

Public Review Document

## **WHITEPAPER: A Modern Approach to EPA and FDA Product Oversight**

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**Jointly developed by:**

U.S. Environmental Protection Agency's Office of Pesticide Programs  
U.S. Food and Drug Administration's Center of Veterinary Medicine.

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**Public Comments:**

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For further information about the docket and instructions for commenting, please consult the ADDRESSES section in the front of the Federal Register document identified under FRL-10689-01-OCSP.

# WHITEPAPER: A Modern Approach to EPA and FDA Product Oversight

***NOTE:** The following document was jointly developed by the U.S. Environmental Protection Agency and the U.S. Food and Drug Administration. This document does not represent a final agency position or policy but is instead intended to explain the need for a modernized approach to product oversight.*

## **Executive Summary**

EPA and FDA are considering how best to update their respective oversight responsibilities for specific products in an efficient and transparent manner and in alignment with each agency’s expertise. We are considering this, in part, due to changes to the definition of “pesticide” in the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) in the mid-1970s, which excluded new animal drugs from regulation as pesticides under FIFRA. Since that time, pesticide and animal drug technologies—and both agencies’ understanding of these technologies—have evolved. The agencies’ current approach to determining whether EPA or FDA is the appropriate regulator of products incorporating these technologies does not effectively accommodate scientific advancement. Further, scientific advancements and improved scientific understanding have highlighted the importance of increased clarity for regulated entities, robust animal safety evaluations of certain products, and applying consistent regulatory standards to similar types of products. An updated approach clarifying oversight over new and existing products would promote the efficient use of each agency’s expertise, improve regulatory clarity, and better protect human, animal, and environmental health.

## I. Background on current EPA/FDA jurisdictional approach

**Beginning when EPA was formed in 1970, EPA and FDA (in particular, FDA’s Center for Veterinary Medicine but, for ease of reference, “FDA” herein) sought to develop an efficient approach for clarifying areas of potential dual jurisdiction.** In 1971, both agencies entered a memorandum of understanding (MOU) that specified which agency would be the primary regulator for products that, at the time, met the definition of both a “pesticide” under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and a “new animal drug” under the Federal Food, Drug, and Cosmetic Act (FD&C Act). Because manufacturers continued to have concerns about duplicative regulation despite the MOU, FIFRA was amended in 1975 to exclude new animal drugs from the definition of “pesticide” in 7 U.S.C. § 136(u).

Since the mid-1970s, pesticide and drug technologies—and both agencies’ understanding of these technologies—have evolved. Nonetheless, in determining whether EPA or FDA is the appropriate regulator of products incorporating these technologies, the agencies continue to rely on the rationale described in an MOU that was written fifty years ago. An updated approach clarifying oversight over new and existing products would promote the efficient use of each agency’s expertise and provide clarity to the regulated industry and other stakeholders.

## II. Challenges with the current approach

**The current approach does not accommodate scientific advancement in a way that facilitates efficient and transparent alignment of product oversight according to each agency’s mission and expertise.**

Since the 1970s, new technologies have emerged, and our scientific understanding has improved. For example, genetically engineered (“GE”) pest animals, which are gaining interest as a pest control tool, were not envisioned fifty years ago when the original regulatory approach was developed. Further, as scientific understanding has improved, it has become clear that in some cases the current approach has resulted in misalignment between product regulation and the agency best equipped to regulate the product.

**Scientific advances in products administered topically to animals have highlighted the need for robust animal safety evaluation and consistent regulatory standards for these products.** For example, the agencies have historically determined oversight for products topically administered to animals to treat fleas and ticks based on whether the chemical is systemically absorbed into the bloodstream (FDA oversight) or remains on the skin (EPA oversight). Both EPA and FDA have developed different levels of expertise and infrastructure to regulate similar products administered topically to animals, including to evaluate animal safety. This is an inefficient use of government resources. FDA maintains robust animal safety expertise to regulate products administered to animals. Additionally, the agencies operate under different standards for product approval and adverse incident reporting, which may result in the inconsistent regulation and post-market monitoring of similar products.

The agencies now understand that many of these topically administered products regulated by EPA are systemically absorbed into the bloodstream. This improved scientific understanding, combined with the development of novel ingredients, longer-lasting products, and other technological advances, has highlighted additional potential animal safety concerns (supported by new toxicological data and reported adverse incidents). In the past several years, reports of adverse effects on animals associated

with certain EPA-registered products to control fleas and ticks on dogs and cats have garnered public and congressional attention and further highlighted the importance of robust animal safety evaluations. These reports have also raised the question about whether a consistent approach to regulating these types of products would improve animal safety and public confidence in the safety of these products for animals.

**The current approach has hampered the agencies' ability to clearly explain oversight responsibilities, which may be stifling innovation.** Firms sometimes need to contact both agencies before knowing who will regulate their product, which results in uncertainty for both industry and the agencies and may interfere with predictability and enforceability. Additionally, the current approach may stifle innovation by making firms hesitant to invest in product development when they are uncertain how their product will be regulated. As new products are developed and technology continues to evolve, the current regulatory approach last updated in the 1970s is expected to grow more inefficient for the agencies and stakeholders alike.

### III. Benefits of a modernized approach

**Clarifying product oversight based on improved scientific understanding and in alignment with each agency's mission and expertise would help the agencies adapt their approach to better respond to current science and technologies.** Breakthrough technologies, like genome-editing, have created unique opportunities and prompted the development of novel products. Among these products are animals genetically altered for a pesticidal use (e.g., mosquitos genetically engineered to control the mosquito population in the environment).

In 2016, federal agencies, including EPA and FDA, agreed in the National Strategy for Modernizing the Regulatory System for Biotechnology to work to ensure an efficient, transparent, and predictable process for products developed with biotechnology and to clarify regulatory responsibility over genetically engineered insects. Since then, there have been additional efforts spanning multiple administrations, including executive orders and interagency strategies, that call for modernized regulatory approaches to biotechnology (e.g., Coordinated Framework and updates, Executive Orders). Most recently, Executive Order 14081, issued September 12, 2022, directed FDA, EPA, and USDA to improve the clarity and efficiency of the regulatory process for biotechnology products. These efforts underline the need for coordination between the agencies to meet the needs of new and future biotechnologies.

Improved scientific understanding about existing products, like products administered topically to animals, also reinforces the importance of clarifying product oversight to ensure alignment with each agency's mission and expertise. These products frequently contain novel chemicals, use novel technologies, and may be longer-lasting, raising new animal safety questions. For example, reports of serious adverse incidents that may be associated with flea and tick collars have further highlighted the value of a robust program to evaluate and monitor the safety of products administered topically to animals. Therefore, this is an opportune moment to consider how the products the agencies regulate, old and new, align with their expertise and mission and to make changes to improve efficiency.

**To better protect animal health, FDA's expertise and infrastructure could be leveraged to evaluate and monitor the safety of products topically administered to animals.** Both agencies agree that FDA's animal safety evaluation process is best equipped to evaluate and monitor products topically

administered to animals. While EPA considers animal safety for these products, EPA's expertise is in evaluating the efficacy of products intended to control pests and the effects of such products, including effects on the environment. EPA has fewer resources (e.g., staff, expertise, regulatory authorities, adverse incident tracking systems, and funding) than FDA to evaluate animal safety and conduct ongoing post-market monitoring of the safety of these products for animals. In contrast, FDA has more extensive expertise in animal safety with established pre-market evaluation and post-market monitoring infrastructure. FDA also has more robust animal safety data and adverse incident reporting requirements. For these reasons, FDA is currently providing staff resources to help EPA review safety information for certain flea and tick collars.

**Aligning product regulation with each agency's expertise and mission ensures that they are regulated in a manner appropriate to their risks and avoids duplicative resource expenditures by the agencies.**

With respect to these products, FDA's mission is to protect human and animal health. FDA has expertise to evaluate drug claims (i.e., disease claims and structure/function claims), animal safety, and where relevant, food safety. EPA's mission is to protect human health and the environment and EPA has scientific expertise to evaluate products to control pest animals in the environment, and where relevant, food safety for pesticide residues. Maintaining redundant programs at both agencies, such as replicating FDA's robust program to evaluate animal safety at EPA, would require significant resources and expanded adverse incident and safety data regulations and/or guidance for EPA. Alternatively, alignment would reduce the need for the agencies to develop and maintain duplicative expertise and infrastructure.

**A modernized approach would support clear communication with stakeholders, including consumers, veterinarians, and industry, regarding product regulation, safety information, and reporting of adverse incidents.** Improved regulatory certainty would allow industry to plan product development more efficiently and may encourage the introduction of novel and beneficial products into the marketplace (such as genetic modifications in pest animals for population control). It would also help both agencies provide consumers and veterinary health professionals with the safety information they need, ensure adverse incidents are promptly reported to the appropriate regulatory agency, assess risks accurately, and if necessary, take action to protect human and animal health. Applying the current regulatory approach continues to be inefficient for the agencies and stakeholders to accomplish these goals.

#### IV. Elements of a modernized approach

**EPA and FDA have identified two complementary components of a modernized approach.** The first component is one that would provide the agencies with more flexibility to update and align their regulatory oversight of relevant products consistent with each agency's mission and expertise.

The second component is one that would then provide a seamless process for the transfer of oversight from EPA to FDA of topically administered products for external parasites of animals, which are currently regulated as pesticides. Importantly, this component should be designed to be minimally burdensome and not require an FDA approval for products previously regulated by EPA, except in the limited circumstance that products raise serious safety concerns.

Together, these components would facilitate the agencies' ability to proactively communicate with stakeholders and the public about oversight responsibilities and respond swiftly to an evolving scientific and technological landscape.

We recognize that FDA would need significant new resources over the first five years to transfer approximately 600 topically administered products for external parasites on animals currently regulated by EPA to FDA. Conversely, to build a comparable animal safety program to FDA's existing program, EPA would likely need several times more resources than the amount needed for FDA to oversee these products.

Additionally, EPA may need resources to expand its existing biotechnology program for products to control populations of pest animals and clarify the program's approach to meet the needs of this growing industry.

## V. Appendix

### A. Terminology

Use of "pest" within this document refers to a nuisance animal.

Use of "animal" refers to any eukaryotic organism (multicellular), including mammals, birds, amphibians, mollusks, insects, etc. and excluding humans.

Use of "animal safety" refers to the health of the animal being administered the product rather than to the external parasite being killed or repelled.

Use of "topically administered products for animals" refers to topically administered products intended to treat external parasites of animals.

### B. Acronyms

- i. CVM: Center for Veterinary Medicine
- ii. EPA: Environmental Protection Agency
- iii. FD&C Act: Federal Food, Drug, and Cosmetic Act
- iv. FDA: Food and Drug Administration
- v. FIFRA: Federal Insecticide, Fungicide, and Rodenticide Act
- vi. MOU: Memorandum of Understanding
- vii. NADA: New Animal Drug Application
- viii. OTC: Over the counter
- ix. Rx: Prescription

### C. References

- [1971 MOU](#) (last updated 1973)
- [U.S. Coordinated Framework for the Regulation of Biotechnology joint agency webpage](#)
- [Modernizing the Regulatory System for Biotechnology Products: Final Version of the 2017 Update to the Coordinated Framework for the Regulation of Biotechnology](#)
- [National Strategy for Modernizing the Regulatory System for Biotechnology Products](#)
- [Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy](#)

### Legal Definitions

- a) A **drug** is defined, in part, as (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other

than food) intended to affect the structure or any function of the body of man or other animals (21 U.S.C. § 321(g)(1)).

- b) A **new animal drug** is defined, in part, as any drug intended for use in animals other than man, including any drug intended for use in animal feed but not including the animal feed, the composition of which is such that the drug is not generally recognized as safe and effective for the use under the conditions prescribed, recommended, or suggested in the labeling of the drug (21 U.S.C. § 321(v)).
- c) A **pesticide** is defined, in part, as (1) any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest..., except that the term “pesticide” shall not include any article that is a “new animal drug” within the meaning of section 201(w) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 321(w)), that has been determined by the Secretary of Health and Human Services not to be a new animal drug by a regulation establishing conditions of use for the article, or that is an animal feed within the meaning of section 201(x) of such Act (21 U.S.C. § 321(x)) bearing or containing a new animal drug. (7 U.S.C. § 136(u))

#### D. Additional Information about FDA/CVM and EPA regulatory processes

##### *FDA CVM*

A **new animal drug application** (NADA) is used to seek approval of a new animal drug. Before FDA can approve a NADA, sponsors must demonstrate that the drug is:

1. **Safe:** The drug must be safe for the animals given the drug, humans consuming food derived from treated animals and users administering the drug.
2. **Effective:** Substantial evidence of effectiveness of a new animal drug shall demonstrate that the new animal drug is effective for each intended use and associated conditions of use for and under which approval is sought (21 CFR 514.4).
3. **Properly manufactured:** The drug must be manufactured under validated manufacturing processes in accordance with Good Manufacturing Practice regulations (21 CFR Part 200).
4. **Properly labeled:** The drug must be labeled such that it is not false or misleading (Section 502(a)) and must contain adequate directions for use (Section 502(f)(1)) to inform users how to use and store the drug safely and effectively and adhere to residue withdrawal procedures.

**Following approval of a new animal drug**, sponsors must submit to FDA reports of adverse drug events (referred to as “adverse incidents” throughout this document), product defects/manufacturing defects, periodic drug experience reports (annually or semi-annually in a specific format), and other submissions and reports as applicable (21 CFR 514.80). In addition, establishment registration and drug listing are required.

Continuous monitoring of approved NADAs and Abbreviated NADAs throughout a drug’s lifecycle ensures that FDA obtains information regarding potential problems with the safety and effectiveness of marketed animal drugs and potential product quality issues/manufacturing problems.

##### **Prescription (Rx) vs. Over the Counter (OTC):**

Labeling must contain adequate directions for use, defined as directions under which the layman can use a drug safely and for the purposes for which it is intended (21 CFR 201.5).

Veterinary drugs are exempt from adequate directions for use when such directions cannot be written and when the veterinary drug bears the prescription legend (21 CFR 201.105).

Thus, the primary basis for distinguishing Rx and OTC animal drug products is the ability (or lack of ability in the case of Rx products) to prepare adequate directions for use that would allow persons other than licensed veterinarians to use the product safely and effectively. Under the FD&C Act Section 503(f)(1) (21 U.S.C. § 352(f)(1)), an animal drug that “because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary for its use, is not safe for animal use except under the professional supervision of a licensed veterinarian” is limited to use by or on the order of a licensed veterinarian.

#### *EPA*

Before manufacturers can sell or distribute pesticides in the United States, EPA must evaluate the pesticides thoroughly to ensure that they meet the federal standard for registration under FIFRA. For a pesticide to be approved for registration, EPA must determine that it will not cause any unreasonable adverse effects on the environment, including “water, air, land, and all plants, animals, and people living therein.” (7 U.S.C. § 136(j), (bb)).

In evaluating a pesticide registration application, EPA assesses a wide variety of potential human health and environmental effects associated with use of the product. Companies must generate scientific data necessary to address concerns pertaining to the identity, composition, potential adverse effects, and environmental fate of each pesticide. Data requirements for pesticides are listed in 40 CFR Part 158. The purpose of these data requirements is to demonstrate that the product will not cause unreasonable adverse effects to the environment (including to humans and animals). In the case of pesticide products intended for use on food, EPA relies on these data to determine whether there is a reasonable certainty of no harm to human health from aggregate exposure to these products.

After a product is registered, the pesticide registrant must report any adverse incidents associated with the product to EPA per FIFRA Section 6(a)(2). EPA defines an adverse incident as any exposure or effect from a pesticide’s use that is not expected or intended. Adverse incidents may involve humans, wildlife, plants, or domestic animals. Adverse incident reports tell EPA if there are problems with a pesticide and help EPA determine whether the pesticide’s application directions need to be clarified, restrictions need to be placed on the pesticide’s use, and/or if additional protective safety equipment may be needed.

#### **General Use vs. Restricted Use Pesticides (RUPs):**

General Use Pesticides are typically available for sale to and use by the general public. Restricted Use Pesticides are not available for purchase or use by the general public, as they have the potential to cause unreasonable adverse effects to the environment and injury to applicators or bystanders without added restrictions. The “Restricted Use” classification restricts a product, or its uses, to use by a certified applicator or someone under the certified applicator’s direct supervision (40 CFR 152.160-152.175). Certified applicators are trained in the safe application and use of RUPs. Most pesticide products are not Restricted Use Pesticides, including almost all products topically administered to animals and GE pest animals.