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FDA Proposes to Overhaul Labeling Requirements for Approved or Conditionally Approved New Animal Drugs

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Last updated in 1975, the Food and Drug Administration (FDA) has published a proposed rule revising its labeling requirements for prescription and over-the-counter (OTC) new animal drugs, as well as new animal drugs for use in animal feeds. The proposed rule, published on March 12, 2024, comes with several new requirements that will impact the industry if finalized.

The FDA intends the proposed rule "to provide consistent formatting of new animal drug labeling" and cites several issues as the impetus of these proposed rules—chief among them that the Code of Federal Regulations (C.F.R.) does not currently include a comprehensive set of regulations that set forth requirements for the content and format of labeling of new animal drugs, resulting in an inefficient label review and approval process. According to the agency, its proposal to standardize labeling content and format is intended to make it easier for veterinarians, animal owners, or persons treating animals to use the information to make informed decisions quickly.

Key Requirements

The FDA proposes the creation of a new Subpart H in 21 C.F.R. Part 201. The existing labeling regulations for new animal drugs would be updated, moved, and incorporated into the new proposed regulations.

Proposed Section 201.401 – Scope

The proposed rule revises existing labeling requirements for prescription new animal drugs, OTC new animal drugs, and new animal drugs for use in animal feeds that are subject to 21 C.F.R. Part 558, including veterinary feed directive drugs. The proposed rule does not apply to: (1) legally marketed unapproved new animal drugs for minor species that are indexed in accordance with Section 572 of the Federal Food, Drug, and Cosmetic Act (FDCA); (2) the labeling of heritable intentional genomic alterations in animals; or (3) to promotional labeling or advertising.

Proposed Section 201.403 – Definitions

The proposed rule lists several terms that would have the same definition as those already in the FDCA or elsewhere in regulation.

- Under the proposed rule, prescription new animal drugs would be required to provide a labeling component that includes "full prescribing information." The proposed rule would define the term as "all information necessary for the safe and effective use of a Rx new animal drug." The FDA states that it would base the definition on the requirements for full prescribing information for prescription human drugs and biologics established in 21 C.F.R. § 201.57(c).
- Similarly, all approved or conditionally approved OTC new animal drugs would be required to provide a labeling component that includes "full product information." The proposed definition of the term is "all information necessary for the safe and effective use of an OTC new animal drug." However, the proposed rule would also establish content and format requirements for labels of OTC animal drugs that do not provide full product information, for example, for an approved OTC drug with a small label that the FDA determines lacks sufficient space to comply with the requirement.
- The proposed rule contains several other proposed definitions for terms used in the general requirements proposed regulations. A few examples of the proposed defined terms include "environmental warning," "target animal," "residue warning statement," and "field study."

Proposed Section 201.404 – General requirements

The proposed rule would require the labeling for animal drugs to conform to an application approved or conditionally approved under the FDCA. A few key takeaways:

- This proposed section would require that the labeling be updated if new information becomes available to cause the labeling to be inaccurate, false, or misleading.
- Proposed Section 201.404(e) provides direction for situations when it may be ambiguous how a requirement in proposed Subpart H applies to a particular new animal drug or whether it applies at all. For instance, for small labels for prescription new animal drugs, the "FDA will make the final determination as to whether an immediate container lacks sufficient space for the label to include all of the information" required by the proposed rule.
- Proposed Section 201.404(g) establishes general formatting requirements. For example, the proposed rule provides specific requirements related to the "placement, size, and prominence of the established name relative to the proprietary name" on the labeling for OTC new animal drugs or new animal drugs for use in animal feeds.

Proposed Section 201.405 – Content and format for prescription new animal drug labeling

All approved or conditionally approved prescription new animal drugs would be required to provide a labeling component that includes full prescribing information. For example, the proposed rule includes various options to present the "Indications for Use" section on the label for a prescription new animal drug, depending on the size of the label. If the most appropriate option is unclear, the proposal clarifies that the FDA would make the final determination. The proposed rule also outlines content requirements for several labeling components, including package inserts, secondary containers, and shipping labeling.

Proposed Section 201.407 – Content and format for OTC new animal drug labeling

Comprehensive content and format requirements are established in this section. For example, all approved and conditionally approved OTC new animal drugs would be required to provide a labeling component that includes full product information. Similar in concept to full prescribing information for prescription animal drugs, the proposal for OTC animal drugs contains content requirements for several labeling components, including package inserts, secondary containers, and shipping labeling.

Importantly, the proposed rule draws a distinction between what is required to be included under the "Animal Safety Warnings" subsections for OTC new animal drugs from the similar "Animal Safety Warnings and Precautions" subsection proposed for prescription animal drugs. "Precautions" are typically associated with professional veterinarian care, while OTC animal drugs are intended to be used by laypersons. The FDA proposes that what would be considered "precautions" are not to be included under the subsection "Animal Safety Warnings." Instead, any such recommendations targeted to the layperson would be included in a separate section called "Additional Recommendations" for OTC animal drugs.

Proposed Section 201.409 – Content and format of labeling for new animal drugs for use in animal feeds

This proposed section provides content and format requirements for labeling components for new animal drugs intended for use in animal feeds, including VFD drugs. The content and format requirements in the proposed rule vary depending on the type of animal feed product. Specifically, the proposal identifies information that would be required to be included on approved labeling for Type A medicated articles, Type B medicated feed labels, and Type C medicated feeds.

Proposed Section 201.411 – Exemptions from labeling requirements for approved or conditionally approved new animal drugs

The FDA's proposal includes an opportunity for sponsors to "request an exemption from one or more specific requirements … on the basis that the requirements are not appropriate for the specific approved or conditionally approved new animal drug." Under the proposed rule, the exemption request would need to be submitted to the corresponding application or investigational new animal drug file (INAD) for the new animal drug. The proposed rule contains instructions for sponsors seeking exemptions. However, the FDA states that it "anticipate[s] that such exemptions would be rare."

Proposed Section 201.413 – Labeling requirements for certain approved or conditionally approved new animal drugs

This section consolidates and updates existing labeling requirements for certain approved or conditionally approved new animal drugs. New requirements include a provision containing new labeling requirements for all new animal drugs approved or conditionally approved for use in horses and anthelmintic new animal drugs for certain species.

Compliance schedule

The proposed rule, if finalized, would require sponsors of new animal drugs to comply with the new requirements on a staggered schedule, within six years of the effective date of the final rule. The schedule is staggered based on application numbers, "with approved NADAs with higher application numbers having the earliest

compliance date because they are more recently approved and therefore likely to need the fewest labeling revisions." Proposed Section 201.404(a)(4) provides the proposed compliance schedule contained within Table 1 that would apply to animal drug sponsors that would have to comply with the earliest applicable compliance date unless specific exemptions apply. The table outlining the range of new animal drug application (NADA) numbers in the proposed compliance schedule will be updated in a final rule.

The table proposes the following compliance dates for the submission of conforming labeling to the FDA:

- **On submission:** For NADAs, new animal drug applications for conditional approval (CNADA), or a supplement to a NADA or CNADA subject to 21 C.F.R. § 514.8(c)(2) that would be submitted 180 days after the effective date of the final rule, sponsors would have to submit conforming labeling as part of the application or supplemental application to the FDA.
- **180 days after approval date:** For a NADA, CNADA, or supplement to either a NADA or CNADA subject to 21 C.F.R. § 514.8(c)(2) that is pending on the effective date of the final rule or submitted within 180 days of the effective date, sponsors would have to submit all conforming labeling to the FDA as part of the application and supplemental application or as a supplement to an approved application no later than 180 days after the approval date of the application or supplemental application.
- **1–2 years after the effective date of the final rule:** For NADA number 141-300 or greater, and originally approved before the effective date of the final rule, or an abbreviated NADA (ANADA) that references a NADA subject to certain criteria, sponsors would have to submit all conforming labeling as a supplement to an approved application between one and two years after the effective date of the final rule.
- **2–3 years after the effective date of the final rule:** For NADA numbers 141-000 to 141-299, sponsors would have to submit all conforming labeling as a supplement to an approved application between two and three years after the effective date of the final rule.
- **3–4 years after the effective date of the final rule:** For NADA numbers 115-000 to 140-999, sponsors would have to submit all conforming labeling as a supplement to an approved application between three and four years after the effective date of the final rule.
- **4–5 years after the effective date of the final rule:** For NADA numbers 45-000 to 114-999, sponsors would have to submit all conforming labeling as a supplement to an approved application between four and five years after the effective date of the final rule.
- **5–6 years after the effective date of the final rule:** For NADA numbers 1 to 44-999, sponsors would have to submit all conforming labeling as a supplement to an approved application between five and six years after the effective date of the final rule.

If finalized, the proposed rule would deem any approved or conditionally approved new animal drug that is noncompliant with the applicable requirements in accordance with the compliance schedule to be misbranded under Section 502 of the FDCA.

Next Steps

The FDA's revamp of the animal drug labeling format and content is going to be a significant undertaking for both the agency and animal drug sponsors. Every interested stakeholder in the FDA's proposed rule on Labeling Requirements for Approved or Conditionally Approved New Animal Drugs should consider taking these two

immediate next steps:

1. **Evaluate animal drug product labels now for compliance with the proposed rule:** The FDA has indicated that implementation would be staggered, depending on the category of applications. Given that the evaluation of product labels and the updating of labels takes a significant amount of time, it is prudent to start evaluating whether products would comply with the proposed requirements, anticipating compliance dates, and monitoring for changes that may appear in the final rule.
2. **Consider commenting on the proposed rule through legal counsel or trade organizations:** Considering the depth and breadth of this proposed rule, from content requirements to required styles and fonts to be used for labeling, industry has an opportunity to provide the agency with additional information or considerations as it moves toward finalizing the rule. The deadline for the submission of comments is June 10, 2024.

Alston & Bird's FDA Team, which provides both regulatory and compliance services to our clients, will continue to monitor developments related to the proposed rule.

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