 Draft Rule Concept Summary which was considered.

In instances where a multiple-choice question could not be answered based on the available information, the item was left unanswered and any relevant contextual information, clarifications, or observations associated with the unanswered item was documented separately and incorporated into the section below or at the end of the report.

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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)

BioPhorum Response

BioPhorum, a global collaboration of over 150 biopharmaceutical manufacturers and suppliers **representing more than 98% of the world's biopharmaceutical output,** is submitting this response.

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

BioPhorum Response

BioPhorum

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

BioPhorum Response

The global biopharmaceutical manufacturing industry (including biologics, monoclonal antibodies, cell and gene therapies, vaccines, mRNA platforms) and supporting suppliers.

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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?

Definition required:

- **Product category** – *"A group of similar products that are used for a similar purpose and that could functionally replace each other for that purpose and does not mean variations within a product that do not affect the product's primary function."*

MPCA Definition Constraint

Product category: group of similar products used for a similar purpose.

BioPhorum Response

BioPhorum may seek CUU determinations for **all PFAS-containing products used in biopharma,** including:

- **Production (Manufacturing Process Equipment & Components):** Sterile filtration membranes (PVDF, PTFE), Vent/gas filters, Tubing, gaskets, O-rings, connectors (PVDF, PTFE, FKM, FEP), Hardware systems (lined pipes, TFF cassettes, pumps)
- **Testing (R&D, QC, Analytical Use):** Laboratory materials essential for R&D (PTFE, FEP apparatus)
- **Storage (Cryogenic & Controlled-Temperature Materials):** Cryostorage bags (PTFE, FEP) and, Ultra-low temperature refrigerants used for drug storage (multiple PFAS).
- **Delivery (Drug-Contact & Final Product Components):** Primary drug-contact films, stoppers, vial/syringe coatings (ETFE/PTFE) and On-body delivery devices/systems (OBDDs/OBDSs)

These uses constitute essential components in drug manufacturing, packaging and delivery.

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5. Recommended changes to the definition of "essential for health, safety, or the functioning of society"

Proposed definition: A use of PFAS is considered essential when the function provided by PFAS is necessary to ensure the product or component performs as intended, where losing that function would cause service to be unavailable and result in:

- A significant increase in negative health outcomes;
- An inability to mitigate significant risks to human health or the environment; or
- A significant disruption of key societal services such as:
    - Food, water, shelter, hygiene, or survival needs;
    - Transportation, utilities, gas, electricity, communications;
    - Personal/occupational/public safety needs, especially in extreme conditions;
    - Other basic human welfare services.

MPCA Constraint

A use is essential when the PFAS function is necessary and alternatives do not exist.

BioPhorum Response

BioPhorum strongly recommends **explicit recognition of biopharmaceutical manufacturing** as essential because:

- **100% of biologic drugs rely on PFAS at some stage** of production, testing, storage, or delivery.
- PFAS removal would immediately halt manufacture of medicines treating cancer, immunological disease, diabetes, infectious disease, neurological disorders, and rare diseases.
- These drugs directly protect life, prevent mortality, and treat chronic illness, meeting all MPCA criteria for essentiality.

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6. Recommended changes to the definition of "alternative"

Proposed definition:

"Alternative" means any non-PFAS chemical, substance, material, manufacturing process change, non-chemical change, or other product that would result in a functionally equivalent product if used in place of PFAS.

BioPhorum Response

BioPhorum urges MPCA to emphasize that:

- **Functional equivalence is not sufficient;** biopharma requires materials that do not interact chemically with the drug stream.
- Many proposed alternatives result in **drug adsorption, yield loss, leachables, or safety failures,** making them unsuitable.

- Alternatives must also be **compatible with GMP requirements,** validated for patient safety, and globally regulatory-approved.

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7. Recommended changes to the definition of "reasonably available"

Proposed definition:

- Alternatives must perform comparably to PFAS.
- Alternatives must be currently available in sufficient quantity.
- Cost is **not** considered, performance and availability only.
- Alternatives used in equivalent products are automatically considered "reasonably available."
- Availability may change due to innovation.

Constraint

MPCA defines “reasonably available” as comparable performance and quantity (not cost).

BioPhorum Response

“Reasonably available” must factor in:

- **20+ years R&D timelines for alternatives to be developed and validated.** Given the need to identify and develop technically suitable PFAS-free materials, then establish robust, resilient global supply chains capable of producing these materials at commercial scale, the timelines for implementing alternatives are expected to exceed 20 years. While initiatives such as the European Innovative Health Initiative (IHI) have launched five-year programs to identify potential replacement materials, these efforts focus primarily on material discovery and do not address the substantial further work required to industrialize those materials, expand manufacturing

capacity, or qualify suppliers under the stringent regulatory and quality systems required in the life-sciences sector.

Even once alternative materials are identified, suppliers and sub-suppliers must develop capability to manufacture them consistently and at the necessary volumes, and then undergo extensive qualification and certification processes. There is potential new suppliers will not initially meet the regulatory, GMP, or ISO-based standards required for Tier 1 supply, meaning additional time is needed for capability building, facility upgrades, and regulatory compliance. Only once these supply chains are robust, stable, and globally scalable can downstream validation activities begin.

The regulatory burden then adds a further sequential and interdependent layer: Tier 1 suppliers must submit updated raw-material and component-level submissions across numerous international markets. Drug manufacturers and biomanufacturers must then submit their own product-level changes to demonstrate safe and effective use of these newly qualified materials within their specific manufacturing processes. Regulatory authorities must therefore evaluate a very large number of linked filings, where product-level approvals depend on prior acceptance of the supplier's data. This multi-market, multi-stage regulatory review structure compounds the overall timeline.

Taken together, material discovery, supplier capability development, supply-chain industrialization, component- and product-level validation, and the high volume of interdependent regulatory approvals across global jurisdictions the end-to-end implementation of fully validated PFAS-free alternatives represents a multi-decade effort extending well beyond 20 years.

- **Biopharma's strict requirement that materials not chemically interact with medicines.**
- **Global regulatory approval timelines of 8–20 years per product, even when alternatives exist.** To appreciate the regulatory scale involved in transitioning PFAS-containing components to fully validated alternatives, it is important to consider the volume of products currently overseen by the U.S. Food and Drug Administration (FDA). According to the FDA's At a Glance report 2020 (1), the agency has over 20,000 prescription drug products approved for marketing in the United States. In addition, the FDA oversees more than 6,500 distinct categories of medical devices, covering everything from simple Class I consumables to complex Class III implantable systems and diagnostic technologies. These figures demonstrate the breadth of products for which manufacturers would need to file amendments if PFAS-containing materials were altered or replaced. For each affected drug or device, Tier 1 suppliers must submit revised component-level data, and manufacturers must subsequently submit product-level updates for regulatory review. In a regulatory environment already responsible for tens of thousands of active product approvals, this scale of sequential, interlinked submissions further underscores why transitioning to PFAS-free alternatives will demand multi-decade timelines, even before considering the added challenges of material identification, supply-chain readiness, and global market synchronization. Note the numbers cited were as of 2020, in the last six years we would have expected many more to be authorized
- **Severe supply chain risks, many alternatives are not produced at scale.**

Severe supply-chain risks persist because many potential PFAS alternatives are not produced on a commercial scale, and in several cases have not yet been industrialized at all. Even when early-stage materials are identified, such as those expected to emerge from initiatives like the IHI five-year

program, these efforts focus only on discovery and do not address the far more extensive work required to build robust, high-volume global supply chains. To be viable for regulated life-science applications, suppliers and sub-suppliers must demonstrate consistent manufacturing capability, secure adequate plant capacity, and meet stringent GMP, ISO, and sector-specific certification requirements. Potential many prospective vendors would not initially meet the quality or regulatory thresholds required for Tier 1 supply, meaning significant investment, facility upgrades, training, and qualification cycles would be necessary before any alternative material could be adopted. Until these supply chains are established, diversified, and proven reliable, PFAS-free materials cannot be considered reasonably available for critical biomanufacturing and tier 1 supply applications. PFAS alternatives are therefore not reasonably available for critical applications.

Works Cited

1. **FDA.** FDA AT A GLANCE - REGULATED PRODUCTS AND FACILITIES. [Online] https://www.fda.gov/media/143704/download.

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8. How broadly should the agency group product categories?

Examples provided:

- "Vehicles" versus specific subtypes such as sedans, SUVs, vans.
- "Printers" vs: receipt, thermal, label, residential, commercial printers.

Definition reminder: *Product category groups similar products with similar purpose.*

BioPhorum Response

BioPhorum recommends **narrow, specific product categories,** because:

- Each bioprocessing component has unique performance, safety and regulatory requirements.
- Grouping categories broadly (e.g. “filters”) obscures the fact that **virus-removal filtration, sterile-filtration, and gas-filtration have entirely different PFAS requirements.**

Over-broad categorization risks misclassification and patient harm.

Alternatively, While many biopharma stakeholders support narrow categories due to technology specificity, others highlighted the need for broader categories, particularly for systems used in FDA-regulated production, so that no critical use falls outside the scope of CUU determinations.

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9. Should each request cover a single product category or multiple categories?

BioPhorum Response

This should be multicategory, biopharma **processes rely on integrated systems** where multiple PFAS-containing components work together.

- A single biologic manufacturing process may rely on **50–200 PFAS-containing components** from different categories.

A “one category at a time” approach would be impractical and not reflective of real manufacturing use.

It would be suggested grouping CUU requests for products used collectively in FDA-regulated manufacturing, noting that changes to one component typically require revalidation of the full system. This would reduce regulatory burden and prevent inconsistent outcomes

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10. What safety or other standards require the use of PFAS in a product? (Include citations)

Important rule requirement: Applicants must:

- Provide citation to the standard.
- Explain exactly why PFAS is needed to meet the standard.
- Clarify whether PFAS is *required* or merely *chosen*.
- Evaluate whether alternatives could meet the same standard.

BioPhorum Response

PFAS are required to meet numerous regulatory and safety standards, including:

- **GMP regulations (21 CFR 211.65)** requiring non-reactive, non-additive materials in equipment. PFAS are uniquely compliant.
- Sterility assurance standards for filtration, where **no PFAS-free membranes can withstand sterilization or maintain performance**.
- Drug packaging standards requiring **chemical inertness and barrier protection**, met only by PTFE/ETFE coatings.

Without PFAS, medicines cannot meet safety requirements.

Stakeholder input emphasized that PFAS-based polymers uniquely meet Good Manufacturing Practices (21 CFR 211.65) requiring non-reactive and non-additive materials. They also noted that PFAS-free films or membranes currently cannot meet required sterility assurance and chemical compatibility standards.

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11. Feedback on the proposed 8-year CUU duration for existing products

Rule requirement summary:

- Existing products: 8-year expiry from issuance.
- Purpose: stagger renewal deadlines, reduce administrative burden.

- Novel products: five-year expiry.

You are asked to comment on:

- Concerns with unintended consequences.
- Alternative methods to stagger renewal cycles.

BioPhorum Response

An 8-year duration is incompatible with:

- **Could be 20+ year pharmaceutical validation cycles based on the information supplied in Question 7.**
- **Stability studies that can last 5–10 years per product.** Depending on the material or product, stability studies may need to span 5–10 years to support the full shelf-life, particularly for Tier 1 raw materials and single-use components, recognizing that some drug products require shorter (e.g., 3-year) studies, while biologics or components with longer shelf-life expectations require extended stability programs.
- **Global regulatory approval timelines that may exceed the CUU renewal horizon.**

BioPhorum recommends **permanent** exemption for CUU for biopharma PFAS due to thermal destruction at end-of-life and essentiality.

Some suppliers indicated that, due to the volume of specialised components and the administrative effort involved, they may be forced to halt shipments to Minnesota rather than risk non-compliance if renewal cycles are too short or burdensome.

12. Feedback on potentially eligible trade-secret data categories

Potentially eligible categories:

- Chemical name
- Chemical identifying number
- Chemical concentration or formula
- Reformulation or redesign details
- Non-chemical alternative descriptions
- Supply chain information

You are asked:

- Any concerns about unintended consequences?
- Recommendations for additional or excluded categories.

BioPhorum Response

Biopharma supports expanding trade secret protection because:

- Supply chains are **n-tiered and highly proprietary;** component-level PFAS identification is often impossible.
- Disclosure requirements would violate supplier IP and jeopardize safety-critical supply.
- Many PFAS-containing components (e.g., multilayer films, membranes) are protected formulations.

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13. Potential ongoing costs to society if a CUU determination is issued

Examples provided:

- Environmental costs
- Human health impacts
- Remediation or cleanup costs

BioPhorum response

If CUU is granted for biopharma:

- The societal cost associated with PFAS used in biomanufacturing is regarded as low, since these materials are typically incinerated at end-of-life and therefore do not persist in the environment. This is particularly true for drug-substance and drug-product manufacturing processes; however, some drug-delivery devices or primary packaging may not always be thermally destroyed, and these exceptions should be acknowledged.
- Conversely, **denial** of CUU risks:
    - Drug shortages
    - Halted clinical pipelines
    - Loss of access to critical therapies
    - Global manufacturing relocation
    - Increased mortality

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14. Administrative cost of requesting a CUU determination (Part 1 of 2)

Requirement context:

- Applies if the company **already possesses PFAS data (CAS-level)** for all components.
- Provide estimated staff hours used to establish baseline.

Options:

- Not applicable
- Less than 40
- 40–100
- 101–500
- More than 500
- Other

BioPhorum Response

Due to multi-tiered supply chains and proprietary formulations:

- Manufacturers **do not possess CAS-level PFAS data** for upstream components.
- Obtaining this data from Tier 2–6 suppliers is **often impossible.** Several manufacturers highlighted that multi-tiered supply chains make component-level PFAS disclosure time-consuming or impossible.
- Estimated effort: **hundreds to thousands of hours,** depending on the product line. often requiring.

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15. Administrative cost (Part 2 of 2)

Requirement context:

- Applies if the company does **not** already have PFAS data (CAS-level).
- Estimate staff hours needed to obtain data from Tier 2/3 suppliers.

Same hour-range choices as above.

BioPhorum Response

Due to multi-tiered supply chains and proprietary formulations:

- Manufacturers **do not possess CAS-level PFAS data** for upstream components.
- Obtaining this data from Tier 2–6 suppliers is **often impossible.** Several manufacturers highlighted that multi-tiered supply chains make component-level PFAS disclosure time-consuming or impossible.
- Transitioning each product line involves a major workload, typically estimated by the team as requiring thousands of hours, given the

need to reassess materials, conduct full validation programs, and complete linked regulatory filings.

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16. Expenditure considerations for non-PFAS alternatives (Part 1 of 2)

Requirement context: Applicants must indicate:

- Whether alternatives require **capital expenditure (CapEx)** → e.g., tooling, molds, equipment.
- Or **operational expenditure (OpEx)** → e.g., more expensive raw materials.
- Provide a ratio or identify dominant cost driver.

BioPhorum Response

Where alternatives exist (rare), implementing them requires:

- For new/novel PFAS replacements the suppliers will need to recover the development and commercialization costs which will feed into the price when brought to market.
- New equipment, tooling, and validation, **significant CapEx.**
- Higher-cost materials, **substantial OpEx**.
- Additional regulatory filings and process redesign.

Most substitution scenarios require **both**, with CapEx as the primary driver.

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17. Expenditure considerations (Part 2 of 2)

If no viable alternative exists:

- State whether an R&D feasibility study was conducted.
- Provide cost of that study.

BioPhorum Response

BioPhorum members report that:

- Feasibility studies for PFAS replacements require **multi-year programs.**
- Costs can reach **millions of dollars**, depending on the application.
- Many studies fail because no viable alternatives exist.

18. Research & development safety validation cycles

Applicants must describe:

- Typical duration from concept → market entry.
- Whether this aligns with **5-year renewal cycles**.
- Technical barriers requiring longer validation.

BioPhorum Response

Typical end-to-end timelines:

- **5–8 years:** minimal substitution (where alternative is already known)
- **20+ years: full replacement requiring new materials, testing, validation, and regulatory approvals.** Achieving full PFAS replacement across biopharmaceutical and medical-device applications is a multi-decade undertaking, well beyond 20 years, because it requires the discovery of entirely new materials, the development and industrialization of robust global supply chains, extensive multi-year stability and performance validation, and sequential regulatory approvals across thousands of affected products. As outlined in the detailed questions above, many alternative materials are not yet identified or produced at commercial scale; suppliers will need years of capability building and certification; manufacturers must revalidate processes and update filings; and regulators face a substantial volume of interdependent submissions from both Tier 1 suppliers and product manufacturers. Taken together, these interconnected scientific, industrial and regulatory barriers reinforce that PFAS-free materials cannot be

substituted quickly and that full replacement timelines necessarily extend over multiple decades.
- This does **not** align with the proposed five-year renewal cycle.

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19. Additional information or documentation

Supporting documents may include [BioPhorum response to the Annex XV report on the proposal for universal PFAS restrictions (part II) - BioPhorum] which includes:

- PFAS document
- Safety standards
- Alternative assessments
- Supply chain or production data

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20. Additional questions or comments regarding the CUU rule

MPCA notes: They may be unable to answer specific rule-content questions at this stage.

BioPhorum Response

BioPhorum emphasizes:

- The biopharma sector is **unique** in that PFAS use directly supports patient safety and survival.
- No PFAS-free substitutes exist for most pharmaceutical applications.
- A CUU framework must recognize the **global public health impact** of PFAS restrictions.

Please find here our fully detailed report which can be downloaded [BioPhorum response to the Annex XV report on the proposal for universal PFAS restrictions (part II) - BioPhorum]

We trust that the accompanying feedback will assist the Minnesota Pollution Control Agency in developing a framework that is both protective of environmental objectives and appropriately calibrated to the scientific, regulatory, and operational realities of the biopharmaceutical sector. Given the essential role these materials play in safeguarding patient health worldwide, it is critical that any final rule reflects an evidence-based understanding of their necessity, the complexity of alternatives, and the potential implications for global public health.

BioPhorum and its members remain committed to supporting the Agency throughout the rulemaking process. We are open to answering any follow-up questions, providing additional technical information, or supplying further documentation where needed. We would also be happy to meet with the Agency to discuss any aspect of our submission in more detail, should that be helpful.

Thank you for the opportunity to contribute to this important consultation.

Yours faithfully,

Victoria Mwanza
BioPhorum Global Change Facilitator
BioPhorum