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Animal Health Institute Packaging Material Exemption Request

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Section 13(D) of 38 M.R.S. § 2146 requires the Maine Department of Environmental Protection (the Department) to review packaging material associated with products covered by certain federal laws and regulations to determine if it should be excluded from the "packaging material" definition under subsection 1, paragraph I. The Department invited assistance to identify any federal content or construction standards that preclude or significantly diminish a producer's ability to increase the recyclability or reduce the volume of packaging material. The Animal Health Institute represents US manufacturers of animal medicines, and submits this request on behalf of its members.

1. Which federal laws or regulations preclude or significantly diminish a producer's ability to increase the recyclability or reduce the volume of packaging material? Please provide specific citations and language.

Animal drugs, biological products, parasiticides, medical devices and diagnostics used to treat, or administered to, animals and associated packaging are regulated by the U.S. Food and Drug Administration (FDA) under the Federal Food, Drug, and Cosmetic Act (FFDCA) (21 U.S.C. Sec. 301 et seq.), the U.S. Department of Agriculture (USDA) under the federal Virus-Serum-Toxin Act (VSTA) (21 U.S.C. Sec. 151 et seq.), and the U.S. Environmental Protection Agency (EPA) under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) (7 U.S.C. Sec. 136 et seq.).

FDA-Regulated Products:

Animal health companies follow the US Pharmacopoeia (USP), an independent, scientific standard setting body. USP standards are legally recognized. The standards state that plastic packaging systems must protect and be compatible with drug products. The ingredients of the drug products should not be absorbed onto the surface or migrate into the body of the plastic packaging system. USP <665> covers fluid-contact, plastic components used for drug substances (with exclusions) and drug products associated with 'traditional' pharmaceuticals, 'small molecule' drug products, biopharmaceuticals, and vaccines. It applies to both single-use systems as well as multi-use systems. Additionally, USP <1665> governs Characterization and Qualification of Plastic Components and Systems used to Manufacture Pharmaceutical Drug Products and Biopharmaceutical Drug Substances and Products.

Pharmaceutical packaging, in addition to providing a barrier and stability to the product, must not present additional risk to the patient (by way of contaminants/leachables); and must not interfere or create compatibility issues with the drug that may result in degradation. Changes to packaging for animal medicines can require extensive research and additional regulatory approval. Section 506A of the FFDCA and FDA's regulation at 21 CFR 514.8 provide for four reporting categories for post-approval changes. Under FDA's Guidance for Industry #83, Chemistry, Manufacturing, and Controls Changes to an Approved New Animal Drug Application (NADA) or Abbreviated New Animal Drug Application (ANADA), a major change is a

change that has a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug as these factors may relate to the safety or effectiveness of the drug.

A major change requires the submission of a supplement and approval by FDA prior to distribution of the drug made using the change. The holder of an approved application under FFDCA § 512 must assess the effects of the change before distributing a drug made with a manufacturing change (21 CFR 514.8(b)(1)(ii)). The following are examples of changes considered to have a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug as these factors may relate to the safety or effectiveness of the drug:

1. For liquid (e.g., solution, suspension, elixir) and semisolid (e.g., creams, ointments) dosage forms, a change to or in polymeric materials (e.g., plastic, rubber) of the primary packaging components.

2. For liquid (e.g., solution, suspension, elixir) and semisolid (e.g., creams, ointments) dosage forms in permeable or semi-permeable container closure systems, a change in the ink and/or adhesive used on the permeable or semi-permeable packaging component.

3. A change in the primary packaging components for any drug product when the primary packaging components control the dose delivered to the animal (e.g., the valve or actuator of a metered-dose inhaler or addition of a dosing gun).

4. For sterile drug products, any change that may affect drug product sterility assurance such as:

- A change from a glass ampule to a glass vial with an elastomeric closure.
- A change to a flexible container system (bag) from another container system.
- A change to a prefilled syringe dosage form from another container system.
- A change from a single unit dose container to a multiple dose container system.
- Changes that add or delete silicone treatments to container closure systems (such as elastomeric closures or syringe barrels).
- Changes in the size and/or shape of a container for a sterile drug product.

5. Deletion of a secondary packaging component intended to provide additional protection to the drug (e.g., a carton to protect from light, an overwrap to limit transmission of moisture or gases) or a change in the composition of, or the addition of, a secondary packaging component that may affect the impurity profile of the drug.

6. A change to a new container closure system if the new container closure system does not provide the same or better protective properties than the approved container closure system.

7. For a liquid or semisolid dosage form, an increase in the size of a container that results in an increase of the labeled amount of drug product.

For each packaging change, the supplement (or annual report) must contain information determined by FDA to be appropriate and include the information developed by the applicant in assessing the effects of the change (FFDCA § 506A(b), (c)(1), (d)(2)(A), and (d)(3)(A)). The type of information that must be included in a supplemental application (or annual report) is specified in 21 CFR 514.8(b)(2)(iii), (b)(3)(iv), (b)(3)(vi), and (b)(4)(iii).

USDA-Regulated Products:

The USDA's Animal Plant Health Inspection Service (APHIS) sets forth packaging requirements for biologics at 9 CFR Part 112. Under this regulatory framework, packaging must protect the integrity of a regulated product, including maintaining the appropriate temperature for a product. Biologics are defined as viruses, serums, toxins (excluding substances that are selectively toxic to microorganisms, e.g., antibiotics), or analogous products at any stage of production, shipment, distribution, or sale, which are intended for use in the treatment of animals and which act primarily through the direct stimulation, supplementation, enhancement, or modulation of the immune system or immune response. The term "biological products" includes but is not limited to vaccines, bacterins, allergens, antibodies, antitoxins, toxoids, immunostimulants, certain cytokines, antigenic or immunizing components of live organisms, and diagnostic components, that are of natural or synthetic origin, or that are derived from synthesizing or altering various substances or components of substances such as microorganisms, genes or genetic sequences, carbohydrates, proteins, antigens, allergens, or antibodies.

Labeling for biological products is highly prescriptive, and there is extensive information that must be included with the final product. Reducing packaging is not possible where the instructions or other information must be included on the label. Final containers of biological product prepared at a licensed establishment, or imported, in cartons or other containers must not be removed from such cartons or containers for sale or distribution, unless each final container bears, or is packaged in a carton with, complete and approved labeling which is affixed to or included with each container by the licensed establishment producing the product.

The broad definition of "packaging material" in Maine's statute as including anything used for the containment, protection, delivery, presentation or distribution of a product, could include many biological product components which are often required to be disposed of as SHARPS, including anything that contains a needle or blood product (whole blood or serum), for example:

- Unused vaccine in a syringe with a needle
- Sample tube with any amount of blood or serum
- Anything made of breakable glass

EPA-Regulated Products:

The U.S. EPA regulates animal parasiticides. Material must be packaged in a container that is designed, constructed and marked to comply with the requirements of 49 CFR 173.4, 173.5, 173.6, 173.24, 173.24a, 173.24b, 173.28, 173.155, 173.203, 173.213, 173.240(c) & (d), 173.241(c) & (d), Part 178 and Part 180 that are applicable to a Packing Group III material, or, if subject to a special permit, according to the applicable requirements of 49 CFR Part 107, subpart B. These requirements apply to the pesticide product as it is packaged for transportation in commerce.

40 CFR Part 157 -- Packaging Requirements for Pesticides and Devices contains child-resistant packaging requirements for pesticides. The EPA's 2006 Standards for Pesticide Containers and Containment Final Rule provides very prescriptive language around rinsing prior to recycling. This greatly reduces a producer's ability to increase recyclability because it is dependent on end user education and compliance with this federal standard.

2. If content or construction standards are not directly specified in the citations referenced in response to Question 1, please explain how the cited federal laws or regulations indirectly specify content or construction standards.

The requirement for research and prior approval or review for federally-regulated products creates an impossible dilemma for producers: they are chasing a moving target of producer responsibility requirements as state legislation changes; and often cannot make any changes without federal agency approval or review, with no assurances that their changes will be approved, or when; or that states won't move the goalpost further.

3. To which product or group of products do the federal laws or regulations referenced in response to Question 1 and any circumstances specified in response to Question 2 apply?

Animal drugs and medical devices are regulated by the FDA under the FFDCA. Sponsors must specify for the agency the materials of construction and packaging used for each drug product and provide data showing those factors will maintain stability of the product over its shelf life. Consequently, each drug product has its own unique approved packaging. Changes to product packaging take months of development followed by full FDA review and approval.

Biological products – including vaccines and diagnostic test kits – are approved by USDA under the VSTA. Manufacturers are required to ensure packaging maintains the integrity of the product, so temperature is a major consideration. Packaging must also accommodate detailed USDA labeling requirements.

Parasiticide products used on or around animals are regulated by the EPA under FIFRA. FIFRA § 25(c)(3) authorizes EPA to establish standards with respect to the package, container, or wrapping in which a pesticide or device is enclosed to protect children and adults from serious injury or illness resulting from accidental ingestion or contact with pesticides or devices regulated under FIFRA. Additionally, FIFRA § 25(c)(3) requires EPA's Child-Resistant Packaging (CRP) standards to be consistent with those established under the Poison Prevention Packaging Act of 1970.

4. Do the federal laws or regulations referenced in response to Question 1 and any circumstances specified in response to Question 2 apply to some or all packaging material associated with the product or group of products identified in response to Question 3? If some, identify the packaging material that is affected.

These federal laws apply to the ***product's*** approval, regulation or registration, therefore all packaging is implicated.

5. Who should the Department contact with questions regarding this exemption request?

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Conclusion

Maine is the only state that does not broadly exempt animal health products from its EPR mandate. The lack of harmonized standards for sustainable packaging creates complexities in already strained supply chains. Packaging arrangements are shared globally, so separating out changes for the U.S. is challenging, and would be impossible on a state-by-state basis.

Sustainable packaging can often conflict with goals to minimize pharmaceutical waste (e.g. implementing multi-layer blister packaging to extend shelf-life of products), creating a conflict in desired outcome of

environmental impact. Most regulatory authority guidance requires demonstration of equivalence/superiority with packaging changes, which results in challenges when introducing higher levels of recyclability.

FDA-regulated drug products require regulatory approval before making packaging changes that might impact the product. The requirements for packaging for biological products, medical devices, parasiticides, and diagnostics are no less problematic in terms of the barriers to simply switch to different packaging. The health and safety reasons for these regulations should be given their appropriate weight.

There is a lengthy lead time for all phases of providing animal health products to veterinarians, livestock producers and pet owners. Discovery, research, regulatory approval or registration, manufacturing and distribution all require long lead times. Without this exemption, our ability to deliver safe and effective animal health products for the treatment and prevention of disease in animals will be threatened.

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