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Mr. Bradley Baker
Resource Management Program Manager
Land and Materials Administration
Maryland Department of the Environment
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Baltimore, MD 21230-1719

Submitted Electronically: mde.epr@maryland.gov

RE: Comments on Proposed Regulations - COMAR 26.04.14 - Extended Producer Responsibility and Request for Exemption of Cold Chain Packaging for Prescription Drugs and Biologics

Dear Mr. Baker:

The National Association of Specialty Pharmacy (NASP) respectfully submits these comments on the proposed amendments to COMAR 26.04.14 regarding Extended Producer Responsibility (EPR) for packaging and paper products in the State of Maryland. NASP urges the Department to clarify and expand the exemption in COMAR 26.04.14 § .02.16(b) to explicitly exempt all primary, secondary, and tertiary packaging associated with cold chain shipments for prescription drugs and biological products.

While NASP appreciates the Department's recognition that primary packaging for FDA-regulated drugs and medical devices merits exemption from EPR obligations, the current regulatory language creates an unjustified and operationally impossible mandate that secondary and tertiary cold chain packaging associated with drug and biologic products be subject to EPR compliance. This proposed approach:

1. Contradicts the statutory intent to exempt medical products from EPR obligations.
2. Fails to account for the mandatory nature of cold chain requirements for specialty pharmacy products.
3. Imposes duplicative and unnecessary regulatory complexity and cost on an already heavily regulated healthcare sector that works to support and carefully manage patients with serious, life-threatening medical conditions.

4. Creates perverse incentives that may increase the risk of temperature excursions and compromise patient safety and drug efficacy.

NASP respectfully requests that the Department revise COMAR 26.04.14 § .02.16(b) to exempt all packaging—primary, secondary, and tertiary—associated with prescription drugs and biological products consistent with the statutory exemption language and the public health imperatives that drive cold chain requirements.

Background On Specialty Pharmacy and Cold Chain Management for Specialty Drugs and Biologics

Specialty pharmacies are highly specialized entities that dispense, deliver and provide patient support services for complex, often high-cost medications used to treat serious, chronic, and rare diseases. These include, but are not limited to:

- Biologic therapies (monoclonal antibodies, recombinant proteins, gene therapies, cell therapies);
- Injectable medications (interferons, growth factors, immunosuppressants);
- Oral chemotherapy agents;
- Antiretroviral medications; and
- Complex injectables requiring patient training and monitoring.

Specialty pharmacies are accredited by national, independent, third-party specialty accreditors (e.g., URAC, ACHC, and JCAHO) and operate under extensive oversight by the U.S. Food and Drug Administration (FDA) and state boards of pharmacy. Cold chain management is not a business choice—it is a regulatory mandate designed to protect patient safety and ensure therapeutic efficacy.

Biologic products differ fundamentally from traditional small-molecule drugs because they are derived from living organisms and contain complex protein or genetic structures that are extraordinarily sensitive to temperature variation. Even brief temperature excursions outside of their required range (exposure to incorrect temperatures for even a few hours) can irreversibly compromise product integrity, efficacy or patient safety in use.

Examples of Temperature-Controlled Specialty Drugs and Biologics

- Humira® (adalimumab): a chronic, patient self-administered biologic medication used to treat a variety of chronic autoimmune and autoinflammatory conditions, such as rheumatoid arthritis, ulcerative colitis, and plaque psoriasis. Humira must be refrigerated at 2-8°C and shipped to a patient home in validated, temperature-controlled packaging to maintain product stability in transit and ensure patient safety and efficacy upon administration.

- Mekinist® (trametinib**)**: an oral medication used for the treatment of unresectable or metastatic solid tumors with genetic mutations for adult and pediatric patients six years of age and older. Mekinist must be stored at 2°C to 8°C, dispensed in the original bottle with the desiccant, protected from moisture and light and not placed in pill boxes to maintain product viability and patient safety.
- Pulmozyme® (dornase alfa): a recombinant enzyme inhalation solution used for the management of cystic fibrosis patients to improve lung function. Pulmozyme ampules must be stored and transported between 2°C to 8°C in their protective foil to protect from light and heat. Once the protective foil pouch is opened, the unused ampules must be kept refrigerated in the protective foil pouch to protect from light and heat. The medication cannot be used if the ampules are exposed to room temperature (22°C to 28°C) for more than a total of 60 hours.

What Cold Chain Packaging Requires

The following represents secondary and tertiary packaging materials that are essential components of FDA-compliant cold chain systems but would NOT be exempt under the proposed regulation: COMAR 26.04.14 § .02.16(b):

A. Thermal Packaging Components

- Styrofoam/Expanded Polystyrene (EPS) Coolers: Rigid foam insulation boxes that maintain temperature stability; irreplaceable for ultra-cold and frozen products.
- Molded Fiber/Pulp Coolers: Paper-based insulation alternatives.
- Reflective Foil-Lined Insulation: Multi-layer insulation wrapping to maintain temperature.
- Vacuum-Insulated Panels: Advanced insulation materials for sensitive products.
- Polyurethane Foam Liners: Additional insulation layer inside coolers.

B. Thermal Conditioning Agents (Packaging Materials Used to Maintain Temperature)

- Gel Ice Packs: Phase-change materials in plastic housings (typically HDPE or PP) that maintain temperature during transport; can hold consistent cold for 24-72+ hours depending on design.
- Dry Ice Packaging: Used for ultra-cold transport (-78°C); sealed in Styrofoam or cardboard containers.
- Liquid Nitrogen Shippers: Specialized containers for cell therapies and gene therapies requiring cryogenic temperatures.

- PCM (Phase Change Material) Liners: Specialized insulation that releases cold gradually.

C. Protective Padding and Void Fill

- Bubble Wrap: Plastic air-filled cushioning to protect medications from temperature shock and physical damage during transit.
- Plastic Air Pillows: Void fill to reduce package movement.
- Kraft Paper Void Fill: Paper-based cushioning.
- Crinkle Paper: Recycled paper packing material.
- Corrugated Cardboard Filler: Carton board used for stacking/spacing.

D. Shipping Containers

- Cardboard Shipping Boxes: Outer container for protection during transport; different grades and coatings required for temperature control.
- Corrugated Mailers: Secondary container for smaller shipments.
- Rigid Plastic Containers: Hard-shell shipping cases for sensitive products.
- Insulated Liners (Plastic/Rubber): Plastic or rubber barriers inside shipping containers.

E. Labeling, Monitoring, and Documentation Packaging

- Temperature Data Logger Packaging: Protective cases for electronic thermometers that track temperature throughout transit.
- Thermal Indicator Labels: Single-use labels that change color if temperature excursions occur (alert systems for pharmacy staff).
- Shipping Labels and Protective Sleeves: Plastic-coated labels and label protectors.
- Desiccant Packets: Moisture-absorbing packets (typically plastic) that prevent condensation inside coolers.
- Oxygen Absorbers: Packages to prevent oxidation of sensitive biologics.

F. Sealing and Closure Materials

- Tape (Paper, Plastic, or Kraft): Used to seal boxes and maintain package integrity.
- Plastic Seals and Security Ties: Tamper-evident packaging.
- Plastic Shrink Wrap: Secondary wrapper around coolers.
- Plastic Film/Wrapping: Protection from moisture and contamination.

Patient Safety Concerns Without Regulatory Exemption

Under the current proposed regulation, secondary and tertiary packaging for drugs is not exempt even though the primary container is exempt. This creates a fundamental regulatory contradiction that undermines the purpose of the statutory exemption, which recognizes that drug packaging must preserve product integrity and meet FDA requirements. While the regulation exempts the primary container (the vial, syringe, or blister pack holding the drug), it does not exempt the secondary and tertiary packaging (ice packs, coolers, insulation) that is equally essential to preventing temperature excursions that would degrade the primary container's contents.

Many specialty drugs and biologics treat rare diseases and extremely small patient populations and are not stocked at local retail pharmacies due to their complex management, high cost, limited shelf life, and low dispensing volume. As a result, these therapies are dispensed through highly accredited specialized pharmacies that primarily operate centralized distribution models, shipping medications directly to patients' homes using validated cold chain packaging, and managing the patient through direct communications during the medication's/biologics' use.

If the regulation is not amended, Maryland's most vulnerable patients could lose access to critical therapies. The state's complex EPR requirements would drastically increase shipping costs and create regulatory uncertainty for specialty pharmacies, making it extremely difficult for specialty pharmacies to continue providing these essential medications. The regulation also risks creating financial pressure on pharmacies to modify cold chain packaging practices in ways that could increase the likelihood of temperature excursions, product loss, or compromised drug integrity. Together, these outcomes threaten patient access to safe and effective treatment and undermine the public health objectives the statute should support.

Volume and Cost Impact: Why This Affects Specialty Pharmacy Disproportionately

Unlike consumer products that are packed once and distributed to many customers, specialty pharmacy medications are typically shipped individually or in small batches directly to patients' homes using temperature-controlled packaging. These shipments require significantly more packaging material by weight due to insulation, refrigerants and monitoring components necessary to maintain validated temperature ranges.

Many specialty pharmacies are clinically specialized to dispense a limited number of therapies or disease states due to the intensive patient management, clinical expertise, accreditation requirements, and infrastructure required to safely support these medications, limiting their ability to diversify services or absorb new regulatory costs. Under the proposed regulation without exemption, these pharmacies would be subject to cumulative producer fees under a per-pound EPR pricing model, along with registration fees, PRO membership fees, administrative costs, and ongoing compliance obligations. For many specialty pharmacies shipping drugs and biologics into Maryland, these combined costs could reach the tens to hundreds of thousands of dollars annually, a level that is unsustainable, particularly for independent specialty pharmacy providers.

Legal and Policy Arguments for Exemption

Maryland's EPR statute (Environment Article 9-2501 et seq.) explicitly exempts "primary packaging for a product regulated as a drug or medical device by the U.S. Food and Drug Administration, including associated components and consumable medical equipment." Cold chain packaging materials (ice packs, insulation, thermal management systems) are "associated components" that are integral to ensuring drugs and biologics reach patients in a safe and efficacious condition.

Interpreting the statutory exemption to exclude secondary/tertiary packaging improperly narrows the exemption in a manner that is inconsistent with the legislative intent, effectively rendering it unworkable for temperature-sensitive drugs and biologics. Federal FDA requirements mandate that drugs and biologics be maintained within specified temperature ranges throughout the entire supply chain, and packaging must be designed to preserve those conditions as temperature excursions would render products non-compliant.

Maryland's state pharmacy regulations similarly presume the use of validated cold chain packaging for temperature sensitive medications. Subjecting required packaging to EPR obligations creates a direct conflict between state pharmacy board requirements, state environmental regulations, and federal drug safety law and regulations. Maryland's EPR regulations should be implemented in a manner that avoids such conflicts and preserves compliance with federal FDA and state patient safety requirements.

Requested Regulatory Revisions

NASP respectfully requests that the Department revise COMAR 26.04.14 § .02.16(b) as follows:

<u>Current Language (to be revised):</u>

"Exempt material means a material, or any portion of a material that is... iv. Primary packaging for a product regulated as a drug or medical device by the U.S. Food and Drug Administration, including associated components and consumable medical equipment..."

"Exempt material does not mean secondary or tertiary packaging associated with products listed in (a)."

Proposed Revised Language:

"Exempt material means a material, or any portion of a material that is... iv. All packaging—primary, secondary, and tertiary—for a product regulated as a drug, biologic, or medical device by the U.S. Food and Drug Administration, including all materials necessary to maintain product stability, temperature control, safety, and efficacy during storage, handling, and distribution to patients, including associated components and consumable medical equipment..."

NASP urges the Maryland Department of the Environment to recognize that cold chain packaging is inseparable from drug efficacy and FDA compliance. Where primary drug packaging is exempt, the packaging materials necessary to maintain validated temperature control during storage and distribution must likewise be exempt to preserve patient safety and therapeutic effectiveness.

Specialty pharmacies already operate under extensive oversight by state boards of pharmacy and are subject to federal requirements governing drug storage, handling, and distribution, as well as rigorous accreditation standards. Imposing additional EPR compliance requirements creates conflict and confusion, unnecessary regulatory duplication, and increases healthcare costs without environmental benefit.

Accordingly, NASP respectfully requests that the Department revise COMAR 26.04.14 § .02.16(b) to explicitly exempt all cold chain packaging (primary, secondary, and tertiary) used for prescription drugs and biologics, consistent with statutory intent and public health considerations.

NASP welcomes the opportunity to work collaboratively with the Department to refine language that protects Maryland's environmental goals while preserving patient access to safe and effective life-saving specialty medications. For additional information please contact me at Sheila.Arquette@naspnet.org.

Respectfully submitted,

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President and CEO