

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

#### 21 CFR Parts 201, 500, 501, 510, 514, and 516

[Docket No. FDA-2023-N-5160]

RIN 0910-AI43

#### Labeling Requirements for Approved or Conditionally Approved New Animal Drugs

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Proposed rule.

**SUMMARY:** The Food and Drug Administration (FDA) is proposing to revise the requirements for the content and format of labeling for approved or conditionally approved new animal drugs to provide for a more comprehensive set of requirements in one location in the Code of the **Federal Register** (CFR). As part of this revision, certain current requirements would be updated and moved, and certain obsolete requirements would be removed. The proposed requirements would apply to the labeling of prescription and over-the-counter (OTC) new animal drugs, as well as new animal drugs for use in animal feeds.

**DATES:** Either electronic or written comments on the proposed rule must be submitted by June 10, 2024. Submit written comments (including recommendations) on information collection issues under the Paperwork Reduction Act of 1995 by April 11, 2024.

**ADDRESSES:** You may submit comments as follows. Please note that late, untimely filed comments will not be considered. The <https://www.regulations.gov> electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of June 10, 2024. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are received on or before that date.

#### Electronic Submissions

Submit electronic comments in the following way:

- **Federal eRulemaking Portal:** <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your

comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

#### Written/Paper Submissions

Submit written/paper submissions as follows:

- **Mail/Hand Delivery/Courier (for written/paper submissions):** Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

**Instructions:** All submissions received must include the Docket No. FDA-2023-N-5160 for "Labeling Requirements for Approved or Conditionally Approved New Animal Drugs." Received comments, those filed in a timely manner (see **ADDRESSES**), will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- **Confidential Submissions—**To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management

Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

**Docket:** For access to the docket to read background documents, the plain language summary of the proposed rule of not more than 100 words are required by the "Providing Accountability Through Transparency Act," or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

Submit comments on information collection issues under the Paperwork Reduction Act of 1995 to the Office of Management and Budget (OMB) <https://www.reginfo.gov/public/do/PRAMain>. Find this particular information collection by selecting "Currently under Review—Open for Public Comments" or by using the search function. The title of this proposed collection is "Labeling Requirements for Approved or Conditionally Approved New Animal Drugs."

#### FOR FURTHER INFORMATION CONTACT:

*With regard to the proposed rule:* Suzanne Sechen, Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 240-402-0814, [Suzanne.Sechen@fda.hhs.gov](mailto:Suzanne.Sechen@fda.hhs.gov).

*With regard to the information collection:* Amber Sanford, Office of Operations, Food and Drug Administration, Three White Flint North, 10A-12M, 11601 Landsdown St., North Bethesda, MD 20852, 301-796-8867, [PRAMain@fda.hhs.gov](mailto:PRAMain@fda.hhs.gov).

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## I. Executive Summary

### A. Purpose and Coverage of the Proposed Rule

FDA proposes to revise the existing regulations regarding the content and format of labeling for approved or conditionally approved new animal drugs. These proposed regulations would apply to the labeling of prescription and OTC new animal drugs, as well as new animal drugs for use in animal feeds. Certain existing regulations regarding the labeling of new animal drugs would be updated and moved from their current location and incorporated into the proposed regulations, including a new subpart H in part 201 (21 CFR part 201). FDA also proposes to amend or remove certain current regulations to ensure consistency with the proposed regulations.

Proposed subpart H would not apply to heritable intentional genomic alterations in animals. Proposed subpart H would also not apply to labeling of indexed legally marketed unapproved new animal drugs for minor species. In addition, proposed subpart H would not apply to promotional labeling or advertising.

### B. Summary of the Major Provisions of the Proposed Rule

The proposed rule would revise the existing requirements for the content and format of labeling for approved or conditionally approved new animal drugs. If finalized, sponsors of these new animal drugs would need to comply with these proposed regulations on a staggered schedule, over the course of 6 years, according to a schedule based on application number, 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.

If finalized, this rule would enable FDA to provide sponsors with predictable requirements for the content and format of labeling for new animal drugs and codify FDA's longstanding practices with respect to the review of labeling submitted as part of a new animal drug application (NADA), certain abbreviated new animal drug applications (ANADAs) that reference a new animal drug for which the NADA has been withdrawn, or a new animal drug application for conditional approval (CNADA).

Currently a comprehensive set of regulations establishing labeling requirements for the content and format of labeling for new animal drugs does not exist in the CFR. These proposed regulations would provide sponsors with predictable requirements for the content and format of labeling for new animal drugs. Also, these proposed regulations would help sponsors more efficiently prepare labeling for new animal drugs to be submitted as part of an NADA, CNADA, or certain ANADAs by providing clear and consistent requirements for the information that would need to be included on each component of labeling for a new animal drug, as well as the format in which the information is to be presented.

FDA is proposing specific requirements for content and format of the labeling for approved or conditionally approved prescription and OTC new animal drugs, as well as approved or conditionally approved new animal drugs for use in animal feeds.

The proposed regulations would provide the following:

- The content and format of labeling components applicable to approved or conditionally approved new animal drugs.
- Definitions of labeling terms for approved or conditionally approved new animal drugs.
- A schedule for sponsors of approved or conditionally approved and

marketed new animal drugs to comply with these proposed regulations within a maximum of 6 years from the effective date of any final rule.

- Provisions for foreign language translation of the labeling for approved or conditionally approved new animal drugs.
- A process for sponsors of new animal drugs to request exemptions from the proposed labeling requirements.
- Consolidation of the labeling requirements for the content and format of labeling for approved or conditionally approved new animal drugs into one section of the regulations. At present, existing requirements are dispersed throughout the regulations.

### C. Legal Authority

FDA's revisions to the content and format requirements for animal drug labeling are authorized by various provisions of the Federal Food, Drug, and Cosmetic Act (FD&C Act). The premarket approval provisions of the FD&C Act authorize FDA to require that new animal drug labeling provide adequate information to permit safe and effective use of the drug.

The FD&C Act requires certain information be included on a drug's label and provides for certain exemptions from these requirements. Also, the FD&C Act authorizes FDA to establish additional exemptions by regulation.

The FD&C Act requires that new animal drug applications include specimens of the labeling proposed to be used for the drug. A new animal drug will be deemed unsafe if its labeling fails to conform to the approved labeling in the applicable approved new animal drug application, conditionally approved new animal drug application, or new animal drug index listing. Unsafe drugs are deemed adulterated under the provisions of the FD&C Act. The FD&C Act prohibits the marketing of drugs that are adulterated or misbranded as well as their adulteration or misbranding while in interstate commerce.

In addition to the other statutory provisions described above, the FD&C Act gives the FDA general rulemaking authority to issue regulations for the efficient enforcement of the FD&C Act.

### D. Costs and Benefits

If this proposed rule is finalized, industry and FDA would incur cost savings from a reduction in the quantity and time burden of new animal drug labeling amendments and informal communications related to new animal drug labeling. There may be additional

benefits to users of approved or conditionally approved new animal drugs from greater predictability and ease of reading new animal drug labeling in the form of time saved searching for content, as well as benefits to animal or human health, which we are unable to quantify.

We expect that new animal drug sponsors would incur one-time costs to read and understand the rule, revise

standard operating procedures (SOPs) related to labeling, and train employees on the revised SOPs. New animal drug sponsors would also bear costs to update labeling and prepare supplemental labeling applications to conform to the proposed requirements. FDA would incur costs to review these supplemental applications.

FDA estimates that the annualized benefits over 10 years would range from

\$0.143 million to \$0.243 million at a 2 percent discount rate, with a primary estimate of \$0.193 million. The annualized costs would range from \$2.16 million to \$2.77 million at a 2 percent discount rate, with a primary estimate of \$2.45 million.

**II. Table of Abbreviations/Commonly Used Acronyms in This Document**

Abbreviation/acronym	What it means
ADAA .....	Animal Drug Availability Act.
ANADA .....	Abbreviated New Animal Drug Application
CFR .....	Code of Federal Regulations.
CNADA .....	Conditionally Approved New Animal Drug Application.
FD&C Act .....	Federal Food, Drug, and Cosmetic Act.
FDA .....	Food and Drug Administration.
FR .....	Federal Register.
HHS .....	Health and Human Services.
INAD .....	Investigational New Animal Drug.
MUMS .....	Minor Use Minor Species.
NADA .....	New Animal Drug Application.
NDC .....	National Drug Code.
NEPA .....	National Environmental Policy Act.
OMB .....	Office of Management and Budget.
OTC .....	Over-the-counter.
PCBs .....	Polychlorinated biphenyls.
PRA .....	Paperwork Reduction Act of 1995.
RLNAD .....	Reference-Listed New Animal Drug.
Rx .....	Prescription.
U.S. ....	United States.
U.S.C. ....	United States Code.
VFD .....	Veterinary Feed Directive.
VMF .....	Veterinary Master File.

**III. Background**

*A. Introduction*

In accordance with the definition in section 201(k) of the FD&C Act (21 U.S.C. 321(k)) the “label” is a display of written, printed, or graphic matter upon the immediate container of any article. Under section 201(m) of the FD&C Act, the term “labeling” means “all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article.” Labeling, therefore, includes the label of any article, including new animal drugs.

Under existing regulations, proposed labeling must be included as part of an application filed with FDA for approval of a new animal drug, in accordance with section 512(b)(1)(F) of the FD&C Act (21 U.S.C. 360b(b)(1)(F)). Labeling for nonprescription, known as over-the-counter (OTC), new animal drugs should include adequate directions for use by the layperson under all conditions of use for which the new animal drug is intended, recommended, or suggested in any of the labeling or advertising sponsored by the applicant (see § 514.1(b)(3)(ii) (21 CFR 514.1(b)(3)(ii)). Labeling for prescription

new animal drugs should bear adequate information for use under which veterinarians can use the new animal drug safely and for the purposes for which it is intended, including those purposes for which it is to be advertised or represented, in accordance with § 201.105 (21 CFR 201.105) (see § 514.1(b)(3)(iii)). All labeling for prescription or OTC new animal drugs must provide any necessary use restrictions prominently and conspicuously displayed (see § 514.1(b)(3)(iv)).

Labeling for new animal drugs intended for use in the manufacture of medicated feeds must include: (1) specimens of labeling to be used for such new animal drug with adequate directions for the manufacture and use of finished feeds for all conditions for which the new animal drug is intended, recommended, or suggested in any of the labeling, including advertising, sponsored by the applicant; and (2) representative labeling proposed to be used for Type B and Type C medicated feeds containing the new animal drug (see § 514.1(b)(3)(v)). Sponsors of new animal drug applications commit to providing labeling for the new animal drug that prescribes, recommends, or

suggests its use only under the conditions stated in the labeling included as part of the application (see § 514.1(b)(11)). All representations of labeling in the application apply to the new animal drug produced until changes are made in conformity with § 514.8 (21 CFR 514.8) (see § 514.1(b)(11)).

Sponsors of new animal drug applications may submit draft labeling for FDA’s preliminary consideration of an application (see § 514.1(b)(3)(vi)). For example, sponsors sometimes include draft labeling content pertinent to key components of an application that are submitted for preliminary FDA review (e.g., manufacturing components and composition, evidence to establish safety and effectiveness, and environmental assessment).

Under section 502(a)(1) of the FD&C Act (21 U.S.C. 352(a)(1)), a drug shall be deemed to be misbranded if its labeling is false or misleading in any particular. A new animal drug for which an approval or conditional approval is in effect will be considered unsafe if its labeling fails to conform to the approved or conditionally approved application (section 512(a)(1)(A) and (B) of the FD&C Act).

### B. Need for the Regulation

Based on FDA's experience in reviewing labeling for approved or conditionally approved prescription new animal drugs and informal feedback from sponsors of such new animal drugs in the past 60 years, it has become clear that sponsors would benefit from having more detailed requirements on the content, format, and order of information on labeling so that they can efficiently prepare adequate labeling for approved or conditionally approved prescription new animal drugs to be submitted as part of an NADA, CNADA, or certain ANADAs that reference a new animal drug for which the NADA has been withdrawn.

For example, existing § 201.105(c) provides requirements for labeling "on or within the package" from which prescription animal drugs are dispensed, and paragraph (d) of that section provides requirements for all labeling for prescription new animal drugs. Labeling for prescription new animal drugs typically consists of multiple components, such as the label, one or more package inserts, secondary container labeling, multiple unit carton labeling, shipping labeling, and/or display carton labeling. However, neither paragraph (c) nor (d) of § 201.105 provides direction on the format or order of information with respect to specific labeling components. Furthermore, it is not clear whether the information required by paragraph (d) of § 201.105 needs to be presented on all components of labeling for prescription new animal drugs, or if not, what critical information needs to be provided on specific labeling components, particularly smaller components of limited size.

Whereas existing § 201.105 provides at least some requirements for the content of labeling for prescription new animal drugs, there are currently no regulations that provide requirements for the general content and format of labeling for OTC new animal drugs and new animal drugs administered in animal feeds.

The lack of direction regarding format and content for each component of labeling has resulted in confusion for sponsors as they prepare labeling for FDA's review and sometimes results in poor quality labeling submissions. Poor quality labeling submissions increase the time needed by sponsors to revise and resubmit adequate labeling, and they increase time needed by FDA to review and approve labeling, and consequently, the application.

New animal drug labeling that presents information in an inconsistent manner can contribute to medication errors by making it difficult for veterinarians and animal owners to readily locate and understand critical directions and safety information. Information in the labeling for approved or conditionally approved new animal drugs presented in a consistent manner communicates information that is important to the safe use of a new animal drug in the medication use process (*i.e.*, from prescription, to procurement, preparation, and dispensing and administration of the medication to the animal).

Other regulations specifically pertaining to the labeling of certain new animal drugs include § 500.25 (21 CFR 500.25), "Anthelmintic drugs for use in animals," § 500.55 (21 CFR 500.55), "Exemption from certain drug-labeling requirements," § 510.105 (21 CFR 510.105), "Labeling of drugs for use in milk-producing animals," § 510.106 (21 CFR 510.106), "Labeling of antibiotic and antibiotic-containing drugs intended for use in milk-producing animals," and § 510.410 (21 CFR 510.410), "Corticosteroids for oral, injectable, and ophthalmic use in animals; warnings and labeling requirements."

The proposed rule would locate the labeling requirements for "Anthelmintic drugs for use in animals," currently in § 500.25, with other labeling requirements for new animal drugs.

The proposed rule would remove the exemption in § 500.55, "Exemption from certain drug-labeling requirements," because we believe that full disclosure labeling is needed for all prescription new animal drugs to ensure veterinarians are able to use these products safely and effectively.

In addition, the proposed rule would remove the labeling requirements in § 510.105, "Labeling of drugs for use in milk-producing animals," and § 510.106, "Labeling of antibiotic and antibiotic-containing drugs intended for use in milk-producing animals." The labeling requirements in these regulations do not provide adequate flexibility for targeted and informative statements with respect to human food safety warnings, including milk discard times, withdrawal periods, and residue warning statements for the labeling of new animal drugs intended for use in milk-producing animals.

Section 510.410, "Corticosteroids for oral, injectable, and ophthalmic use in animals; warnings and labeling requirements," contains background information and warning and labeling requirements for this category of new

animal drugs. We propose a conforming amendment to remove § 510.410 and to move portions of that section to be located with the other labeling requirements for new animal drugs.

### C. FDA's Current Regulatory Framework

Current § 201.105 provides conditions that must be met for exempting prescription animal drugs from section 502(f)(1) of the FD&C Act, which requires the labeling to bear adequate directions for use. Section 201.105(b) requires the following information to appear on the label for prescription animal drugs for such products to be exempt from section 502(f)(1) of the FD&C Act:

- a standard statement restricting use to or on the order of a licensed veterinarian,
- dosage,
- route of administration if it is not oral,
- quantity or proportion of each active ingredient as well as information required, in accordance with section 502(e) of the FD&C Act,
- names of inactive ingredients if the drug is for other than oral use (with some exemptions), and
- an identifying lot or control number.

For containers too small or otherwise unable to fit a label with enough space to display all the required information, § 201.105(b) allows eliminating some information from these labels and placing it on other approved labeling.

Labeling for prescription new animal drugs must bear adequate information for use, including indications, effects, dosages, routes, methods, and frequency and duration of administration; any relevant warnings, hazards, contraindications, side effects, and precautions under which veterinarians can use the drug safely and for the intended purposes; and ingredient information as required for the label (see § 201.105(c) through (e)). All prescription animal drug labeling, except for labels and cartons, must bear the issuance dates of the latest revisions of such labeling (see § 201.105(e)). Applicants may submit a written request to the Commissioner of Food and Drugs for an exemption from inclusion of adequate information for use required in § 201.105(c)(1) from the dispensing package of prescription new animal drugs for which directions, hazards, warnings, and use information are commonly known to licensed veterinarians (see § 201.105(c)(2)).

A prescription drug intended for both human and veterinary use must comply with paragraphs (e) and (f) of § 201.105, in addition to § 201.100, which provides

requirements for prescription drugs for human use (see § 201.105(f)).

#### *D. History of the Rulemaking*

In 1955, FDA issued regulations at § 1.106(c) establishing requirements primarily for the label of prescription animal drugs (20 FR 9525 at 9533, December 20, 1955). The initial requirements were expanded in 1960 to cover the labeling of such drugs more fully (25 FR 12592, December 9, 1960). As part of FDA's reorganization of its regulations, in 1975 § 1.106(c) was redesignated as § 201.105 (40 FR 13494 at 13496, March 27, 1975). Most provisions in current § 201.105 are similar to the 1960 version of § 1.106(c).

#### **IV. Legal Authority**

FDA's revisions to the content and format requirements for animal drug labeling are authorized by various provisions of the FD&C Act, including sections 201, 301, 501, 502, 503, 504, 512, 571, and 701 (21 U.S.C. 321, 331, 351, 352, 353, 354, 360b, 360ccc, and 371). Section 201 contains definitions relevant to the proposed content and format requirements, including for the terms "label" and "labeling". Pursuant to section 201(k) of the FD&C Act, the term "label" means "a display of written, printed, or graphic matter upon the immediate container of any article." That provision requires that any words, statements, or other information appearing on the label also appear on the outside container or wrapper of the retail package, or be easily legible through the outside container or wrapper. Section 201(m) of the FD&C Act defines "labeling" to mean "all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article."

Section 301 of the FD&C Act prohibits the marketing of drugs that are adulterated or misbranded as well as their adulteration or misbranding while in interstate commerce. Section 501(a)(5) of the FD&C Act deems a new animal drug to be adulterated if it is unsafe within the meaning of section 512 of the FD&C Act. Under section 512 of the FD&C Act, a new animal drug will be deemed unsafe if its labeling fails to conform to the applicable approved application under section 512 of the FD&C Act, conditionally approved application under section 571 of the FD&C Act, or index listing under section 572 of the FD&C Act (21 U.S.C. 360ccc-1).

Section 502 of the FD&C Act specifies conditions that cause a drug to be misbranded. Under section 502(a) of the FD&C Act, a drug is deemed to be

misbranded if its labeling is false or misleading "in any particular." Section 201(n) of the FD&C Act deems a product's labeling misleading if it fails to reveal facts regarding the consequences that may result from using the article under the conditions of use prescribed in the labeling or under such conditions of use as are customary or usual. Under section 502(b) of the FD&C Act, a drug in package form is deemed to be misbranded unless its label bears the name and place of business of the manufacturer, packer, or distributor, and it contains an accurate statement of the quantity of the contents in terms of weight, measure, or numerical count. Section 502(c) of the FD&C Act, deems a drug misbranded if any word, statement, or other information required by law or regulation to be included on the label or labeling does not appear with such prominence and conspicuousness, and in such terms, that it is likely to be read and understood by ordinary individuals under customary conditions of purchase and use.

Section 502(e) of the FD&C Act specifies requirements for including the established name of the drug and for listing the active and inactive ingredients on the drug's label. It also provides for certain exemptions from the requirement to list active and inactive ingredients and authorizes the Secretary to establish additional exemptions from some of the requirements in section 502(e) by promulgating regulations where compliance would be impracticable.

Section 502(f) of the FD&C Act deems a drug to be misbranded if its labeling lacks adequate directions for use and adequate warnings against use in those pathological conditions where its use may be dangerous to health, as well as adequate warnings against unsafe dosage or methods or duration of administration or application, in such manner and form, as are necessary for the protection of users.

Section 502(j) of the FD&C Act deems a drug to be misbranded if it is dangerous to health when used in the dosage or manner, or with the frequency or duration, prescribed, recommended, or suggested in its labeling.

Under section 502(w)(1) of the FD&C Act, a new animal drug that has been conditionally approved is deemed to be misbranded if its labeling fails to conform with the approved application or fails to include the labeling information required under section 571(f) of the FD&C Act. Section 571(f) requires the label and labeling of a new animal drug with a conditional approval to contain the statement "conditionally

approved by FDA pending a full demonstration of effectiveness under application number," in addition to other information as required by the Secretary. Effective September 30, 2023, section 502(w)(3) requires the labeling of new animal drugs that have received approval under section 512 of the FD&C Act to include the application number in the format "Approved by FDA under (A)NADA # xxx-xxx."

Section 503(f) of the FD&C Act provides certain labeling requirements specific to prescription animal drugs, including a required cautionary statement. Section 503(f)(2) exempts prescription animal drugs from having to comply with some of the requirements in section 502 of the FD&C Act, including the requirement for there to be adequate directions for use (section 502(f)), provided certain dispensing and labeling requirements specified in section 503(f) are met.

Section 504 of the FD&C Act authorizes the Secretary to issue regulations specific to veterinary feed directive (VFD) drugs for use in or on animal feed, including regulations prescribing a cautionary statement and other information to be included on the labeling of VFD drugs and animal feed containing such drugs. Under section 504(b), VFD drugs and feed containing such drugs will be deemed to be misbranded if their labeling fails to include such required information.

In addition, the premarket approval provisions of the FD&C Act authorize FDA to require that animal drug labeling provide adequate information to permit safe and effective use of the drug. Under section 512 of the FD&C Act, FDA will approve a NADA only if the drug is shown to be both safe and effective under the conditions of use set forth in the drug's labeling. Under section 571 of the FD&C Act, FDA will conditionally approve a new animal drug application (CNADA) only if the drug is shown to be safe, and there is a reasonable expectation of effectiveness for use, under the conditions of use set forth in the drug's labeling. Section 512(b)(1)(F) of the FD&C Act requires that the application for approval of a new animal drug include specimens of the labeling proposed to be used for the drug. A new animal drug that has been approved or conditionally approved by FDA will be deemed to be unsafe (and therefore adulterated under section 501(a)(5) of the FD&C Act) if its labeling does not conform to its approved application.

In addition to the other statutory provisions described above, section 701(a) of the FD&C Act gives the Secretary general rulemaking authority

to issue regulations for the efficient enforcement of the FD&C Act.

FDA has previously issued implementing regulations governing the format and content of labeling for animal drugs. This proposed rule, when finalized, would revise the content and format of labeling requirements applicable to approved and conditionally approved new animal drugs and would consolidate these requirements in subpart H of part 201.

## V. Description of the Proposed Rule

FDA proposes to add subpart H to part 201 (hereafter called proposed subpart H) to revise the existing requirements for the content and format of labeling for approved or conditionally approved new animal drugs. Proposed subpart H would be titled “Labeling Requirements for Approved or Conditionally Approved New Animal Drugs” and would apply to new animal drugs that are approved under section 512 of the FD&C Act or conditionally approved under section 571 of the FD&C Act. These regulations would not apply to legally marketed unapproved new animal drugs for minor species that are indexed in accordance with section 572 of the FD&C Act. These regulations would not apply to the labeling of heritable intentional genomic alterations in animals, or to promotional labeling or advertising.

Sponsors of approved or conditionally approved and marketed new animal drugs would need to comply with these requirements per the schedule in proposed § 201.404(a)(4), (b), (c), or (d). Consistent with current practice, we expect that sponsors of new animal drugs that are the subject of an ANADA approved or submitted pursuant to section 512(n) of the FD&C Act (*i.e.*, a generic new animal drug) will submit a supplemental application to their ANADA to conform the labeling of their generic new animal drugs with the revised labeling of the reference-listed new animal drug (RLNAD). Therefore, in the preliminary regulatory impact analysis we examine the costs and benefits of these requirements for ANADAs that reference a NADA that has not been withdrawn. However, for generic new animal drugs that are the subject of an ANADA that reference a new animal drug for which the NADA has been voluntarily withdrawn for reasons other than safety or effectiveness, or that reference a new animal drug for which the NADA that has been withdrawn on the basis of one or more of the grounds included under section 512(e) of FD&C Act and for which the ANADA’s approval was not affected by the withdrawal, labeling for

such ANADAs would need to comply with proposed subpart H per the proposed schedule described in proposed § 201.404(a)(4)(iii).

The proposed requirements are based on FDA’s experience in reviewing labeling submitted for the approval or conditional approval of new animal drugs and its experience in implementing existing regulations for labeling of new animal drugs, as well as input received from new animal drug sponsors, end users of animal drugs, information collected from post approval surveillance, and other stakeholders. We intend for these proposed regulations to provide consistent formatting of new animal drug labeling by identifying the specific labeling components that would be required and permitted for each new animal drug, the information needed for each component, and the order in which information would appear on labeling. Consistent and standardized content and format of new animal drug labeling may make it easier for end users (veterinarians, animal owners, or persons treating the animals) to access, read, and use the information to make informed decisions quickly, while promoting safe use of the drug. Such labeling may contribute to reducing medication errors.

Providing clear and consistent requirements in these proposed regulations should help to reduce the amount of time needed by sponsors of new animal drugs to prepare high quality proposed labeling for their new animal drugs. The submission of higher quality proposed labeling by sponsors of new animal drugs may reduce the amount of time needed by FDA to review and approve labeling, and consequently, the new animal drug application.

We include the following eight sections in proposed subpart H:

- § 201.401 Scope.
- § 201.403 Definitions.
- § 201.404 General requirements.
- § 201.405 Content and format for prescription new animal drug labeling.
- § 201.407 Content and format for OTC new animal drug labeling.
- § 201.409 Content and format of labeling for new animal drugs for use in animal feeds.
- § 201.411 Exemptions from labeling requirements for approved or conditionally approved new animal drugs.
- § 201.413 Labeling requirements for certain approved or conditionally approved new animal drugs.

### A. Scope (Proposed § 201.401)

The proposed rule would revise the existing requirements for the content and format of labeling for prescription (Rx) new animal drugs, OTC new animal drugs other than those for use in animal feeds in accordance with part 558 (21 CFR part 558), and new animal drugs for use in animal feeds that are subject to part 558, including VFD drugs, that are subject of the specific applications identified in proposed § 201.401(a)(1) through (4).

Subpart H would apply to the labeling of new animal drugs that are the subject of an NADA approved or submitted pursuant to section 512 of the FD&C Act (see proposed § 201.401(a)(1)), new animal drugs that are the subject of a CNADA conditionally approved or submitted pursuant to section 571 of the FD&C Act (see proposed § 201.401(a)(2)), and new animal drugs that are the subject of an ANADA approved or submitted pursuant to section 512(n) of the FD&C Act (*i.e.*, a generic new animal drug) that reference a new animal drug for which the NADA has been voluntarily withdrawn for reasons other than safety or effectiveness, or that reference a new animal drug for which the NADA has been withdrawn on the basis of one or more of the grounds included under section 512(e) of the FD&C Act and for which the generic new animal drug’s approval was not affected by the withdrawal (see proposed § 201.401(a)(3)).

For some proprietary Type B or Type C medicated feeds, the formulation and labeling are approved and maintained in an NADA or CNADA file. In other situations, the underlying data and labeling for the proprietary Type B or Type C medicated feed to support the approved uses are maintained in a Veterinary Master File (VMF). The latter would include, as an example, situations in which a proprietary Type B or Type C medicated feed is manufactured via modification to an approved formulation published in the CFR or where a feed manufacturer creates its own proprietary formulation. The labeling of these proprietary medicated feeds is maintained in a VMF and would be required to comply with proposed subpart H (see proposed § 201.401(a)(4)).

The proposed requirements would apply to the applications described in proposed § 201.401(a)(1) through (4) for new animal drugs that are approved before the effective date of any final rule based on this proposed rule, pending on the effective date of any final rule based on this proposed rule, or submitted on

or after the effective date of any final rule based on this proposed rule (see proposed § 201.401(c)). The schedule for compliance is provided in proposed § 201.404(a)(4).

The proposed requirements would deem any approved or conditionally approved new animal drug subject to this subpart that does not fully comply with the applicable requirements in accordance with the schedule proposed in § 201.404(a)(4) to be misbranded under section 502 of the FD&C Act and, if that drug is a VFD drug, also under section 504(b) of the FD&C Act (see proposed § 201.401(c)).

The proposed requirements would not apply to the labeling of legally marketed unapproved new animal drugs for minor species that are indexed in accordance with section 572 of the FD&C Act (see proposed § 201.401(d)(1)) or to the labeling of heritable intentional genomic alterations in animals (see proposed § 201.401(d)(2)).

The proposed requirements would not apply to promotional labeling or advertising (see proposed § 201.401(d)(3)). Promotional labeling for new animal drugs is generally any labeling other than labeling required in an application for a new animal drug (see § 514.1(b)(3)). Materials that may be considered promotional labeling or advertising include, for example, brochures, booklets, mailing pieces, or reminder labeling. These materials are described in more detail for prescription human drugs and prescription new animal drugs in existing 21 CFR 202.1.

#### B. Definitions (Proposed § 201.403)

Proposed § 201.403 would establish definitions for terms used in proposed subpart H.

The proposed definitions for the following terms would be the same as those already in the FD&C Act or elsewhere in the regulations:

- “active ingredient”
- “adverse drug experience”
- “ANADA”
- “drug product”
- “established name”
- “extralabel use”
- “free-choice medicated feed”
- “inactive ingredient”
- “label”
- “labeling”
- “lot number”
- “control number”
- “batch number”
- “NADA”
- “new animal drug”
- “sponsor”
- “strength”
- “Type A medicated article”
- “Type B medicated feed”
- “Type C medicated feed”

- “veterinary feed directive (VFD)”
- “VFD drug”

We would base the definition of “full prescribing information” for prescription new animal drugs on the requirements for full prescribing information for prescription human drugs and biologics established in § 201.57(c) (21 CFR 201.57(c)).

For OTC new animal drugs, we would create a similar term, called “full product information.” We would define “full product information” as all information necessary for the safe and effective use of an OTC new animal drug.

We would base the definitions of other terms on the requirements established in § 201.57(c) for full prescribing information of prescription human drugs and biologics. These terms include “adverse reaction,” “boxed warning,” and “contraindication.” The proposed definition of “precaution” would be based on the requirements for the “Other special care precautions” labeling section described in § 201.57(c)(6)(ii). The proposed definition of “warning” would be based on general requirements for the “Warnings and Precautions” section described in § 201.57(c)(6)(i).

We would define “active moiety” as the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance.

We would define “field study” as a type of adequate and well-controlled study designed to assess the effectiveness and/or safety of a new animal drug in the target animal under conditions that closely approximate the actual conditions of use.

The term “indication” would mean “the use for which the new animal drug is approved or conditionally approved.”

We would define “milk discard time” as the interval between the time of the last administration of a new animal drug and the time when the milk can be safely consumed.

We would define “residue warning statement” as a statement that warns against the use of the new animal drug in animals for which the withdrawal period and/or milk discard time has not been determined, and/or provides other information to prevent illegal drug residues in food products from animals treated with the new animal drug.

The term “target animal” would mean the species, or collection of species, of

animals, and if applicable, the specific subset(s) of animals (*e.g.*, life stage, production class, age, gender) for which the new animal drug is approved or conditionally approved. Particularly for food-producing animals, new animal drugs may be approved for use only during a specific life stage (*e.g.*, growing, pregnant, lactating), production class (*e.g.*, growing beef steers and heifers fed in confinement for slaughter, broiler chickens, finishing pigs), age, or gender of the animal.

We would define “environmental warning” as a warning that identifies any potential hazard to the human environment associated with the use of the new animal drug. We would define “user safety warning” as a warning that identifies any serious adverse reaction or potential hazard to human health associated with human exposure during use of a new animal drug via contact, inhalation, ingestion, injection, or by other means.

The term “withdrawal period” would mean the interval between the time of the last administration of a new animal drug and the time when the animal can be safely slaughtered for food.

The proposed regulations would provide definitions for terms associated with key labeling components for new animal drugs, including “immediate container,” “package insert,” “secondary container,” “small label,” “shipping labeling,” “representative Type B medicated feed labeling,” and “representative Type C medicated feed labeling.”

#### C. General Requirements (Proposed § 201.404)

The proposed rule would require the labeling for approved or conditionally approved new animal drugs to conform to an application approved under section 512 of the FD&C Act or conditionally approved under section 571 of the FD&C Act (see proposed § 201.404(a)(1)).

The proposed rule would require the labeling to be informative and accurate and neither promotional in tone nor false or misleading in any particular and would require the labeling to be updated if new information becomes available to cause the labeling to become inaccurate, false, or misleading, in accordance with § 514.8 of this chapter (see proposed § 201.404(a)(2) and (3)).

The proposed rule would require labeling conforming to this subpart to be submitted to FDA per the earliest applicable compliance date provided in the schedule, unless § 201.404(b), (c), or (d) was applicable (see proposed § 201.404(a)(4)). See also section VI for

discussion of Proposed Effective/ Compliance Dates.

Labeling included in NADAs, CNADAs, or supplements to NADAs or CNADAs subject to § 514.8(c)(2) that are submitted to FDA for approval more than 180 days after the effective date of any final rule based on this proposed rule would be required to conform to the regulations as part of the application (see proposed § 201.404(a)(4)(i)).

The proposed rule would require sponsors with NADAs, CNADAs, or supplements to NADAs or CNADAs subject to § 514.8(c)(2) that are pending with FDA on the effective date of any final rule based on this proposed rule, or submitted within 180 days after the effective date of any final rule based on this proposed rule, to submit conforming labeling as part of the application or supplemental application, or alternatively, as a supplement to the approved application or supplemental application within 180 days after the approval date of the application or supplemental application, as determined by FDA (see proposed § 201.404(a)(4)(ii)).

The proposed rule would establish a timeline for submission of supplements with conforming labeling for marketed new animal drugs originally approved before the effective date of any final rule based on this proposed rule, based on NADA number (see proposed § 201.404(a)(4)(iii) through (vii)).

For an ANADA that references a new animal drug for which the NADA has been voluntarily withdrawn for reasons other than safety or effectiveness, or that references a new animal drug for which the NADA has been withdrawn on the basis of one or more grounds included under section 512(e) of the FD&C Act and the ANADA's approval was not affected by the withdrawal, the labeling for such an ANADA would be required to be submitted between the [effective date of a final rule plus 1 year] and the [effective date of a final rule plus 2 years] (see proposed § 201.404(a)(4)(iii)). For an ANADA that references a new animal drug for which the NADA has not been withdrawn, consistent with current practice, we expect that the sponsor of such a generic new animal drug will submit a supplemental application to the ANADA to conform the labeling of the generic new animal drug with the revised labeling of the RLNAD once the labeling of the RLNAD has been revised in accordance with the schedule in proposed § 201.404.

Sponsors of proprietary Type B or Type C medicated feeds for which the underlying data and labeling are maintained in a VMF would be required

to submit conforming labeling to the VMF within 180 days after all conforming labeling has been approved for the NADA or CNADA that is the approved or conditionally approved source of the new animal drug used to manufacture the proprietary medicated feed (see proposed § 201.404(b)).

The labeling for new animal drugs conditionally approved before the effective date of a final rule would not be required to comply with proposed subpart H until an application for full approval is submitted unless a supplement subject to § 514.8(c)(2) is submitted to the CNADA after the effective date of a final rule (see proposed § 201.404(c)). The conditional approval is valid for 1 year and can be renewed annually for up to a total of 5 years by the sponsor showing active progress towards demonstrating substantial evidence of effectiveness. The conditional approval will be terminated if substantial evidence of effectiveness is not demonstrated (section 571(d) of the FD&C Act).

The proposed rule would also establish an alternative schedule for submitting conforming labeling for combination new animal drugs intended for use in animal feed or drinking water and approved, on or before the effective date of a final rule, in accordance with section 512(d)(4) of the FD&C Act, *i.e.*, per the Animal Drug Availability Act (ADAA) of 1996. Section 512(d)(4) was amended as part of the Minor Use Minor Species (MUMS) Act of 2004 to clarify that only products approved under section 512(b)(1) of the FD&C Act can be used in ADAA combinations. Thus, ADAA combination new animal drugs exclude conditionally approved drugs subject to section 571 of the FD&C Act. These ADAA combination new animal drugs generally provide for more than one approved new animal drug (as a Type A medicated article) to be mixed into medicated feed or drinking water. These ADAA combination new animal drug approvals result in new representative ("Blue Bird") labeling for medicated feeds containing the combination (see proposed § 201.409).

Representative labeling for medicated feed containing the approved combination of new animal drugs includes information from the approved labeling for the individual drugs. Thus, it would be appropriate that the labeling for individual drugs included in the combination be updated to conform to any final regulations before representative labeling for the feeds containing the combination approval is updated. However, the ADAA

combination approval would occur after the individual drugs are approved; therefore, the NADA number for the combination approval would be higher than the NADA numbers for the individual new animal drugs. Thus, according to the schedule proposed in § 201.404(a)(4), the conforming labeling for a combination approval would likely need to be submitted before the conforming labeling for the individual drugs in the combination. To address this problem, the proposed rule would require the conforming labeling for the combination new animal drug to be submitted within 180 days of the approval of all conforming labeling for the individual new animal drugs used in the combination (see proposed § 201.404(d)).

The range of NADA numbers provided as "breakpoints" in the proposed schedule for the submission of conforming labeling are intended to provide for a relatively uniform number of labeling supplements during each 1-year interval. The schedule would require more recently approved new animal drugs to conform to the requirements first because they are more likely to be consistent with the new requirements than the labeling of older new animal drugs. Sponsors of older new animal drug applications would have a longer amount of time to comply with the new requirements. Table 1 provides these NADA ranges in the first column. Table 1 provides in the second column the number of currently approved and marketed NADAs within the ranges of NADAs calculated by FDA as of September 2023 and adjusts for ADAA combination new animal drugs that would need to conform after all individual new animal drugs in the combination have conformed (see proposed § 201.404(d)). The first row of the second column of table 1 includes ANADAs that reference a new animal drug for which the NADA has been voluntarily withdrawn for reasons other than safety or effectiveness, or that reference a new animal drug for which the NADA has been withdrawn on the basis of one or more of the grounds included under section 512(e) of FD&C Act and for which the ANADA's approval was not affected by the withdrawal. Table 1 also provides in the third column the number of currently approved and marketed ANADAs with a RLNAD that has not been withdrawn, as calculated by FDA as of September 2023; these ANADAs are included in the row that corresponds to the NADA number for the RLNAD.

TABLE 1—NUMBER OF AFFECTED APPLICATIONS AS OF SEPTEMBER 2023<sup>1</sup>

NADA Nos.	NADA	ANADA with a RLNAD <sup>2</sup>	Total
N-141-300 +; certain ANADAs .....	<sup>3</sup> 104	9	113
N-141-000 to N-141-299 .....	101	86	187
N-115-000 to N-140-999 .....	105	87	192
N-045-000 to N-114-999 .....	116	68	184
N-000-001 to N-044-999 .....	86	66	152
Total .....	512	316	828

<sup>1</sup> These numbers will be updated in a final rule.

<sup>2</sup> These are ANADAs with a RLNAD that has not been withdrawn, and they are in the row that corresponds to the NADA number for the RLNAD.

<sup>3</sup> This number includes six ANADAs that reference a withdrawn NADA.

The proposed rule would provide direction for situations in which it may not be clear how a requirement in subpart H applies to a particular new animal drug, or whether it applies. FDA approves and conditionally approves new animal drugs for many species of animals. For some new animal drugs, certain sections or subsections of labeling required by proposed subpart H would not be applicable. For example, new animal drugs approved or conditionally approved for use in non-food-producing animals (e.g., cats, dogs) would not require the labeling subsection entitled either “Withdrawal Periods and Residue Warnings” or “Withdrawal Periods”. As another example, certain new animal drugs may not have contraindications. We would make the final determination in these situations as to the applicability of requirements in subpart H to specific new animal drugs (see proposed § 201.404(e)).

In addition, some sections in subpart H propose different options to meet the labeling requirements. For example, proposed § 201.405(b) would provide various options for presenting the “Indications for Use” section on the label for a prescription new animal drug, depending on size of the label. In those situations where the most appropriate option is not clear, we would make the final determination (see proposed § 201.404(e)). Ordinarily, such determinations would be made during the review of the new animal drug and its labeling.

When sponsors would submit labeling for purposes of conforming to the requirements of proposed subpart H according to the schedule in proposed § 201.404(a)(4), the proposed rule would require all labeling components for an approved or conditionally approved new animal drug to be provided in one submission. FDA would refuse to file labeling submissions intended to conform to this subpart that are incomplete. This would ensure that the

content and format is consistent across all the labeling components for a particular new animal drug. Also, this would enable FDA to review and compare all labeling components at the same time to ensure that they conform to the proposed regulations when finalized (see proposed § 201.404(f)).

The proposed rule would establish general requirements for the format of labeling of approved or conditionally approved new animal drugs in proposed § 201.404(g). The format and content of labeling for prescription new animal drugs, OTC new animal drugs, or new animal drugs for use in animal feeds would be required to comply with the general requirements in proposed § 201.404(g), as applicable, in addition to format and content specific requirements for each type of new animal drug (see proposed §§ 201.405, 201.407, or 201.409, respectively).

The proposed rule would establish requirements for the placement, size, and prominence of the established name relative to the proprietary name for approved or conditionally approved prescription new animal drugs in proposed § 201.404(g)(1). These requirements are in accordance with § 201.10(g)(1) and (2) (21 CFR 210.10(g)(1) and (2)) and section 502(e)(1)(B) of the FD&C Act.

The proposed rule would establish requirements for the placement, size, and prominence of the established name relative to the proprietary name of approved or conditionally approved OTC new animal drugs and labeling for approved or conditionally approved new animal drugs for use in animal feeds, excluding representative Type B and Type C medicated feed labeling (see proposed § 201.404(g)(2)).

The proposed rule would provide the requirements for the placement, size, and prominence of the established name on representative Type B and Type C medicated feed labeling for approved or conditionally approved new animal

drugs for use in animal feeds (see proposed § 201.404(g)(3)).

The proposed rule would require labeling text to be easy to read and with letters that do not touch. For certain text on labeling for new animal drugs, we believe that black text on a white background and use of a single type style is the easiest to read. Accordingly, the proposed rule would require that the running text, section headings, and subsection headings of package inserts must be in black type and on a white background and use a single type style because package inserts provide full prescribing information for prescription new animal drugs and full product information for OTC new animal drugs. Black text on a white background also would be required for representative labeling for Type B and C medicated feeds. For all other labeling components for new animal drugs, other color combinations would be allowed, provided that there is sufficient contrast between text and the background colors to ensure readability. See proposed § 201.404(g)(4) and (5).

The proposed rule would establish requirements for presentation of graphics and designs on labeling for approved or conditionally approved new animal drugs (see proposed § 201.404(g)(6)). Representative labeling for Type B and C medicated feeds would not be permitted to have logos, graphics, or designs other than illustrations or tables that FDA determines are necessary for proper use of the medicated feed. This proposed format is consistent with the purpose of representative labeling for Type B and C medicated feeds for use as template labeling and is also consistent with the format of representative labeling for Type B and C medicated feeds currently used in the medicated feeds industry. The proposed rule would require the presentation of graphics and designs on other labeling components for approved or conditionally approved new animal drugs to comply with § 201.15(b)(1) (21

CFR 201.15(b)(1) and proposed § 201.404(a)(2) (see proposed § 201.404(g)(6)). If graphics are incorporated into the background of these labeling components, for any text appearing over the graphics there would need to be sufficient contrast between the text and the graphics colors to ensure readability of the text. The use of compressed arrows on labeling would be limited to the subsection entitled either “Withdrawal Periods and Residue Warnings” or “Withdrawal Periods,” in accordance with the requirements in proposed § 201.404(g)(8) (see proposed § 201.404(g)(6)).

The proposed rule would establish minimum letter height or type size requirements that would vary for each labeling component and ensure appropriate space on each component while maintaining readability of text (see proposed § 201.404(g)(7)).

Section headings and subsection headings would be required to be in bold type that prominently distinguishes them from other approved labeling information. Section headings would be required to be left justified or centered, whereas subsection headings would be required to be left justified. An exception would be the subsection of labeling entitled either “Withdrawal Periods and Residue Warnings” or “Withdrawal Periods,” in which the subsection heading, and the contents of the subsection, would be required to be centered within compressed arrows (see proposed § 201.404(g)(8)).

The proposed rule would require that, if the National Drug Code is included on labeling of new animal drugs, then it must appear in accordance with 21 CFR 207.33 (see proposed § 201.404(h)).

The proposed rule would require all words, statements, and other information on the labeling for approved or conditionally approved new animal drugs to appear in English. In addition, the proposed rule would also establish requirements for additional foreign language translations of new animal drug labeling (see proposed § 201.404(i)).

For approved or conditionally approved prescription new animal drugs, the proposed rule would require that if any section or wording of a labeling component is translated into a foreign language, the entire full prescribing information would also be required to be translated into the foreign language. In certain situations, FDA may also require additional wording on other labeling components for the prescription new animal drug to be translated into the foreign language. These requirements would ensure that all information necessary for the safe

and effective use of the prescription new animal drug would be provided in the foreign language (see proposed § 201.404(i)(1)).

For approved or conditionally approved OTC new animal drugs, the proposed rule would require that if any section or wording of a labeling component is translated into a foreign language, the entire full product information would also be required to be translated into the foreign language. In certain situations, FDA may also require additional wording on other labeling components for the OTC new animal drug to be translated into the foreign language. These requirements would ensure that all information necessary for the safe and effective use of the OTC new animal drug would be provided in the foreign language (see proposed § 201.404(i)(2)).

For approved or conditionally approved new animal drugs for use in animal feeds, the proposed rule would require that if the labeling contains any representation in a foreign language, all labeling must also appear in the foreign language (see proposed § 201.404(i)(3)).

For all situations where labeling for new animal drugs is translated into a foreign language, the translated wording would be required to comply with the format and content requirements for prescription, OTC, or new animal drugs for use in animal feeds in proposed § 201.405(a), § 201.407(a), or § 201.409, respectively.

FDA may limit the number of languages into which labeling information is translated to ensure clarity of information and the safe and effective use of the new animal drug. This proposed limitation would avoid multipage labeling in multiple languages. We intend for this limitation to reduce medication errors and reduce the time needed to locate information on labeling (see proposed § 201.404(i)(4)).

The proposed rule would allow the predominant language to be substituted for English on the labeling for new animal drugs distributed solely in the Commonwealth of Puerto Rico or in a Territory where the predominant language is other than English. We may determine that such new animal drugs may be altogether exempt from the requirements in proposed § 201.404(i) (see proposed § 201.404(j)).

#### *D. Content and Format for Prescription (Rx) New Animal Drug Labeling—Overview (Proposed § 201.405)*

The proposed rule provides content and format requirements for all components of labeling for approved or conditionally approved prescription

(Rx) new animal drugs. Proposed § 201.405 would not apply to approved or conditionally approved new animal drugs intended for use in or on animal feed under the professional supervision of a licensed veterinarian because, in accordance with section 504(a) of the FD&C Act, such drugs are approved or conditionally approved as VFD drugs. Proposed § 201.409 would establish the content and format requirements for all components of labeling for approved or conditionally approved new animal drugs intended for use in animal feeds that are subject to part 558, including VFD drugs.

The proposed rule would require that labeling sections or subsections that do not apply be omitted from the labeling for approved or conditionally approved Rx new animal drugs (see proposed § 201.405). For example, Rx new animal drugs approved or conditionally approved for use in non-food-producing animals (e.g., cats, dogs) would not require the labeling subsection entitled either “Withdrawal Periods and Residue Warnings” or “Withdrawal Periods”.

FDA determines the final content of each applicable section of labeling during the review of each new animal drug as part of the approval process.

Full prescribing information for Rx new animal drugs would include all information necessary for safe and effective use of the Rx new animal drug. Thus, all approved or conditionally approved Rx new animal drugs would be required to provide a labeling component that includes full prescribing information. The proposed rule would identify the information that would be required to be included on the labeling component that would provide full prescribing information for Rx new animal drugs. If a package insert is provided with an Rx new animal drug, the proposed rule would require the package insert to include full prescribing information. If only partial information is provided on a package insert, the user may mistakenly assume the package insert includes complete information on the safe and effective use of the drug when in fact it does not. If no package insert is provided with an Rx new animal drug, the secondary container labeling would be required to include full prescribing information (see proposed § 201.405(a)).

The label is the labeling component that appears on the immediate container, which is the container in contact with the drug. The proposed rule would establish content and format requirements for the label for an approved or conditionally approved Rx new animal drug (see proposed § 201.405(b)) and for a small label for an

approved or conditionally approved Rx new animal drug that FDA determines lacks sufficient space to comply with proposed § 201.405(b) (see proposed § 201.405(c)).

For purposes of proposed subpart H, the proposed rule would define a package insert for an approved or conditionally approved Rx new animal drug as a labeling component that contains full prescribing information and is included with the immediate container or secondary container or is attached to the label (see proposed § 201.403). Where the package insert is attached to the label, which is sometimes referred to as, for example, “extended labeling,” “onserts,” or “outserts,” for purposes of proposed subpart H, the package insert providing full prescribing information and attached to the label would need to comply with proposed § 201.405(a). The label would need to comply with proposed § 201.405(b) or (c), as applicable.

FDA considers the secondary container for a new animal drug to be the packaging that surrounds the immediate container. The proposed rule would establish content and format requirements for secondary container labeling for an approved or conditionally approved Rx new animal drug (see proposed § 201.405(d)). If a package insert is provided with an Rx new animal drug, then the secondary container labeling would be required to comply with proposed § 201.405(d), and the package insert would be required to provide full prescribing information to comply with proposed § 201.405(a). If no package insert is provided with an Rx new animal drug, the proposed rule would require full prescribing information to appear on the secondary container labeling (see proposed § 201.405(a)).

In accordance with the definition of “label” in section 201(k) of the FD&C Act, information on the label must also appear on an outside container or wrapper of the retail package, if it exists, or be easily legible through the outside container or wrapper. For purposes of these proposed regulations, FDA considers the secondary container to be an “outside container or wrapper of the retail package” for new animal drugs. Therefore, if a secondary container exists, the proposed rule would require the secondary container labeling to include all information that would be on the label in accordance with proposed § 201.405(b) or (c), unless the information on the label is easily legible through the secondary container (see proposed § 201.405(a) and (d)).

Shipping labeling is associated with the outermost carton containing a new animal drug, which is intended for shipping, but not displaying the product. The proposed rule would establish content and format requirements for the shipping labeling of approved or conditionally approved Rx new animal drugs, including a requirement that such shipping labeling identify the new animal drug, the manufacturer, and drug storage and handling information. However, approved or conditionally approved Rx new animal drugs that are controlled substances would not include information that identifies the drug, in accordance with § 1301.74(e) (21 CFR 1301.74(e)), to guard against storage or in-transit losses (see proposed § 201.405(e)).

Depending on how a sponsor intends to sell or display an approved or conditionally approved Rx new animal drug, there may be other containers such as display cartons and multiple unit (multi-unit) cartons that contain immediate containers or secondary containers. These containers may be packaged in shipping cartons. The proposed rule would establish content and format requirements for the labeling of these other containers for Rx new animal drugs (see proposed § 201.405(f)).

Labeling sections and subsections for Rx new animal drugs would not be numbered. Headings of sections and subsections that would be required to appear verbatim on labeling are identified in the proposed regulations in quotations. Similarly, certain other labeling text would be required to appear verbatim on labeling; this text is also identified in the proposed regulations in quotations.

The proposed rule would require the labeling of approved or conditionally approved Rx new animal drugs to comply with other applicable requirements in proposed subpart H (see proposed § 201.405).

#### 1. Labeling Providing Full Prescribing Information (Proposed § 201.405(a))

FDA uses the term “full prescribing information” to identify all information necessary for the safe and effective use of approved or conditionally approved Rx new animal drugs. The proposed rule would establish content and format requirements for the component of labeling that provides full prescribing information for approved or conditionally approved Rx new animal drugs (see proposed § 201.405(a)).

If a package insert is provided with an approved or conditionally approved Rx new animal drug, the proposed rule

would require the package insert to include full prescribing information (see proposed § 201.405(a)). If a package insert is provided with an approved or conditionally approved Rx new animal drug, any secondary container labeling would be required to comply with proposed § 201.405(d).

If a package insert is not provided with an approved or conditionally approved Rx new animal drug, then secondary container labeling would be required, and the secondary container labeling would be required to provide full prescribing information (see proposed § 201.405(a)). If full prescribing information is provided on the secondary container labeling, in accordance with section 201(k) of the FD&C Act, proposed § 201.405(a) would allow the secondary container labeling to exclude any portions of full prescribing information that would be required to appear on the label if such information is easily legible through the secondary container (see proposed in § 201.405(d)).

The proposed rule would require the following information to be presented in full prescribing information for approved or conditionally approved Rx animal drugs and in the following order:

*a. Drug product identification.* The proposed rule would require this section of full prescribing information to include the proprietary name of the finished drug product and the established name of the drug product. If not included as part of the established name of the drug product, the route(s) of administration and dosage form of the finished drug product would be required to be included in this section as well (see proposed § 201.405(a)(1)(i) through (iv)).

The established name and strength or concentration of each active ingredient would also be required. The strength or concentration of each active ingredient would be allowed to be excluded from full prescribing information provided on a package insert if the package insert applies to multiple strengths or concentrations for the same Rx new animal drug (see proposed § 201.405(a)(1)(v)).

If FDA determines that identifying the pharmacological class of an Rx new animal drug on labeling would be helpful in facilitating its safe and effective use by the prescribing veterinarian, the proposed rule would require that the pharmacological class be included in this section of full prescribing information (see proposed § 201.405(a)(1)(vi)).

For Rx new animal drugs that are controlled substances, symbols provided in part 1302 (21 CFR part

1302) to identify the controlled substance schedule would also appear in this section of full prescribing information. See proposed § 201.405(a)(1)(vii).

*Prescription statement.* The proposed rule would require this section of full prescribing information to include the prescription statement, “Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.” Prescription new animal drugs are limited to use under the professional supervision of a licensed veterinarian (section 503(f)(1)(A) of the FD&C Act). The prescription statement would indicate that the Rx new animal drug is restricted to use by or under the order of a licensed veterinarian. Including the prescription statement on full prescribing information would be consistent with its inclusion on the label for Rx new animal drugs, which is required by section 503(f)(4) of the FD&C Act. The requirement for including the prescription statement as part of full prescribing information is proposed under the authority granted to FDA under sections 502(a), 201(n), and 701(a) of the FD&C Act. See proposed § 201.405(a)(2).

*c. Conditional approval statement.* For conditionally approved Rx new animal drugs, the proposed rule would require this section of full prescribing information to include, in accordance with section 571(f)(1)(A) of the FD&C Act, the statement indicating conditional approval by FDA and the application number: “conditionally approved by FDA pending a full demonstration of effectiveness under application number [insert number]”. This statement would be required to be prominent and conspicuous (see proposed § 201.405(a)(3)).

*d. Boxed warnings.* For Rx new animal drugs requiring boxed warnings, the proposed rule would require this section of full prescribing information to include the boxed warnings. Boxed warnings convey the most significant risks associated with the use of a Rx new animal drug. If applicable to the product, they would appear at this prominent location. An upper case “WARNING” heading would be included in the box, and the box, heading, and contents would be bolded. The boxed warning would be brief, with reference to more detailed information in other sections of full prescribing information if applicable (see proposed § 201.405(a)(4)).

*e. Extralabel use prohibition statement.* For approved new animal drugs prohibited from extralabel use, in accordance with § 530.41 (21 CFR 530.41), the proposed rule would

require this section of full prescribing information to include an extralabel use prohibition statement that begins with the phrase: “Federal law prohibits the extralabel use of this drug . . .” and concludes with a description of the prohibition as described in § 530.41 (see proposed § 201.405(a)(5)). For example, “Federal law prohibits the extralabel use of this drug in lactating dairy cows.”

Certain new animal drugs are prohibited from extralabel use in some or all animals, in accordance with § 530.41. This information is critical for inclusion on labeling. If a user fails to comply with an extralabel use prohibition statement, there could be serious safety consequences for the target animal, or in the case of a food-producing animal, also for humans consuming food derived from the target animal.

*f. “Description.”* The proposed rule would require this section of full prescribing information to have the heading “Description,” followed by a description of the new animal drug. The description would include the proprietary name of the finished drug product and established name of the drug product, and the route(s) of administration and dosage form if not included as part of the established name. The description would also include identifying characteristics of the dosage form, such as color, shape, coating, scoring, and imprinting. All approved and available strengths or concentrations of the new animal drug to which full prescribing information applies would need to be identified in this section of full prescribing information. If the drug product was sterile, this fact would also be identified in this section of full prescribing information (see proposed § 201.405(a)(6)).

The established name of each inactive ingredient would be required to be included in the “Description” section of full prescribing information. The proposed rule would require all inactive ingredients to be listed in decreasing order of predominance, by weight or concentration (see proposed § 201.405(a)(6)(viii)). FDA believes that listing inactive ingredients in decreasing order of predominance based on either weight or concentration would provide the most clinically useful information to users.

In accordance with section 502(e)(1)(A)(iii) of the FD&C Act, the proposed rule would not require the listing of inactive ingredients on full prescribing information under circumstances that would result in disclosure of trade secret information. Therefore, where sponsors believe the

listing of inactive ingredients on product labeling would result in disclosure of trade secret information, they would be able to request exemption from this labeling requirement under proposed § 201.411. If an exemption from the listing of inactive ingredients to avoid divulgence of trade secret information is granted under § 201.411, this section of full prescribing information would be required to state: “Certain inactive ingredients are not listed to avoid disclosing trade secret information.” (see proposed § 201.405(a)(6)(viii)(A)).

Section 502(e)(1)(B) of the FD&C Act allows an exemption from listing inactive ingredients on the label of Rx drugs if doing so would be impracticable. The current regulations at § 201.105(b)(5) for Rx animal drugs state that names of flavorings, perfumes, certain color additives, and “trace amounts of harmless substances added solely for individual product identification” may be exempt from listing on the labels for products other than for oral use. The regulations at § 201.105 predate the requirements in section 502(e)(1)(B) of the FD&C Act and are outdated. The proposed rule would replace the requirements for labels for approved or conditionally approved Rx new animal drugs currently provided in § 201.105(b) with the requirements in proposed § 201.405(b) and (c) (see discussion in section V.D.2. and 3). Thus, the labels for approved or conditionally approved Rx new animal drugs would no longer qualify for the exemptions currently identified in § 201.105(b)(5).

If under proposed § 201.411 FDA grants an exemption from listing inactive ingredients because their listing would be impracticable, this section of full prescribing information would need to state the following: “Certain inactive ingredients are not listed because their listing would be impracticable.” (see proposed § 201.405(a)(6)(viii)(B)).

*g. “Indications for Use.”* This section of full prescribing information would be required to have the heading “Indications for Use,” followed by the approved or conditionally approved indication(s) and target animal(s) in the following format: “For [indication(s)] in [target animal(s)]” (see proposed § 201.405(a)(7)(i)).

Consistent with regulations for the labeling of Rx human products in § 201.57(c)(2)(i)(A), if a Rx new animal drug is approved or conditionally approved for use only under specific conditions, e.g., in conjunction with a primary mode of therapy, special diet, surgery, behavioral modification, or some other drug, the proposed rule

would require that this information be specified in the “Indications for Use” section of full prescribing information (see proposed § 201.405(a)(7)(iii)).

If, in approving or conditionally approving an application, FDA requires, for safety and/or effectiveness reasons, a statement(s) on labeling identifying animals for which the Rx new animal drug has not been approved or conditionally approved, the proposed rule would require that statement(s) to appear in the “Indications for Use” section of full prescribing information (see proposed § 201.405(a)(7)(iii)). We currently require the statement(s) proposed in § 201.405(a)(7)(iii) to appear on labeling of some approved new animal drugs, particularly new animal drugs for use in food-producing animals, to clarify the target animal for which the drug is approved. The statements are typically required if we determine that unapproved use of a drug in animals similar to the target animal(s) is reasonably foreseeable and we believe that inclusion of such a statement on the labeling of the new animal drug could increase the safe and effective use of the drug. For example, feedlot beef cattle are not intended to provide milk for human consumption. Therefore, we will not likely require an evaluation of the human food safety of a new animal drug in lactating dairy cows if the new animal drug is only to be approved for use in feedlot cattle. However, we will often require a statement on labeling that the drug is not for use in lactating dairy cows intended to produce milk for human consumption to avoid use of the drug in this unapproved and unevaluated manner.

The statement(s) proposed in § 201.405(a)(7)(iii) is not intended to prohibit extralabel use of approved new animal drugs allowed under specific circumstances, in accordance with section 512(a)(4) of the FD&C Act and part 530 (21 CFR part 530), but would help to clarify that some specific uses are extralabel and have not been evaluated for safety and effectiveness by FDA. Currently, there is no uniform place on the labeling for new animal drugs for such statements to appear. If we require such statements on labeling to ensure safe and effective use of a new animal drug, the proposed rule would require the statements to be placed within the “Indications for Use” section of full prescribing information. Inclusion of such statements in the “Indications for Use” section would not necessarily preclude also including similar statements in other sections or subsections of full prescribing information if warranted. For example,

it may be appropriate to include a similar statement as a residue warning statement in the “Withdrawal Periods and Residue Warnings” subsection to expand upon human food safety risks of the extralabel use of the new animal drug in animals other than the target animal.

*h. “Dosage and Administration.”* The proposed rule would require this section of full prescribing information to have the heading “Dosage and Administration,” followed by the dosage and administration information for the new animal drug for each indication and target animal (see proposed § 201.405(a)(8)).

Sometimes FDA requires additional labeling for Rx new animal drugs that provides important information for the animal owner or person treating the animal. If such additional labeling is required, the proposed “Dosage and Administration” section of full prescribing information would advise the veterinarian to provide the additional labeling to the animal owner or person treating the animal (see proposed § 201.405(a)(8)(i)).

The remainder of this section of full prescribing information would be required to include information necessary for treatment of the animal with the Rx new animal drug in accordance with FDA approval or conditional approval, including: route(s) of administration and specific site(s) of administration, if applicable; dose or dose range; intervals between doses, if applicable; and duration of treatment. For some injectable products, FDA may require a statement of the maximum volume per injection site to facilitate the drug’s safe and effective use, and the proposed rule would require this information to be included in this section of full prescribing information. Also, certain animal populations may require modifications to the dosage and administration for safe and effective use. These modifications would be required to appear in this section of full prescribing information. Other required dosage and administration information would also be included in this section of full prescribing information. See proposed § 201.405(a)(8).

*i. “Contraindications.”* For Rx new animal drugs with contraindications, the proposed rule would require this section of full prescribing information to have the heading “Contraindications,” followed by the contraindications (see proposed § 201.405(a)(9)). As defined in proposed § 201.403, a contraindication would include any situation in which the new animal drug should not be used because the risk of use clearly outweighs any possible benefit to the

animal and includes only known hazards.

*j. “Warnings and Precautions.”* The proposed rule would require this section of full prescribing information for all approved or conditionally approved Rx new animal drugs, and it would have the heading “Warnings and Precautions” (see proposed § 201.405(a)(10)). As defined in proposed § 201.403, warnings would describe any serious adverse reactions or potential hazards associated with the use of the new animal drug. In addition, precautions would be defined as any special care to be exercised for safe and effective use of the new animal drug, which may include recommended screening, monitoring, or diagnostic tests. Multiple subsections, if applicable, would be included in the “Warnings and Precautions” section of full prescribing information as described below and in the following order, and the warnings and precautions would be provided in the applicable subsection:

*i. “Withdrawal Periods and Residue Warnings” or “Withdrawal Periods.”* All Rx new animal drugs approved or conditionally approved for use in food-producing animals would be required to have as the first subsection of the “Warnings and Precautions” section of full prescribing information a subsection entitled either “Withdrawal Periods and Residue Warnings” or “Withdrawal Periods” (see proposed § 201.405(a)(10)(i)). This subsection would provide all human food safety warnings, including milk discard times, withdrawal periods, and residue warning statements, as applicable to the new animal drug.

As defined in proposed § 201.403, a withdrawal period is the interval between the time of the last administration of a new animal drug and the time when the animal can be safely slaughtered for food. Withdrawal periods apply to all food-producing animals. As defined in proposed § 201.403, a milk discard time is the interval between the time of the last administration of a new animal drug and the time when the milk can be safely consumed. Milk discard times apply to female animals that produce milk for human consumption. A new animal drug approved for use in female animals that produce milk for human consumption may have both a milk discard time and a withdrawal period.

As defined in proposed § 201.403, a residue warning statement warns against the use of the new animal drug in animals for which the withdrawal period and/or milk discard time has not been determined, and/or provides other

information to prevent illegal drug residues in food products from animals treated with the new animal drug.

If there are any residue warning statements for the new animal drug, the proposed rule would require this subsection of full prescribing information to have the title “Withdrawal Periods and Residue Warnings.” If there are no residue warning statements associated with the new animal drug, this subsection of full prescribing information would be required to have the title “Withdrawal Periods” (see proposed § 201.405(a)(10)(i)(A)).

If the new animal drug is approved or conditionally approved for use in food-producing animals excluding female animals that produce milk for human consumption, the proposed rule would require this subsection of full prescribing information to include the withdrawal period(s) followed by any residue warning statements (see proposed § 201.405(a)(10)(i)(B)).

If the new animal drug is approved or conditionally approved for use in food-producing animals excluding female animals that produce milk for human consumption and there is no withdrawal period, the proposed rule would require this subsection of full prescribing information to state, “No withdrawal period is required when used according to labeling.” This statement would be followed by any residue warnings statements (see proposed § 201.405(a)(10)(i)(C)).

If the new animal drug is approved or conditionally approved for use in female animals that produce milk for human consumption, the proposed rule would require this subsection of full prescribing information to include the milk discard time(s), followed by the withdrawal period(s), followed by any residue warning statements (see proposed § 201.405(a)(10)(i)(D)).

If the new animal drug is approved or conditionally approved for use in female animals that produce milk for human consumption, and there is a milk discard time(s) but no withdrawal period, the proposed rule would require this subsection of full prescribing information to include the milk discard time(s), followed by the statement, “No withdrawal period is required when used according to labeling.” This statement would be followed by any residue statements (see proposed § 201.405(a)(10)(i)(E)).

If the new animal drug is approved or conditionally approved for use in female animals that produce milk for human consumption and there is no milk discard time but there is a withdrawal period(s), the proposed rule

would require this subsection of full prescribing information to include the withdrawal period(s), followed by the statement, “No milk discard time is required when used according to labeling.” This statement would be followed by any residue warnings statements (see proposed § 201.405(a)(10)(i)(F)).

If the new animal drug is approved or conditionally approved for use in female animals that produce milk for human consumption and there is no milk discard time and no withdrawal period, the proposed rule would require this subsection of full prescribing information to state, “No milk discard time and no withdrawal period is required when used according to labeling.” This statement would be followed by any residue warnings statements (see proposed § 201.405(a)(10)(i)(G)).

Currently, new animal drugs approved for use in food-producing animals that have no milk discard time and/or withdrawal period may or may not indicate this information on labeling. If this information is not provided on labeling, potentially it could be confusing to the user of the new animal drug as to whether or not there is a milk discard time or withdrawal period for the new animal drug. Requiring this subsection of full prescribing information for all new animal drugs approved or conditionally approved for use in food-producing animals, and requiring a statement, if appropriate, to indicate that there is no milk discard time or withdrawal period when the new animal drug is used according to labeling, will better ensure the safe use of animal drugs in food-producing animals.

To further highlight for users this critical subsection of full prescribing information, the title of this subsection and all information in this subsection would be required to be centered and placed entirely within compressed arrows, in accordance with proposed § 201.404(g)(8). The compressed arrows would be black for package inserts, or a color that clearly contrasts from background colors for other approved labeling (see proposed § 201.405(a)(10)(i)(A)). Currently, the compressed arrows are used voluntarily, although not consistently, on the labeling for many new animal drugs approved for use in food-producing animals. Currently other statements not associated with human food safety may also appear within the compressed arrows. The proposed rule would limit the use of compressed arrows to the subsection entitled either “Withdrawal Periods and Residue Warnings” or

“Withdrawal Periods” (see proposed § 201.404(g)(6)), which would only contain human food safety information.

ii “*User Safety Warnings.*” The proposed rule would require this subsection of the “Warnings and Precautions” section of full prescribing information to have the heading “User Safety Warnings,” followed by the user safety warnings. As defined in proposed § 201.403, a user safety warning would be a warning that identifies serious adverse reactions or potential hazards to human health associated with human exposure during use of a new animal drug via contact, inhalation, ingestion, injection, or by other means. This information would be required to prevent or decrease the risk of harm to humans.

The first statements that would be included in this subsection of full prescribing information are: “Not for use in humans. Keep out of reach of children.” The subsection would next list all additional user safety warnings listed in decreasing order of severity or frequency. The final information that would be included in this subsection of full prescribing information would be a sentence explaining how to obtain Safety Data Sheet(s) for the drug. Chemical manufacturers, distributors, and/or importers are required pursuant to 29 CFR 1910.1200(g) to provide Safety Data Sheets for each hazardous chemical to downstream users to communicate information on these hazards. Safety Data Sheets include information such as the properties of each chemical; their physical, health, and environmental health hazards; protective measures; and safety precautions for handling, storing, and transporting the chemical. The sentence in this subsection of full prescribing information would be required to be formatted as follows: “To obtain a Safety Data Sheet(s), contact [insert name of manufacturer] at [insert manufacturer’s telephone number] or [insert manufacturer’s website].” See proposed § 201.405(a)(10)(ii).

iii. “*Animal Safety Warnings and Precautions.*” For Rx new animal drugs with target animal safety warnings and precautions, the proposed rule would require this subsection of the “Warnings and Precautions” section of full prescribing information to have the heading “Animal Safety Warnings and Precautions,” followed by the target animal safety warnings and precautions (see proposed § 201.405(a)(10)(iii)). Target animal safety warnings identify any serious adverse reactions or potential hazards to the target animal(s) associated with the use of the new animal drug. Precautions for Rx new

animal drugs often include recommendations for specific screening, monitoring, diagnostic tests, or special care that should be taken by the prescribing veterinarian for safe and effective use of the new animal drug (see definition in proposed § 201.403). The heading of the subsection would include the term “animal safety warnings”, *i.e.*, “Animal Safety Warnings and Precautions,” because we believe the term “animal safety warnings” is more familiar to users of Rx new animal drugs than “target animal safety warnings.”

Precautions are sometimes difficult to distinguish from target animal safety warnings. Currently, target animal safety warnings and precautions are sometimes presented separately on the labeling for Rx new animal drugs. However, because the two sets of information are often closely related, it is advantageous to combine them into one subsection of full prescribing information.

Warnings and precautions are combined in the “Highlights” and “Full Prescribing Information” for human Rx drugs and biologics (see §§ 201.56 and 57). Similarly, combining target animal safety warnings and precautions in the “Animal Safety Warnings and Precautions” subsection of full prescribing information would be less burdensome for sponsors of Rx new animal drugs because sponsors would not be required to distinguish one from the other.

iv. “*Environmental Warnings.*” For approved or conditionally approved new animal drugs that have environmental warnings, the proposed rule would require this subsection of the “Warnings and Precautions” section of full prescribing information to have the heading “Environmental Warnings,” followed by the environmental warnings (see proposed § 201.405(a)(10)(iv)). FDA’s regulations at 21 CFR part 25 implementing the National Environmental Policy Act (NEPA), 42 U.S.C. 4321 *et seq.*, address the environmental impact considerations required for products regulated by FDA, including new animal drugs. Under NEPA, the responsible Agency official examines the environmental risks of the proposed action and the alternative courses of action, selects a course of action, and ensures that any necessary mitigating measures are implemented as a condition for approving the selected course of action (see 21 CFR 25.40(e)). In some instances, sponsors may choose to include environmental warnings on the labeling for their new animal drugs as a means to mitigate or reduce the potential for environmental impacts to

occur from the use or disposal of the drug (see 21 CFR 25.45). These warnings would generally include information to prevent or decrease the risk of any environmental effects. The proposed rule would require any environmental warnings applicable to the new animal drug that are included in an approved or conditionally approved application be provided in this subsection of full prescribing information (see proposed § 201.405(a)(10)(iv)).

v. “*Other Warnings.*” For new animal drugs having warnings not more appropriately placed in other “Warnings and Precautions” subsections, the proposed rule would require the last subsection of the “Warnings and Precautions” section of full prescribing information to have the heading “Other Warnings,” followed by those warnings (see proposed § 201.405(a)(10)(v)).

k. “*Adverse Reactions.*” For Rx new animal drugs that we determine have adverse reactions, this section of full prescribing information would be required to have the heading “Adverse Reactions,” followed by the adverse reactions (see proposed § 201.405(a)(11)). Adverse reactions would be defined in proposed § 201.403 as undesirable effects, reasonably associated with the use of the drug product, that may occur as part of the pharmacological action of the drug or that may be unpredictable in occurrence. The proposed rule would require this section of full prescribing information to include adverse reactions that occur with use of the Rx new animal drug and with use of drugs in the same pharmacologically active and chemically related classes, if applicable. Furthermore, we may require additional information as necessary for the prescribing veterinarian to interpret the adverse reactions, such as the total number of animals exposed to the drug and the extent and nature of exposure.

The proposed rule would also require that adverse reactions be presented within the following categories, as applicable, in decreasing order of severity or frequency: preapproval experience, foreign market experience known prior to U.S. approval for drugs also commercially marketed outside of the United States, and post-approval experience (see proposed § 201.405(a)(11)). For previously approved Rx new animal drugs for which the labeling would be updated in accordance with the schedule provided in this rule, if the preapproval experience and/or foreign market experience categories were not included on full prescribing information when the drug was approved, we may allow one or both of these subsections to be

excluded from the “Adverse Reactions” section of full prescribing information if we determine that including such information is not necessary to ensure the safe and effective use of the drug. Post-approval experience would typically be added to labeling of the drug after it has been approved in the United States and if additional adverse drug experiences (as defined by § 514.3) associated with the use of the drug have been identified.

l. “*Contact Information.*” The proposed rule would require this section of full prescribing information to have the heading “Contact Information,” followed by the sponsor’s contact information for veterinarians or consumers to facilitate requesting additional information or to report suspected adverse drug experiences. FDA’s contact information for voluntary reporting of adverse drug experiences for animal drugs would also be required. Requiring contact information on new animal drug labeling increases the likelihood that a user will report adverse drug events to the sponsor and/or to the Center for Veterinary Medicine (CVM). Increasing the likelihood of receiving adverse drug event reports would allow new animal drug sponsors and CVM to better monitor and detect emerging safety issues with approved or conditionally approved new animal drugs on the market. Any increase in adverse drug event reporting and monitoring resulting from this proposed requirement would benefit both animal and human health.

The sponsor’s contact information would be the name of the manufacturer, packer, or distributor, whichever is identified in the “Name and place of business” section of full prescribing information per proposed § 201.405(a)(22). If more than one business is identified in the “Name and place of business” section of full prescribing information, the drug sponsor would select the most appropriate of these businesses to use in the “Contact Information” section to provide additional information about the Rx new animal drug and to contact regarding suspected adverse drug experiences.

The statements in this section of full prescribing information would be required to be structured as follows: “Contact [insert name of business] at [insert business telephone number] or [insert business web address]. To report suspected adverse drug experiences, contact [insert name of business] at [insert business telephone number]. For additional information about reporting adverse drug experiences for animal drugs, contact FDA at [insert current

FDA telephone number for voluntary reporting of adverse drug experiences] or [insert current FDA web address for voluntary reporting of adverse drug experiences].” See proposed § 201.405(a)(12). Sponsors can search FDA’s website or contact FDA by telephone to find the current FDA telephone number and web address for voluntary reporting of adverse drug experiences for animal drugs.

*m. “Information for Animal Owner.”* For Rx new animal drugs required to have additional information to be communicated by the prescribing veterinarian to the animal owner or person treating the animal to ensure safe and effective use of the Rx new animal drug, the proposed rule would require this section of full prescribing information to have the heading “Information for Animal Owner,” followed by the specific information.

For some new animal drugs, FDA may determine it is necessary for sponsors to provide the animal owner or person treating the animal with additional labeling, such as a “client information sheet,” to ensure the safe and effective use of the Rx new animal drug. If we determine that such additional labeling is necessary, a printed copy of the additional labeling would be required to be attached to or accompany the package insert or secondary container labeling if no package insert is provided. See proposed § 201.405(a)(13).

*n. “Clinical Pharmacology.”* For Rx new animal drugs required to include clinical pharmacology information on labeling, the proposed rule would require this section of full prescribing information to have the heading “Clinical Pharmacology,” followed by the clinical pharmacology information for the Rx new animal drug in the target animal(s). The required information would be relevant for understanding the relationship between dose, systemic drug exposure, safety, and clinical effectiveness. This information may help the prescribing veterinarian to predict how the Rx new animal drug would perform in the different animal patient populations likely to be encountered under clinical use conditions. This section of full prescribing information would be required to include the following three separate subsections, as applicable to the Rx new animal drug: “Mechanism of action,” “Pharmacodynamics,” and “Pharmacokinetics” (see proposed § 201.405(a)(14)).

*o. “Microbiology.”* For antimicrobial Rx new animal drugs, the proposed rule would require this section of full prescribing information to have the heading “Microbiology,” followed by a

description of microbiologic data associated with the studies used to support the effectiveness of the drug against the indicated pathogens. The microbiology data would be required to be restricted to organisms named in the approved or conditionally approved indications.

If in vitro data for antimicrobial new animal drugs are included in this section of full prescribing information and the data have not been correlated to clinical effectiveness, then such in vitro data would be required to be immediately preceded by the following statement: “The following in vitro data are available, but their clinical significance is unknown.” See proposed § 201.405(a)(15).

*p. “Target Animal Safety.”* The proposed rule would require this section of full prescribing information to have the heading “Target Animal Safety,” followed by a summary of the basis for the conclusion that the new animal drug is safe in the target animal(s) when used as approved or conditionally approved (see proposed § 201.405(a)(16)).

*q. “Effectiveness.”* The proposed rule would require this section of full prescribing information to have the heading “Effectiveness,” followed by a summary of the basis for the conclusion that the new animal drug is effective in the target animal(s) when used as approved. For conditionally approved drugs, the “Effectiveness” section of full prescribing information would be required to include a summary of the basis for the reasonable expectation of effectiveness (see proposed § 201.405(a)(17)).

*r. “Net Contents.”* The proposed rule would require this section of full prescribing information, when presented on the secondary container labeling, to have the heading “Net Contents,” followed by the contents of the secondary container. The proposed rule would exclude a “Net Contents” section from package inserts (see proposed § 201.405(a)(18)).

*s. “How Supplied.”* The proposed rule would require this section of full prescribing information to have the heading “How Supplied,” followed by information on available drug strengths, concentrations, and container sizes to which the labeling applies. The information in this section would be required to be revised if new strengths, concentrations, or container sizes are added (see proposed § 201.405(a)(19)).

*t. “Storage, Handling, and Disposal.”* The proposed rule would require this section of full prescribing information to have the heading “Storage, Handling, and Disposal” (see proposed

§ 201.405(a)(20)). Drug storage information would be included in this section and may include, for example, required temperature, humidity, and/or light exposure conditions to maintain the potency of the Rx new animal drug until its established expiration date. Also, any handling and drug disposal information that we determine to be necessary for safe and effective use of the Rx new animal drug would be included in this section. Handling information may include, for example, recommendations to reseal reusable bottles promptly after opening and conditions necessary to maintain potency of reconstituted new animal drugs. Drug disposal information may include, for example, instructions on disposal of unused portions of new animal drugs remaining after treatment, as well as used needles and/or syringes.

*u. NADA/ANADA approval statement.* In accordance with section 502(w)(3) of the FD&C Act, by no later than September 30, 2023, approved new animal drugs must include the following statement on labeling: “Approved by FDA under NADA # xxx-xxx”. By no later than September 30, 2023, approved generic Rx new animal drugs must include the following statement on labeling: “Approved by FDA under ANADA # xxx-xxx”. For approved Rx new animal drugs, the proposed rule would require this section of full prescribing information to include the “NADA approval statement,” indicating the product’s NADA number and that it was approved by FDA. For approved generic Rx new animal drugs that would be covered by these regulations (*i.e.*, those that reference an NADA that has been withdrawn for reasons other than safety or effectiveness or under section 512(e) of the FD&C Act and the ANADA’s approval was not affected by the withdrawal), the proposed rule would require this section of full prescribing information to include the “ANADA approval statement.” The proposed rule would establish format requirements for the approval statement and would require that the approval statement not be so prominent as to obscure other required information. The approval statement could not be incorporated into a seal, stamp, logo, or graphic. See proposed § 201.405(a)(21).

*v. Name and place of business.* The proposed rule would require this section of full prescribing information to identify the name and place of business of the manufacturer, packer, or distributor (see proposed § 201.405(a)(22)).

*w. “Lot Number and Expiration Date.”* The proposed rule would require

this section of full prescribing information when provided on the secondary container labeling. Package inserts are excluded from this requirement because they might apply to multiple lots of secondary or immediate containers of the Rx new animal drug. When full prescribing information is provided on the secondary container labeling, this section would be required to have the heading “Lot Number and Expiration Date,” followed by the identifying lot or control number of the Rx new animal drug within the secondary container (see proposed § 201.405(a)(23)). Should a problem be reported to FDA, a lot or control number would help us more easily to identify and trace back a specific lot of a product. The proposed rule would also require this section to include the expiration date of the Rx new animal drug within the secondary container, in accordance with § 201.17 (21 CFR 201.17). An expiration date better ensures that the new animal drug would not be used after it expires.

Alternatively, the proposed rule would allow for this section of full prescribing information to refer to the location on the secondary container labeling or secondary container where the lot or control number and expiration date are printed (see proposed § 201.405(a)(23)). As an example, if the lot number and expiration date are printed on the bottom flap of a secondary container, then the secondary container labeling may state in this section, “See carton bottom flap for lot number and expiration date.” However, in accordance with § 201.17, the proposed rule would allow an expiration date to be excluded from the secondary container labeling or secondary container if the expiration date provided on the label or immediate container is easily legible through the secondary container.

x. “*Revision Date.*” The proposed rule would require this section of full prescribing information to have the heading “Revision Date,” followed by the date of the most recent revision of the component of labeling that provides full prescribing information, listing the month followed by the year (see proposed § 201.405(a)(24)). This information is important to ensure that the most current approved version of the labeling is being used.

## 2. Prescription New Animal Drug Label (Rx Label) (Proposed § 201.405(b))

The proposed rule would establish content and format requirements for the information presented on the label for approved or conditionally approved Rx new animal drugs (Rx label) (see

proposed § 201.405(b)). As defined in proposed § 201.403, “label” has the same meaning as given in section 201(k) of the FD&C Act, which defines the term “label” to mean a display of written, printed, or graphic matter upon the immediate container of any article. As defined in proposed § 201.403, the immediate container means the container in contact with the new animal drug, and it excludes package liners.

Proposed § 201.405(b) would apply to Rx labels that are of adequate size to contain the proposed required information per that paragraph, whereas proposed § 201.405(c) would apply to small labels for Rx new animal drugs that are not of adequate size to contain all the proposed required information in proposed § 201.405(b).

Prescription new animal drugs labels to which § 201.405(b) would apply may consist of a single panel, a front panel and one side or back panel, or a front panel and multiple side and/or back panels, and the proposed rule would provide for such label designs (see § 201.405(b)). For Rx labels with a front panel and one side or back panel, the proposed rule would require certain information for the front panel (see proposed § 201.405(b)(1)), and the side or back panel (see proposed § 201.405(b)(2)). For Rx labels consisting of a single panel, the proposed rule would require the information identified in proposed § 201.405(b)(1) followed by the information identified in proposed § 201.405(b)(2), in order, on the single panel. For Rx labels with a front panel and multiple side and/or back panels, the information identified in proposed § 201.405(b)(1) followed by the information identified in proposed § 201.405(b)(2) would be required in order, starting on the front panel, continuing on the panel immediately to the right of the front panel, and continuing to fill the panels to the right until all of the information in proposed § 201.405(b)(1) and (b)(2) was presented. In all instances, the information proposed in § 201.405(b)(2)(iii) and (iv), *i.e.*, “Active Ingredient” or “Active Ingredients” and “Inactive Ingredients,” would need to appear on the same panel.

a. *Front panel.* The proposed rule would require the following information to be presented on the front panel of the Rx label for an approved or conditionally approved Rx new animal drug and in the following order. Unless otherwise indicated, this information would be the same as that required by proposed § 201.405(a) for full prescribing information.

i. *Drug product identification.* The proposed rule would require this section of the Rx label to include drug product identification information (see proposed § 201.405(b)(1)(i)). This information may help the user quickly and correctly identify the product and distinguish it from other, similar products. The information included in this section of the Rx label would include the same information as that in the drug product identification section of full prescribing information, as described in proposed § 201.405(a)(1), in addition to a statement that the drug product is sterile, if applicable. Full prescribing information would require a drug product identification section and a “Description” section. Full prescribing information for sterile Rx new animal drugs would be required to identify in the “Description” section that the drug is sterile. However, due to space limitations, no “Description” section is proposed for the Rx label. Instead, the drug product identification section of the Rx label for sterile Rx new animal drugs would be required to state that the drug product is sterile. See proposed § 201.405(b)(1)(i).

ii. *Prescription statement.* The proposed rule would require this section of the Rx label to include the prescription statement (see proposed § 201.405(b)(1)(ii)). In accordance with section 503(f)(4) of the FD&C Act, all Rx new animal drugs must state on the label: “Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.”

iii. *Conditional approval statement.* For conditionally approved new animal drugs, the proposed rule would require this section of the Rx label to include a conditional approval statement, as described in proposed § 201.405(a)(3) for full prescribing information (see proposed § 201.405(b)(1)(iii)).

iv. *Boxed warnings.* For approved or conditionally approved Rx new animal drugs requiring boxed warnings, the proposed rule would require this section of the Rx label to include the boxed warnings, as described in proposed § 201.405(a)(4) for full prescribing information (see proposed § 201.405(b)(1)(iv)).

v. *Indications for Use.* The proposed rule would require this section of the Rx label to have the heading “Indications for Use,” followed by the “Indications for Use” section, as described in proposed § 201.405(a)(7) for full prescribing information. If we determine that there is insufficient space on the Rx label for the complete “Indications for Use” section as described in proposed § 201.405(a)(7), then the proposed rule would require

the sponsor to include in this section of the Rx label the statement required in proposed § 201.405(a)(7)(i), *i.e.*, “For [indication(s)] in [target animal(s)]”. If there is insufficient space on the Rx label for the statement in proposed § 201.405(a)(7)(i), then an abbreviated version of the statement would be required: “For [abbreviated indication(s)] in [target animal(s)]”. In either situation where there is insufficient space on the Rx label for the complete “Indications for Use” section as specified in proposed § 201.405(a)(7), the required statement would be followed by one of the following statements: “See package insert for complete ‘Indications for Use’” if full prescribing information is provided on a package insert; or “See package labeling for complete ‘Indications for Use’” if full prescribing information is provided on the secondary container labeling. See proposed § 201.405(b)(1)(v).

The complete “Indications for Use” section as described in proposed § 201.405(a)(7) may exceed the available space on the Rx label if, for example, it includes specific conditions of use (proposed § 201.405(a)(7)(ii)) or animals for which the new animal drug is not approved or conditionally approved (proposed § 201.405(a)(7)(iii)), and/or the indication(s) is lengthy and/or complex. For example, a new animal drug approved to treat and control multiple species of roundworms, lungworms, lice, and mites in beef cattle would ordinarily identify all of those species in the “Indications for Use” section of the label. However, if space is insufficient on the Rx label to provide the identity of all of the species of the roundworms, lungworms, lice, and mites for which the drug is effective, an acceptable “abbreviated” version of the “Indications for Use” section on the Rx label for this product might include, for example, “For treatment and control of certain species of roundworms, lungworms, lice, and mites in beef cattle. See package insert for complete ‘Indications for Use’.”

vi. *Extralabel use prohibition statement.* For approved Rx new animal drugs prohibited from extralabel use, in accordance with § 530.41, the proposed rule would require this section of the Rx label to include the extralabel use prohibition statement, as described in proposed § 201.405(a)(5) for full prescribing information (see proposed § 201.405(b)(1)(vi)).

vii. *“Withdrawal Periods and Residue Warnings” or “Withdrawal Periods.”* For new animal drugs approved or conditionally approved for use in food-producing animals, the proposed rule

would require this section of the Rx label to have the heading “Withdrawal Periods and Residue Warnings” or “Withdrawal Periods,” followed by all human food safety warnings, including milk discard times, withdrawal periods, and residue warning statements, as described in proposed § 201.405(a)(10)(i) for full prescribing information. If there is insufficient space on the front panel of Rx labels with only a front panel and one side or back panel, the proposed rule would require this section to be provided on the side or back panel of the Rx label immediately following the full prescribing information statement specified in proposed § 201.405(b)(2)(i). See proposed § 201.405(b)(1)(vii).

viii. *“Net Contents.”* The proposed rule would require this section of the Rx label to have the heading “Net Contents,” followed by the contents of the immediate container, in accordance with § 201.51 (see proposed § 201.405(b)(1)(viii)).

ix. *NADA/ANADA approval statement.* For approved new animal drugs or approved generic new animal drugs, the proposed rule would require this section of the Rx label to include the NADA or ANADA approval statement, as described in proposed § 201.405(a)(21) for full prescribing information (see proposed § 201.405(b)(1)(ix)).

b. *Side or back panel.* The proposed rule would require the following information to be presented on the side or back panel of the Rx label for an approved or conditionally approved Rx new animal drug in the following order (see proposed § 201.405(b)(2)). Unless otherwise indicated, this information would be the same as that required by proposed § 201.405(a) for full prescribing information.

i. *Full prescribing information statement.* The proposed rule would require this section of the Rx label to include one of two statements (see proposed § 201.405(b)(2)(i)). If full prescribing information is provided on the package insert, the following statement would be used: “Before using this drug, read package insert for full prescribing information.” If full prescribing information is provided on the secondary container labeling, the following statement would be used: “Before using this drug, read package labeling for full prescribing information.” Because full prescribing information would not be provided on the Rx label, the purpose of the statements would be to remind the veterinarian to read full prescribing information before using the Rx new animal drug.

ii. *“Dosage and Administration.”* The proposed rule would require this section of the Rx label to have the heading “Dosage and Administration,” followed by the “Dosage and Administration” section, as described in proposed § 201.405(a)(8) for full prescribing information. If there is insufficient space on the Rx label for the complete requirements as specified in proposed § 201.405(a)(8), or if it is necessary for additional information provided in full prescribing information that is not provided on the Rx label to be read before administering the drug (*e.g.*, complete warnings and precautions, contraindications, and/or target animal safety), then FDA may exclude this section from the Rx label (see proposed § 201.405(b)(2)(ii)). For example, with respect to the latter situation, if careful observation of the animal after dosing is advised to watch for adverse reactions, this information typically would be described in the “Animal Safety Warnings and Precautions” subsection, which would not be required on the Rx label but would be required on full prescribing information. Excluding the “Dosage and Administration” section from the Rx label in this situation helps to ensure that the veterinarian would read full prescribing information, which would include the “Dosage and Administration” section as well as the “Animal Safety Warnings and Precautions” subsection, before treating the animal. Users would also be reminded to read full prescribing information before using the drug via the full prescribing information statement that would be required in the previous section of the Rx label by proposed § 201.405(b)(2)(i).

iii. *“Active Ingredient” or “Active Ingredients.”* The proposed rule would require this section of the Rx label to have the heading “Active Ingredient” or “Active Ingredients,” followed by the established name and strength or concentration of each active ingredient. If the Rx new animal drug contains one active ingredient, the proposed rule would require this section of the Rx label to be entitled “Active Ingredient.” If the Rx new animal drug contains more than one active ingredient, the proposed rule would require this section of the Rx label to be entitled “Active Ingredients.” The requirement to provide established name and strength or concentration of each active ingredient on the Rx label would be consistent with the requirement for the established name and quantity or proportion of each active ingredient on the label of prescription drugs, in

accordance with section 502(e)(1)(A)(ii), (B), and (g) of the FD&C Act (see proposed § 201.405(b)(2)(iii)). This information is currently required to be on the label for Rx animal drugs, in accordance with § 201.105(b)(4). Proposed § 201.405(b) and (c) would establish the content and format requirements for the label for approved or conditionally approved Rx new animal drugs and would replace the requirements for the label of approved or conditionally approved Rx new animal drugs currently provided in § 201.105(b). Furthermore, § 201.105 would be amended to refer to proposed § 201.405 for the content and format requirements for labeling components for approved or conditionally approved Rx new animal drugs.

iv. *“Inactive Ingredients.”* The proposed rule would require this section of the Rx label to have the heading “Inactive Ingredients,” followed by the established name of each inactive ingredient, as described in proposed § 201.405(a)(6)(viii) for full prescribing information (see proposed § 201.405(b)(2)(iv)).

v. *“Storage, Handling, and Disposal.”* The proposed rule would require this section of the Rx label to have the heading “Storage, Handling, and Disposal,” followed by drug storage, handling, and disposal information, as described in proposed § 201.405(a)(20) for full prescribing information (see proposed § 201.405(b)(2)(v)).

vi. *Name and place of business.* The proposed rule would require this section of the Rx label to identify the name and place of business of the manufacturer, packer, or distributor, as required in section 502(b) of the FD&C Act (see proposed § 201.405(b)(2)(vi)).

vii. *“Lot Number and Expiration Date”* or *“Lot Number.”* The proposed rule would require this section of the Rx label to have the heading “Lot Number and Expiration Date” or “Lot Number,” followed by the identifying lot or control number of the Rx new animal drug within the immediate container (see proposed § 201.405(b)(2)(vii)). A lot or control number would allow us to more easily identify and trace back a specific lot of a product should a problem be reported to FDA. We would also require this section of the Rx label to include the expiration date of the Rx new animal drug within the immediate container, in accordance with § 201.17.

An expiration date on the Rx label better ensures that the new animal drug would not be used after it expires. Alternatively, the proposed rule would allow for this section to refer to the location on the Rx label or immediate container where the lot or control

number and expiration date are printed (see proposed § 201.405(b)(2)(vii)). As an example, if the lot number and expiration date are printed at the top of the immediate container, then the Rx label may state in this section, “See top of container for lot number and expiration date.” If the immediate container provides a single dose of the Rx new animal drug and is packaged individually in a secondary container that provides an expiration date on the secondary container labeling or secondary container, the proposed rule would not require an expiration date on the Rx label or immediate container, in accordance with § 201.17. Under such provision, this section of the Rx label would be required to be entitled “Lot Number.”

viii. *“Revision Date.”* The proposed rule would require the last section of the Rx label to have the heading “Revision Date,” followed by the date of the most recent revision of the Rx label, listing the month followed by the year (see proposed § 201.405(b)(2)(viii)).

### 3. Prescription New Animal Drug Small Label (Rx Small Label) (Proposed § 201.405(c))

The proposed rule would establish content and format requirements for the small label for Rx new animal drugs (Rx small label) (see proposed § 201.405(c)). Some immediate containers, such as blister packs, pre-filled syringes, and small vials, are so small that only a minimal amount of information can be included on their label. The proposed rule would establish requirements for Rx small labels for approved or conditionally approved Rx new animal drugs (see proposed § 201.405(c)). We recognize that the size of the label is dependent upon the size of the immediate container. If an immediate container lacks sufficient space to contain a label that accommodates all of the information required by proposed § 201.405(b), the requirements of proposed § 201.405(c) would instead apply. We would ordinarily make this determination during the review of the new animal drug and its labeling, taking into consideration the readability and legibility of the information.

The proposed rule would require the following information to be presented on the Rx small label for an approved or conditionally approved Rx new animal drug and in the following order (see proposed § 201.405(c)).

a. *Proprietary name of the finished drug product.* The proposed rule would require this section of the Rx small label to include the proprietary name of the finished drug product (see proposed § 201.405(c)(1)). This requirement

already exists for small labels for drugs in general in § 201.10(i)(1), but is repeated in these proposed regulations to include all requirements for labeling of approved or conditionally approved new animal drugs in proposed subpart H.

b. *Established name of the drug product.* The proposed rule would require this section of the Rx small label to include the established name of the drug product (see proposed § 201.405(c)(2)). This requirement already exists for small labels for drugs in general in § 201.10(i)(1), but is repeated in these proposed regulations to include all requirements for labeling of approved or conditionally approved new animal drugs in proposed subpart H.

c. *Active ingredient(s).* The proposed rule would require this section of the Rx small label to include the established name and strength or concentration of each active ingredient, which is consistent with the requirement for the established name and quantity or proportion of each active ingredient on the label of prescription drugs, in accordance with section 502(e)(1)(A)(ii), (B), and (g) of the FD&C Act (see proposed § 201.405(c)(3)). This information is currently required to be on the label for Rx animal drugs, in accordance with § 201.105(b)(4).

Proposed § 201.405(b) and (c) would establish the content and format requirements for the label for approved or conditionally approved Rx new animal drugs and would replace the requirements for the label of approved or conditionally approved Rx new animal drugs currently provided in § 201.105(b). Furthermore, § 201.105 would be amended to cross-reference proposed § 201.405 for the content and format requirements for labeling components for approved or conditionally approved Rx new animal drugs (see discussion in section V.I.).

d. *Controlled substance symbol.* For Rx new animal drugs that are controlled substances, the proposed rule would require this section of the Rx small label to include the controlled substance schedule symbol in accordance with part 1302 designating the schedule for the drug substance (see proposed § 201.405(c)(4)).

e. *Prescription statement.* The proposed rule would require this section of the Rx small label to state: “Rx Animal Use” (see proposed § 201.405(c)(5)). In accordance with section 503(f)(4) of the FD&C Act, the label for all Rx new animal drugs must include the following statement: “Caution: Federal law restricts this drug to use by or on the order of a licensed

veterinarian.” However, since 1960 (25 FR 12592) § 201.105(b)(6) exempts “containers too small or otherwise unable to accommodate a label with sufficient space” to include the full prescription statement provided that the full statement may be placed on the outer container only. We are proposing the “Rx Animal Use” statement for a Rx small label for Rx new animal drugs. This statement would appropriately identify the Rx status of the new animal drug and would require minimal space.

*f. “For [target animal(s)] only.”* The proposed rule would require this section of the Rx small label to include a brief listing of the approved target animal(s) as follows: “For [target animal(s)] only” (see proposed § 201.405(c)(6)). The brief listing of the approved target animal(s) would be used in place of full “Indications for Use” information because Rx small labels lack sufficient space. This listing would not require as much space on the Rx small label.

*g. Full prescribing information statement.* The proposed rule would require this section of the Rx small label to include one of two statements. If full prescribing information is provided on the package insert, the following statement would be used: “Read package insert for full prescribing information.” If full prescribing information is provided on the secondary container labeling, the following statement would be used: “Read package labeling for full prescribing information.” See proposed § 201.405(c)(7). Because full prescribing information would not be provided on the Rx small label, the purpose of the statements would be to remind the veterinarian to read full prescribing information before using the Rx new animal drug.

*h. “Net Contents.”* The proposed rule would require this section of the Rx small label to have the heading “Net Contents,” followed by the contents of the immediate container, in accordance with § 201.51 (see proposed § 201.405(c)(8)).

*i. Name and place of business.* The proposed rule would require this section of the Rx small label to identify the name and place of business of the manufacturer, packer, or distributor, as required in section 502(b) of the FD&C Act (see proposed § 201.405(c)(9)).

*j. “Lot, Exp. and Storage” or “Lot and Storage.”* The proposed rule would require this section of the Rx small label to have the heading “Lot, Exp. and Storage” or “Lot and Storage,” followed by the identifying lot or control number of the Rx new animal drug within the immediate container (see proposed

§ 201.405(c)(10)). Should a problem be reported to FDA, a lot or control number would allow us more easily to identify and trace back a specific lot of a product. We would also require this section of the Rx small label to include the expiration date of the Rx new animal drug within the immediate container, in accordance with § 201.17. An expiration date on the Rx small label better ensures that the new animal drug would not be used after it expires.

The proposed rule would also require this section of the Rx small label to include drug storage information for the new animal drug (see proposed § 201.405(c)(10)). Storage information is necessary to maintain potency of the drug before its expiration date. Requiring this information on the Rx small label is needed for safe and effective use of new animal drugs. If the immediate container provides a single dose of the Rx new animal drug and is packaged individually in a secondary container that provides an expiration date on the secondary container labeling or secondary container, the proposed rule would not require an expiration date on the Rx small label or immediate container, in accordance with § 201.17. Under such provision, this section of the Rx small label would be required to be entitled “Lot and Storage.”

*k. “Revision Date.”* The proposed rule would require this section of the Rx small label to have the heading “Revision Date,” followed by the date of the most recent revision of the Rx small label, listing the month followed by the year (see proposed § 201.405(c)(11)).

#### 4. Labeling for Secondary Containers for Rx New Animal Drugs That Include a Package Insert (Rx Secondary Container Labeling) (Proposed § 201.405(d))

The proposed rule would establish content and format requirements for the information on the labeling for secondary containers of approved or conditionally approved Rx new animal drugs that include a package insert (Rx secondary container labeling) (see proposed § 201.405(d)). In this situation, the package insert would be required to include full prescribing information, as described in proposed § 201.405(a).

In accordance with section 201(k) of the FD&C Act, the Rx secondary container labeling could exclude any information described in proposed § 201.405(d) that would be required to appear on the Rx label or Rx small label (see proposed § 201.405(b) or (c), respectively) if such information on the Rx label or Rx small label was easily legible through the secondary container.

The Rx secondary container labeling to which proposed § 201.405(d) would

apply may consist of a front panel and one side or back panel, or a front panel and multiple side and/or back panels. Proposed § 201.405(d) would provide for such Rx secondary container labeling designs. For Rx secondary container labeling with a front panel and one side or back panel, proposed § 201.405(d)(1) would provide required information for the front panel, and proposed § 201.405(d)(2) would provide required information for the side or back panel. For Rx secondary container labeling with a front panel and multiple side and/or back panels, the information identified in proposed § 201.405(d)(1) followed by the information identified in proposed § 201.405(d)(2) would be required in order, starting on the front panel, continuing on the panel immediately to the right of the front panel, and continuing to fill the panels to the right until all of the information in proposed § 201.405(d)(1) and (d)(2) was presented. In all instances, the information proposed in § 201.405(d)(2)(v) and (vi), *i.e.*, “Active Ingredient” or “Active Ingredients” and “Inactive Ingredients,” would need to appear on the same panel.

*a. Front panel.* The proposed rule would require the following information to be presented on the front panel of the Rx secondary container labeling and in the following order (see proposed § 201.405(d)(1)). Unless otherwise indicated, this information would be the same as that required by proposed § 201.405(a) for full prescribing information.

*i. Drug product identification.* The proposed rule would require this section of the Rx secondary container labeling to include drug product identification (see proposed § 201.405(d)(1)(i)). The information would be the same as that included in the drug product identification section for full prescribing information, as described in proposed § 201.405(a)(1), and would also identify if the drug product is sterile. Full prescribing information would require a drug product identification section and a “Description” section. Full prescribing information for sterile Rx new animal drugs would be required to identify in the “Description” section that the drug is sterile. However, due to space limitations, no “Description” section would be required on the Rx secondary container labeling. Instead, the drug product identification section of the Rx secondary container labeling for sterile Rx new animal drugs would be required to state that the drug is sterile.

*ii. Prescription statement.* The proposed rule would require this section of the Rx secondary container

labeling to include the prescription statement, as described in proposed § 201.405(a)(2) for full prescribing information (see proposed § 201.405(d)(1)(ii)).

iii. *Conditional approval statement.* For conditionally approved Rx new animal drugs, the proposed rule would require this section of the Rx secondary container labeling to include a conditional approval statement, as described in proposed § 201.405(a)(3) for full prescribing information (see proposed § 201.405(d)(1)(iii)).

iv. *Boxed warnings.* For approved or conditionally approved Rx new animal drugs requiring boxed warnings, the proposed rule would require this section of the Rx secondary container labeling to include the boxed warnings, as described in proposed § 201.405(a)(4) for full prescribing information (see proposed § 201.405(d)(1)(iv)).

v. *“Indications for Use.”* The proposed rule would require this section of the Rx secondary container labeling to have the heading “Indications for Use,” followed by the “Indications for Use” section, as described in proposed § 201.405(a)(7) for full prescribing information (see proposed § 201.405(d)(1)(v)).

vi. *Extralabel prohibition statement.* For approved new animal drugs prohibited from extralabel use, in accordance with § 530.41, the proposed rule would require this section of the Rx secondary container labeling to include the extralabel use prohibition statement, as described in proposed § 201.405(a)(5) for full prescribing information (see proposed § 201.405(d)(1)(vi)).

vii. *“Net Contents.”* The proposed rule would require this section of the Rx secondary container labeling to have the heading “Net Contents,” followed by the contents of the secondary container (see proposed § 201.405(d)(1)(vii)).

viii. *NADA/ANADA approval statement.* For approved new animal drugs or approved generic new animal drugs, the proposed rule would require this section of the Rx secondary container labeling to include the NADA or ANADA approval statement, as described in proposed § 201.405(a)(21) for full prescribing information (see proposed § 201.405(d)(1)(viii)).

b. *Side or back panel.* The proposed rule would require the following information to be presented on the side or back panel of the Rx secondary container labeling and in the following order (see proposed § 201.405(d)(2)). Unless otherwise indicated, this information would be the same as that required by proposed § 201.405(a) for full prescribing information.

i. *Full prescribing information statement.* The proposed rule would require this section of the Rx secondary container labeling to include the statement: “Before using this drug, read package insert for full prescribing information” (see proposed § 201.405(d)(2)(i)). Because full prescribing information would not be provided on the Rx secondary container labeling, the purpose of the full prescribing information statement would be to remind the veterinarian to read full prescribing information before using the Rx new animal drug.

ii. *“Dosage and Administration.”* The proposed rule would require this section of the Rx secondary container labeling to have the heading “Dosage and Administration,” followed by the “Dosage and Administration” section, as described in proposed § 201.405(a)(8) for full prescribing information (see proposed § 201.405(d)(2)(ii)).

iii. *“Contraindications.”* The proposed rule would require this section of the Rx secondary container labeling to have the heading “Contraindications,” followed by the “Contraindications” section, as described in proposed § 201.405(a)(9) for full prescribing information (see proposed § 201.405(d)(2)(iii)).

iv. *“Warnings and Precautions.”* The proposed rule would require this section of the Rx secondary container labeling to have the heading “Warnings and Precautions,” followed by the “Warnings and Precautions” section, as described in proposed § 201.405(a)(10) for full prescribing information (see proposed § 201.405(d)(2)(iv)).

v. *“Active Ingredient” or “Active Ingredients.”* The proposed rule would require this section of the Rx secondary container labeling to have the heading “Active Ingredient” or “Active Ingredients,” followed by the established name and strength or concentration of each active ingredient, as described in proposed § 201.405(b)(2)(iii) for the Rx label (see proposed § 201.405(d)(2)(v)).

vi. *“Inactive Ingredients.”* The proposed rule would require this section of the Rx secondary container labeling to have the heading “Inactive Ingredients,” followed by the established name of each inactive ingredient, as described in proposed § 201.405(a)(6)(viii) for full prescribing information (see proposed § 201.405(d)(2)(vi)).

vii. *“Storage, Handling, and Disposal.”* The proposed rule would require this section of the Rx secondary container labeling to have the heading “Storage, Handling, and Disposal,” followed by drug storage, handling, and

disposal information, as described in proposed § 201.405(a)(20) for full prescribing information (see proposed § 201.405(d)(2)(vii)).

viii. *Name and place of business.* The proposed rule would require this section of the Rx secondary container labeling to identify the manufacturer, packer, or distributor, as described in proposed § 201.405(a)(22) for full prescribing information (see proposed § 201.405(d)(2)(viii)).

ix. *“Lot Number and Expiration Date.”* The proposed rule would require this section of the Rx secondary container labeling to have the heading “Lot Number and Expiration Date,” followed by the identifying lot or control number of the Rx new animal drug within the secondary container. The proposed rule would also require this section of the Rx secondary container labeling to include the expiration date of the Rx new animal drug within the secondary container, in accordance with § 201.17. Alternatively, the proposed rule would allow for this section to refer to the location on the Rx secondary container labeling or secondary container where the lot or control number and expiration date are printed (see proposed § 201.405(d)(2)(ix)). As an example, if the lot number and expiration date are printed on the bottom flap of a secondary container, then the labeling may state in this section, “See carton bottom flap for lot number and expiration date. However, in accordance with § 201.17, the proposed rule would allow an expiration date to be excluded from the Rx secondary container labeling or secondary container if the expiration date provided on the Rx label, Rx small label, or immediate container is easily legible through the secondary container.

x. *“Revision Date.”* The proposed rule would require this section of the Rx secondary container labeling to have the heading “Revision Date,” followed by the date of the most recent revision of the Rx secondary container labeling, listing the month followed by the year (see proposed § 201.405(d)(2)(x)).

5. *Shipping Labeling for Rx New Animal Drugs (Rx Shipping Labeling) (Proposed § 201.405(e))*

The proposed rule would establish content and format requirements for the information on the shipping labeling for approved or conditionally approved Rx new animal drugs (Rx shipping labeling). As defined in proposed § 201.403, shipping labeling is associated with the outermost carton containing immediate containers, secondary containers, and/or multiple

unit (multi-unit) cartons of a new animal drug and intended for shipment, but not display, of the product. The proposed rule would require the Rx shipping labeling to include, among additional information, drug product identity, the manufacturer, packer, or distributor, and drug storage and handling conditions (see proposed § 201.405(e)). However, the Rx shipping labeling for controlled substances would not include information that would identify the drug, in accordance with § 1301.74(e), to guard against storage or in-transit losses due to theft or diversion.

The proposed rule would require the following information to be presented on the Rx shipping labeling and in the following order (see proposed § 201.405(e)). Unless otherwise indicated, this information would be the same as that required by proposed § 201.405(a) for full prescribing information.

*a. Proprietary name of the finished drug product.* The proposed rule would require this section of the Rx shipping labeling to include the proprietary name of the finished drug product (see proposed § 201.405(e)(1)). This section would be excluded from the Rx shipping labeling for a controlled substance.

*b. Established name of the drug product.* The proposed rule would require this section of the Rx shipping labeling to include the established name of the drug product (see proposed § 201.405(e)(2)). This section would be excluded from the Rx shipping labeling for a controlled substance.

*c. Established name and strength or concentration of each active ingredient.* The proposed rule would require this section of the Rx shipping labeling to provide the established name and strength or concentration of each active ingredient. This section would be excluded from the Rx shipping labeling for a controlled substance (see proposed § 201.405(e)(3)).

*d. Conditional approval statement.* For conditionally approved Rx new animal drugs, the proposed rule would require this section of the Rx shipping labeling to include a conditional approval statement, as described in proposed § 201.405(a)(3) for full prescribing information (see proposed § 201.405(e)(4)). This section would be excluded from the Rx shipping labeling for a controlled substance.

*e. "Net Contents."* The proposed rule would require this section of the Rx shipping labeling to have the heading "Net Contents," followed by the contents of the shipping carton (see proposed § 201.405(e)(5)).

*f. "Storage and Handling."* The proposed rule would require this section of the Rx shipping labeling to have the heading "Storage and Handling," followed by drug storage information (see proposed § 201.405(e)(6)). Also, any handling information required for safe and effective use of the new animal drug would be included in this section. Information on disposal of the new animal drug would not be required to be included on the Rx shipping labeling.

*g. NADA/ANADA approval statement.* For approved new animal drugs or approved generic new animal drugs, the proposed rule would require this section of the Rx shipping labeling to include the NADA or ANADA approval statement, as described in proposed § 201.405(a)(21) for full prescribing information (see proposed § 201.405(e)(7)). This section would be excluded from the Rx shipping labeling for a controlled substance.

*h. Name and place of business.* The proposed rule would require this section of the Rx shipping labeling to identify the name and place of business of the manufacturer, packer, or distributor, as described in proposed § 201.405(a)(22) for full prescribing information (see proposed § 201.405(e)(8)).

*i. "Lot Number and Expiration Date."* The proposed rule would require this section of the Rx shipping labeling to have the heading "Lot Number and Expiration Date," followed by the identifying lot or control number(s) and the expiration date(s) of the Rx new animal drug within the shipping carton (see proposed § 201.405(e)(9)). The shipping carton may contain more than one lot of the new animal drug, and therefore, more than one lot or control number and expiration date may be listed in this section of the Rx shipping labeling.

*j. "Revision Date."* The proposed rule would require the last section of the Rx shipping labeling to have the heading "Revision Date," followed by the date of the most recent revision of the Rx shipping labeling, listing the month followed by the year (see proposed § 201.405(e)(10)).

## 6. Other Approved Labeling for Rx New Animal Drugs (Rx Other Approved Labeling) (Proposed § 201.405(f))

The proposed rule would establish content and format requirements for the information presented on other approved labeling for approved or conditionally approved Rx new animal drugs (Rx other approved labeling) (see proposed § 201.405(f)). Rx other approved labeling includes, but is not

limited to, labeling on display cartons and multi-unit cartons (excluding shipping cartons), containing the immediate containers or the secondary containers of the Rx new animal drug.

The proposed rule would require the following information to be presented on the Rx other approved labeling and in the following order (see proposed § 201.405(f)). Unless otherwise indicated, this information would be the same as required by proposed § 201.405(a) for full prescribing information.

*a. Proprietary name of the finished drug product.* The proposed rule would require this section of the Rx other approved labeling to include the proprietary name of the finished drug product (see proposed § 201.405(f)(1)).

*b. Established name of the drug product.* The proposed rule would require this section of the Rx other approved labeling to include the established name of the drug product (see proposed § 201.405(f)(2)).

*c. Established name and strength or concentration of each active ingredient.* The proposed rule would require this section of the Rx other approved labeling to provide the established name and strength or concentration of each active ingredient (see proposed § 201.405(f)(3)).

*d. Controlled substance symbol.* The proposed rule would require this section of the Rx other approved labeling for controlled substances to include the controlled substance schedule symbol, in accordance with part 1302 designating the schedule for the drug substance (see proposed § 201.405(f)(4)).

*e. Prescription statement.* The proposed rule would require this section of the Rx other approved labeling to include the prescription statement, as described in proposed § 201.405(a)(2) for full prescribing information (see proposed § 201.405(f)(5)).

*f. Conditional approval statement.* For conditionally approved new animal drugs, the proposed rule would require this section of the Rx other approved labeling to include a conditional approval statement, as described in proposed § 201.405(a)(3) for full prescribing information (see proposed § 201.405(f)(6)).

*g. Boxed warnings.* For approved or conditionally approved Rx new animal drugs requiring boxed warnings, the proposed rule would require this section of the Rx other approved labeling to include the boxed warnings, as described in proposed § 201.405(a)(4) for full prescribing information (see proposed § 201.405(f)(7)).

*h. Extralabel use prohibition statement.* For approved new animal drugs prohibited from extralabel use, in accordance with § 530.41, the proposed rule would require this section of the Rx other approved labeling to include the extralabel use prohibition statement, as described in proposed § 201.405(a)(5) for full prescribing information (see proposed § 201.405(f)(8)).

*i. "Net Contents."* The proposed rule would require this section of the Rx other approved labeling to have the heading "Net Contents," followed by the contents of the container to which the Rx other approved labeling applies (see proposed § 201.405(f)(9)).

*j. "Storage, Handling, and Disposal."* The proposed rule would require this section of the Rx other approved labeling to have the heading "Storage, Handling, and Disposal," followed by drug storage, handling, and disposal information, as described in proposed § 201.405(a)(20) for full prescribing information (see proposed § 201.405(f)(10)).

*k. NADA/ANADA approval statement.* For approved new animal drugs or approved generic new animal drugs, the proposed rule would require this section of the Rx other approved labeling to include the NADA or ANADA approval statement, as described in proposed § 201.405(a)(21) for full prescribing information (see proposed § 201.405(f)(11)).

*l. Name and place of business.* The proposed rule would require this section of the Rx other approved labeling to identify the name and place of business of the manufacturer, packer, or distributor, as described in proposed § 201.405(a)(22) for full prescribing information (see proposed § 201.405(f)(12)).

*m. "Lot Number and Expiration Date."* The proposed rule would require this section of the Rx other approved labeling to have the heading "Lot Number and Expiration Date," followed by the identifying lot or control number of the Rx new animal drug within the container to which the Rx other approved labeling applies. This section of the Rx other approved labeling would also be required to include the expiration date of the Rx new animal drug within the container to which the Rx other approved labeling applies, in accordance with § 201.17. In accordance with § 201.17, the proposed rule would allow an expiration date to be excluded from the Rx other approved labeling if the expiration date provided on containers within or their labeling is easily legible through the container to which the Rx other approved labeling applies (see proposed § 201.405(f)(13)).

*n. "Revision Date."* The proposed rule would require the last section of the Rx other approved labeling to have the heading "Revision Date," followed by the date of the most recent revision of the Rx other approved labeling, listing the month followed by the year (see proposed § 201.405(f)(14)).

*E. Content and Format for Over-The-Counter (OTC) New Animal Drug Labeling—Overview (Proposed § 201.407)*

The proposed rules provides content and format requirements for all components of labeling for approved or conditionally approved OTC new animal drugs other than those for use in animal feeds that are subject to part 558 (see proposed § 201.407). Proposed § 201.409 would establish the content and format requirements for all components of labeling for approved or conditionally approved new animal drugs intended for use in animal feeds that are subject to part 558. OTC new animal drugs are new animal drugs that can be used without a prescription from a veterinarian. They are intended for use by the layperson, such as pet owners and livestock producers. In accordance with section 502(f) of the FD&C Act, OTC drugs must bear adequate directions for use on labeling. Adequate directions for use means directions under which the layperson can use a drug safely and for the purposes for which it is intended (see § 201.5).

The proposed rule would require that labeling sections or subsections that do not apply be omitted from the labeling for approved or conditionally approved OTC new animal drugs (see proposed § 201.407). For example, OTC new animal drugs approved or conditionally approved for use in non-food-producing animals (e.g., cats, dogs) would not require the labeling subsection entitled either "Withdrawal Periods and Residue Warnings" or "Withdrawal Periods".

FDA determines the final content of each applicable section of labeling during the review of each new animal drug as part of the approval process.

The proposed rule would identify the information that would be required to be included on the labeling component that would provide full product information for OTC new animal drugs in proposed § 201.407(a). Full product information for OTC new animal drugs would be similar in concept to full prescribing information for Rx new animal drugs in that it would include all information necessary for the safe and effective use of the OTC new animal drug. Thus, all approved or conditionally approved OTC new animal drugs would be required to

provide a labeling component that includes full product information. If a package insert is provided with an OTC new animal drug, the proposed rule would require the package insert to include full product information. If only partial information is provided on a package insert, the user may mistakenly assume the package insert includes complete information on the safe and effective use of the drug when in fact it does not. If no package insert is provided with an OTC new animal drug, the secondary container labeling would be required to include full product information. If no package insert or secondary container labeling is provided with the OTC new animal drug, then full product information would need to be provided on the label (see proposed § 201.407(a)).

The label is the labeling component that appears on the immediate container, which is the container in contact with the drug. The proposed rule would establish content and format requirements for the label for an approved or conditionally approved OTC new animal drug that does not provide full product information (see proposed § 201.407(b)). The proposed rule would establish content and format requirements for a small label for an approved or conditionally approved OTC new animal drug that we determine lacks sufficient space to comply with proposed § 201.407(b) (see proposed § 201.407(c)).

For purposes of proposed subpart H, we would define a package insert for an approved or conditionally approved OTC new animal drug as a labeling component that contains full product information and is included with the immediate container or secondary container or is attached to the label (see proposed § 201.403). Where the package insert is attached to the label, which is sometimes referred to as, for example, "extended labeling," "onserts," or "outserts," for purposes of proposed subpart H, the package insert providing full product information and attached to the label would need to comply with proposed § 201.407(a). The label would need to comply with proposed § 201.407(b) or (c), as applicable.

FDA considers the secondary container for a new animal drug to be the packaging that surrounds the immediate container. The proposed rule would establish content and format requirements for secondary container labeling for an approved or conditionally approved OTC new animal drug (see proposed § 201.407(d)). If a package insert is provided with an OTC new animal drug, then the secondary container labeling would be

required to comply with proposed § 201.407(d) and the package insert would be required to provide full product information to comply with proposed § 201.407(a). If no package insert is provided with an OTC new animal drug, the proposed rule would require full product information to appear on the secondary container labeling (see proposed § 201.407(a)).

In accordance with the definition of “label” in section 201(k) of the FD&C Act, information on the label must also appear on an outside container or wrapper of the retail package, if it exists, or be easily legible through the outside container or wrapper. For purposes of these proposed regulations, FDA considers the secondary container to be an “outside container or wrapper of the retail package” for new animal drugs. Therefore, if a secondary container exists, the proposed rule would require the secondary container labeling to include all information that would be on the label in accordance with proposed § 201.407(b) or (c), unless the information on the label is easily legible through the secondary container (see proposed § 201.407(a) or (d)).

Shipping labeling is associated with the outermost carton containing a new animal drug, which is intended for shipping, but not displaying the product. The proposed rule would establish content and format requirements for the shipping labeling of approved or conditionally approved OTC new animal drugs including a requirement that such shipping labeling identify the new animal drug, the manufacturer, and drug storage and handling information (see proposed § 201.407(e)).

Depending on how a sponsor intends to sell or display an approved or conditionally approved OTC new animal drug, there may be other containers such as display cartons and multiple unit (multi-unit) cartons that contain immediate containers or secondary containers. These containers may be packaged in shipping cartons. The proposed rule would establish content and format requirements for the labeling of these other containers for OTC new animal drugs (see proposed § 201.407(f)).

Labeling sections and subsections for OTC new animal drugs would not be numbered. Headings of sections and subsections that would be required to appear verbatim on labeling are identified in the proposed regulations in quotations. Similarly, certain other labeling text would be required to appear verbatim on labeling; this text is also identified in the proposed regulations in quotations.

The proposed rule would require the labeling of approved or conditionally approved OTC new animal drugs to comply with other applicable requirements in proposed subpart H (see proposed § 201.407).

#### 1. Labeling Providing Full Product Information (Proposed § 201.407(a))

The proposed rule uses the term “full prescribing information” to identify all information necessary for the safe and effective use of approved or conditionally approved Rx new animal drugs, and the proposed regulations use that term for Rx new animal drugs. The concept of a component of labeling providing all information necessary for the safe and effective use of an approved or conditionally approved OTC new animal drug is equally important. FDA proposes that the term used for this information for approved or conditionally approved OTC new animal drugs would be “full product information” because OTC new animal drugs are not prescribed.

The proposed rule would establish content and format requirements for the component of labeling that provides full product information for approved or conditionally approved OTC new animal drugs (see proposed § 201.407(a)).

If a package insert is provided with an approved or conditionally approved OTC new animal drug, the proposed rule would require the package insert to include full product information (see proposed § 201.407(a)). If a package insert is provided with an approved or conditionally approved OTC new animal drug, the label would be required to comply with proposed § 201.407(b) or (c), and any secondary container labeling would be required to comply with proposed § 201.407(d).

If a package insert is not provided with an approved or conditionally approved OTC new animal drug, but a secondary container is provided, then the secondary container labeling would be required to provide full product information (see proposed § 201.407(a)). If full product information is provided on the secondary container labeling, in accordance with section 201(k) of the FD&C Act, proposed § 201.407(a) would allow the secondary container labeling to exclude any portions of full product information that would be required to appear on the label if such information is easily legible through the secondary container (see proposed § 201.407(a)).

If no package insert or secondary container is provided with an approved or conditionally approved OTC new animal drug, then the label would be

required to include full product information (see proposed § 201.407(a)).

The proposed rule would require the following information to be presented in full product information for approved or conditionally approved OTC new animal drugs and in the following order. Unless otherwise indicated, this information would be the same as that required by proposed § 201.405(a) for full prescribing information for approved or conditionally approved Rx new animal drugs.

*a. Drug product identification.* The proposed rule would require this section of full product information to include the proprietary name of the finished drug product and the established name of the drug product. If not included as part of the established name of the drug product, the route(s) of administration and dosage form of the finished drug product would be required to be included in this section as well (see proposed § 201.407(a)(1)(i) through (iv)).

The established name and strength or concentration of each active ingredient would also be required. The strength or concentration of each active ingredient would be allowed to be excluded from full product information provided on a package insert if the package insert applies to multiple strengths or concentrations for the same OTC new animal drug (see proposed § 201.407(a)(1)(v)).

If FDA determines that identifying the pharmacological class of an OTC new animal drug on labeling would be helpful in facilitating its safe and effective use, the proposed rule would require that the pharmacological class be included in this section of full product information (see proposed § 201.407(a)(1)(vi)).

*b. Conditional approval statement.* For conditionally approved OTC new animal drugs, the proposed rule would require this section of full product information to include a conditional approval statement, as described in proposed § 201.405(a)(3) for full prescribing information for conditionally approved Rx new animal drugs (see proposed § 201.407(a)(2)).

*c. “Uses.”* This section of full product information would be required to have the heading “Uses,” followed by the approved or conditionally approved indication(s) and target animal(s) in the following format: “For [indication(s)] in [target animal(s)]” (see proposed § 201.407(a)(3)).

This section of full product information would be similar to the “Indications for Use” section of full prescribing information for Rx new animal drugs, as described in proposed

§ 201.405(a)(7). For OTC new animal drugs, the heading “Uses” may be better understood by the layperson and is consistent with the requirements for labeling of OTC human drugs (see § 201.66(c)(4)).

If FDA approves or conditionally approves an OTC new animal drug for use only under specific conditions, such as in conjunction with a specific diet, then the proposed rule would require that this information be specified in the “Uses” section of full product information (see proposed § 201.407(a)(3)(ii)).

FDA may require a statement in the “Uses” section of full product information describing the relative effectiveness of doses within the approved range of doses (see proposed § 201.407(a)(3)(iii)). This requirement primarily pertains to OTC new animal drugs that affect the structure or function of the body of an animal (section 201(g)(1)(C) of the FD&C Act) but are not intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease (section 201(g)(1)(B) of the FD&C Act), *e.g.*, drugs that increase the rate of weight gain or feed efficiency in food-producing animals. For these new animal drugs, all doses within the range presented on the approved labeling must be effective for their intended use(s) (see 21 CFR 514.4(b)(2)(i)). For new animal drugs intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease, the lowest dose of the dose range must be effective for the intended use(s). However, the doses within the approved range do not need to be more effective than any other doses within the same range. For OTC new animal drugs approved for structure or function indications, if the highest approved dose(s) is not more effective compared to the next lower approved dose(s), the proposed rule would be able to require a statement in the “Uses” section to inform the user that a higher dose(s) is not more effective than the next lower dose(s).

For safety and/or effectiveness reasons, we may require a statement(s) in the “Uses” section of full product information identifying animals for which the OTC new animal drug has not been approved or conditionally approved (see proposed § 201.407(a)(3)(iv)).

*d. Extralabel use statement.* The proposed rule would require this section of full product information to include an extralabel use statement (see proposed § 201.407(a)(4)). In accordance with part 530, extralabel use of approved new animal drugs is not permitted except by or on the order of

a licensed veterinarian and under the conditions described in that chapter. The required statement would be: “It is a violation of Federal law to use this drug product other than as directed in the labeling or as directed by your veterinarian.” It is important for the layperson to know when it is a violation of Federal law to use drugs in animals in an extralabel manner.

*e. Extralabel use prohibition statement.* For approved new animal drugs prohibited from extralabel use, in accordance with § 530.41, the proposed rule would require this section of full product information to include an extralabel use prohibition statement, as described in proposed § 201.405(a)(5) for full prescribing information for Rx new animal drugs (see proposed § 201.407(a)(5)). Few OTC new animal drugs are prohibited from extralabel use under § 530.41. However, for the rare situation in which an approved OTC new animal drug is prohibited from extralabel use under § 530.41, this statement would be included in addition to the appropriate extralabel use statement that would be required by proposed § 201.407(a)(4).

*f. “Description.”* The proposed rule would require this section of full product information to have the heading “Description,” followed by a description of the new animal drug. The description would include the proprietary name of the finished drug product and established name of the drug product, and the route(s) of administration and dosage form if not included as part of the established name. The description would also include identifying characteristics of the dosage form, such as color, shape, coating, scoring, and imprinting. All approved and available strengths or concentrations of the new animal drug to which full product information applies would need to be identified in this section of full product information. If the drug product was sterile, this fact would also be identified in this section of full product information (see proposed § 201.407(a)(6)).

When inactive ingredients are provided on the labeling, the proposed rule would require they be listed in the “Description” section in decreasing order of predominance, by weight or concentration (see proposed § 201.407(a)(6)(viii)). We encourage sponsors to list all inactive ingredients on labeling to better inform users about the product.

*g. “Warnings.”* The proposed rule would require this section of full product information for all approved or conditionally approved OTC new animal drugs, and it would have the

heading “Warnings” (see proposed § 201.407(a)(7)). This section of full product information would be similar to the “Warnings and Precautions” section proposed for full prescribing information for Rx new animal drugs, as described in proposed § 201.405(a)(10). However, “precautions” would be excluded from this section of full product information and instead be provided in the “Additional Recommendations” section of full product information, as described in proposed § 201.407(a)(8). A more complete explanation of the basis for this proposal is provided in the discussion of the “Animal Safety Warnings” subsection for OTC new animal drugs in proposed § 201.407(a)(7)(iii).

*i. “Withdrawal Periods and Residue Warnings” or “Withdrawal Periods.”* All OTC new animal drugs approved or conditionally approved for use in food-producing animals, would be required to have as the first subsection of the “Warnings” section of full product information a subsection with the heading “Withdrawal Periods and Residue Warnings” or “Withdrawal Periods.” This subsection would provide human food safety warnings, including milk discard times, withdrawal periods, and residue warning statements, as applicable to the new animal drug (see proposed § 201.407(a)(7)(i)). This subsection of full product information would be the same as described in proposed § 201.405(a)(10)(i) for full prescribing information for Rx new animal drugs.

*ii. “User Safety Warnings.”* The proposed rule would require this subsection of the “Warnings” section of full product information to have the heading “User Safety Warnings,” followed by the user safety warnings (see proposed § 201.407(a)(7)(ii)). This subsection of full product information would be the same as described in proposed § 201.405(a)(10)(ii) for full prescribing information for Rx new animal drugs.

*iii. “Animal Safety Warnings.”* For OTC new animal drugs with contraindications, target animal safety warnings that identify any serious adverse reaction or potential hazard to the target animal(s) associated with the use of the new animal drug, adverse reactions, or post-approval adverse drug experiences, the proposed rule would require this subsection of the “Warnings” section of full product information to have the heading “Animal Safety Warnings,” followed by the contraindications, target animal safety warnings, adverse reactions, and post-approval adverse drug experiences

(see proposed § 201.407(a)(7)(iii)). This proposed subsection of full product information would differ in some ways from the “Animal Safety Warnings and Precautions” subsection of full prescribing information proposed for Rx new animal drugs, as described in proposed § 201.405(a)(10)(iii), and these differences are the basis for the different proposed titles of these sections, *i.e.*, “Warnings” for OTC new animal drugs versus “Warnings and Precautions” for Rx new animal drugs.

The definition of “precautions” in proposed § 201.403 is “any special care to be exercised for safe and effective use of the new animal drug. This may include recommended screening, monitoring, or diagnostic tests.” Precautions related to Rx new animal drugs may include screening, special care and monitoring, or diagnostic tests intended to be performed by a veterinarian. Furthermore, precautions related to Rx new animal drugs are often related to, and difficult to distinguish from, target animal safety warnings. On the other hand, OTC new animal drugs do not require professional veterinary expertise to properly administer the drug, provide adequate post-treatment care, or monitor effects after use of the drug. For OTC new animal drugs, precautions provide additional recommendations to the layperson and are distinguishable from target animal safety warnings. For example, this may include information on when to administer the drug relative to feeding, or a recommendation to have a sound mastitis monitoring program before using the drug, etc. This advice is distinguishable from warnings for OTC new animal drugs. Therefore, for better clarity to the layperson, we propose that precautions for OTC new animal drugs not be included in the “Animal Safety Warnings” section of full product information and instead would be included in a separate section called “Additional Recommendations,” as described in proposed § 201.407(a)(8).

In addition, the “Animal Safety Warnings” subsection of full product information for OTC new animal drugs would differ from the “Animal Safety Warnings and Precautions” subsection of full prescribing information for Rx new animal drugs in terms of presentation of warning information. For OTC new animal drugs, all potential risks of the drug to the target animal would be included: contraindications, target animal safety warnings, adverse reactions, and post-approval adverse drug experiences as determined by FDA. For Rx new animal drugs, this information would be provided in

different sections of full prescribing information.

For OTC new animal drugs, including all potential risks to the target animal in one subsection of full product information might be clearer for the layperson and increase the likelihood that all of the information would be read. Furthermore, identifying the risks to the target animal on labeling as “contraindications,” “target animal safety warnings,” “adverse reactions,” or “post-approval adverse drug experience” may be confusing to a layperson because they may not know the differences between the terms. The subsection heading “Animal Safety Warnings” would be understood by the layperson as meaning risks to the target animal. Therefore, the proposed rule would require that all risks to the target animal for OTC new animal drugs be simply identified as “Animal Safety Warnings” and placed in this subsection of full product information. All risk information listed under “Animal Safety Warnings” would be required to be listed in decreasing order of severity to emphasize the most critical risks to the target animal (see proposed § 201.407(a)(7)(iii)).

iv. “*Environmental Warnings.*” For new animal drugs having environmental warnings, the proposed rule would require this subsection of the “Warnings” section of full product information to have the heading “Environmental Warnings,” followed by the environmental warnings (see proposed § 201.407(a)(7)(iv)). This subsection of full product information would be the same as described in proposed § 201.405(a)(10)(iv) for full prescribing information for Rx new animal drugs.

v. “*Other Warnings.*” For OTC new animal drugs having warnings not more appropriately placed in other “Warnings” subsections, the proposed rule would require the last subsection of the “Warnings” section of full product information to have the heading “Other Warnings,” followed by those warnings (see proposed § 201.407(a)(7)(v)). This subsection of full product information would be the same as described in proposed § 201.405(a)(10)(v) for full prescribing information for Rx new animal drugs.

h. “*Additional Recommendations.*” For OTC new animal drugs having precautions, the proposed rule would require this section of full product information to have the heading “Additional Recommendations,” followed by all precautions (see proposed § 201.407(a)(8)). As described in its proposed definition, precautions include any special care to be exercised

for safe and effective use of the new animal drug. As discussed with respect to proposed § 201.407(a)(7)(iii), regarding “Animal Safety Warnings,” precautions are distinguishable from target animal safety warnings for OTC new animal drugs. However, because the term “precautions” as intended by these proposed regulations may not be known or understood by the layperson, the title “Additional Recommendations” is proposed.

i. “*Other Effects You May Notice.*” For OTC new animal drugs that have effects on the target animal(s) that are not considered contraindications, target animal safety warnings, adverse reactions, or post-approval adverse drug experiences, and FDA determines these effects are required to be described on labeling, the proposed rule would require this section of full product information to have the heading “Other Effects You May Notice,” followed by a description of the effects (see proposed § 201.407(a)(9)). We consider this information important for owners of animals, and this information is currently provided on the labeling of some OTC new animal drugs.

For example, some OTC new animal drugs approved for increased rate of weight gain and/or feed efficiency in feedlot beef cattle have effects on the leanness or tenderness of the carcass of those animals. Similarly, OTC new animal drugs that increase milk production in dairy cows or the efficiency by which they produce milk may alter the fat percent content of the milk. These effects, which are currently described on the approved labeling for these products, are not considered negative health effects on the target animal nor are they of human food safety concern. However, these effects could be mistaken for symptoms of an underlying health problem in the target animal, such as poor nutritional status. For this reason, information of this type may be considered material under section 201(n) of the FD&C Act such that it would be required to be disclosed in the labeling for these products on the basis that such disclosures may preclude unnecessary concern and inappropriate medical treatment. Similarly, some topically applied OTC new animal drugs for companion animals might permanently (but harmlessly) alter the color of the fur at the application site. These types of potential effects that are not safety concerns, but rather provide important information to the layperson, would be included in this section of full product information.

j. “*Directions.*” The proposed rule would require this section of full

product information to have the heading “Directions,” followed by the directions for use of the OTC new animal drug for each indication and target animal (see proposed § 201.407(a)(10)). The corresponding section of full prescribing information for Rx new animal drugs would be called “Dosage and Administration,” as described in proposed § 201.405(a)(9). However, for OTC new animal drugs, the term “Directions” may be better understood by the layperson. In addition, the term “Directions” is also used in labeling of OTC human drugs (see § 201.66(c)(6)).

The “Directions” section of full product information is intentionally proposed for placement after the “Warnings” section. This is in contrast to the “Dosage and Administration” section in full prescribing information for Rx new animal drugs, which, except for “Boxed Warnings,” would be placed before “Contraindications,” “Warnings and Precautions,” “Adverse Reactions,” and other information about the effects of the drug. The intent in presenting “Directions” after the “Warnings” section in full product information for OTC new animal drugs is to increase the likelihood that the layperson will read the “Warnings” section before using the drug. This placement approach is similar to that used in labeling of OTC human drugs (see § 201.66(c)(6)).

The “Directions” section of full product information would be required to include information necessary for treatment of the animal with the OTC new animal drug in accordance with FDA approval or conditional approval, including route(s) of administration; specific site(s) of administration, if applicable; dose or dose range, intervals between doses, if applicable; and duration of treatment. For some injectable products, FDA may require a statement of maximum volume per injection site to facilitate the drug’s safe and effective use, and the proposed rule would require this information to be included in this section of full product information. Other required dosage and administration information would be included in this section of full product information. See proposed § 201.407(a)(10).

k. “*Net Contents.*” The proposed rule would require this section of full product information, when presented on the label or the secondary container labeling, to have the heading “Net Contents,” followed by the contents of the immediate container, in accordance with § 201.62 (21 CFR 201.62), or the secondary container, respectively. The proposed rule would exclude a “Net Contents” section from package inserts (see proposed § 201.407(a)(11)).

l. “*How Supplied.*” The proposed rule would require this section of full product information to have the heading “How Supplied,” followed by information on available strengths, concentrations, and container sizes to which the labeling applies (see proposed § 201.407(a)(12)). This section of full product information would be the same as described in proposed § 201.405(a)(19) for full prescribing information for Rx new animal drugs.

m. “*Storage, Handling, and Disposal.*” The proposed rule would require this section of full product information to have the heading “Storage, Handling, and Disposal,” followed by drug storage information, as well as any required handling and drug disposal information (see proposed § 201.407(a)(13)). This section of full product information would be the same as described in proposed § 201.405(a)(20) for full prescribing information for Rx new animal drugs.

n. “*Questions/Comments?*” The proposed rule would require this section of full product information to have the heading “Questions/Comments?,” followed by the sponsor’s contact information for consumers to facilitate requesting additional information or to report suspected adverse drug experiences. FDA’s contact information for voluntary reporting of adverse drug experiences for animal drugs would also be required (see proposed § 201.407(a)(14)). The “Questions/Comments?” section of full product information would be similar to the “Contact Information” section in proposed § 201.405(a)(12) for full prescribing information for Rx new animal drugs.

The “Questions/Comments?” heading might be clearer than “Contact Information” to the layperson using OTC new animal drugs. Furthermore, the heading “Questions?” or “Questions or comments?” is used for OTC human drug labeling (see § 201.66(c)(9)). Also, the phrase “To report side effects, contact . . .” is proposed for full product information for OTC new animal drugs rather than “To report suspected adverse drug experiences, contact . . .,” which is the phrase proposed for full prescribing information for Rx new animal drugs. The term “side effects” may be better understood by the layperson than the term “suspected adverse drug experiences.” Also, the term “side effects” may be used in labeling of OTC human drugs (see § 201.66(c)(5)(vii) (21 CFR 201.66(c)(5)(vii))).

The sponsor’s contact information would be the name of the manufacturer, packer, or distributor, whichever is

identified in the “Name and place of business” section of full product information (see proposed § 201.407(a)(16)). If more than one business is identified in the “Name and place of business” section of full product information, the drug sponsor would select the most appropriate of these businesses to use in the “Questions/Comments?” section to provide additional information about the OTC new animal drug and to contact regarding suspected adverse drug experiences.

The statements in this section of full product information would be required to be structured as follows: “Contact [insert name of business] at [insert business telephone number] or [insert business web address]. To report side effects, contact [insert name of business] at [insert business telephone number]. For additional information about reporting side effects for animal drugs, contact FDA at [insert current FDA telephone number for voluntary reporting of adverse drug experiences] or [insert current FDA web address for voluntary reporting of adverse drug experiences].” Sponsors can search FDA’s website or contact FDA by telephone to find the current FDA telephone number or web address for voluntary reporting of adverse drug experiences for animal drugs.

o. “*NADA/ANADA approval statement.*” For approved new animal drugs or approved generic new animal drugs, the proposed rule would require this section of full product information to include an “NADA approval statement” or “ANADA approval statement,” respectively (see proposed § 201.407(a)(15)). This section of full product information would be the same as described in proposed § 201.405(a)(21) for full prescribing information for Rx new animal drugs.

p. “*Name and place of business.*” The proposed rule would require this section of full product information to identify the name and place of business of the manufacturer, packer, or distributor (see proposed § 201.407(a)(16)). This section of full product information would be the same as described in proposed § 201.405(a)(22) for full prescribing information for Rx new animal drugs.

q. “*Lot Number and Expiration Date.*” The proposed rule would require this section of full product information when provided on the secondary container labeling or the label. Package inserts are excluded from this requirement because they might apply to multiple lots of secondary or immediate containers of the OTC new animal drug. When full product

information is provided on the secondary container labeling or the label, this section would be required to have the heading “Lot Number and Expiration Date,” followed by the identifying lot or control number of the OTC new animal drug within the secondary container or immediate container (see proposed § 201.407(a)(17)). A lot or control number would help us more easily to identify and trace back a specific lot of a product should a problem be reported to FDA. The proposed rule would also require this section to include the expiration date of the OTC new animal drug within the secondary container or immediate container, in accordance with § 201.17. An expiration date better ensures that the new animal drug would not be used after it expires.

Alternatively, the proposed rule would allow for this section of full product information to refer to the location on the secondary container labeling, secondary container, label, or immediate container where the lot or control number and expiration date are printed (see proposed § 201.407(a)(17)). As an example, if the lot number and expiration date are printed on the bottom flap of a secondary container, then the secondary container labeling may state in this section, “See carton bottom flap for lot number and expiration date.” However, if full product information is provided on the secondary container labeling, in accordance with § 201.17, the proposed rule would allow an expiration date to be excluded from the secondary container labeling or secondary container if the expiration date provided on the label or immediate container is easily legible through the secondary container.

*r. “Revision Date.”* The proposed rule would require this section of full product information to have the heading “Revision Date,” followed by the date of the most recent revision of the component of labeling that provides full product information, listing the month followed by the year (see proposed § 201.407(a)(18)). This information is important to ensure that the most current approved version of the labeling is being used.

## 2. OTC New Animal Drug Label Not Providing Full Product Information (OTC Label) (Proposed § 201.407(b))

The proposed rule would establish content and format requirements for the information presented on the label for approved or conditionally approved OTC new animal drugs (OTC label) where the label does not provide full product information (see proposed

§ 201.407(b)). As described previously in section V.E.1 regarding labeling providing full product information, the label for an OTC new animal drug would include full product information only if there is no package insert or secondary container labeling.

Proposed § 201.407(b) would apply to OTC labels that are of adequate size to contain the proposed required information per that paragraph, whereas proposed § 201.407(c) would apply to small labels for OTC new animal drugs that are not of adequate size to contain all the proposed required information in proposed § 201.407(b).

OTC new animal drugs labels to which § 201.407(b) would apply may consist of a single panel, a front panel and one side or back panel, or a front panel and multiple side and/or back panels, and the proposed rule would provide for such label designs (see proposed § 201.407(b)). For OTC labels with a front panel and one side or back panel, the proposed rule would require certain information for the front panel (see proposed § 201.407(b)(1)), and the side or back panel (see proposed § 201.407(b)(2)). For OTC labels consisting of a single panel, the proposed rule would require the information identified in proposed § 201.407(b)(1) followed by the information identified in proposed § 201.407(b)(2), in order, on the single panel. For OTC labels with a front panel and multiple side and/or back panels, the information identified in proposed § 201.407(b)(1) followed by the information identified in proposed § 201.407(b)(2) would be required in order, starting on the front panel, continuing on the panel immediately to the right of the front panel, and continuing to fill the panels to the right until all of the information in proposed § 201.407(b)(1) and (2) was presented. In all instances, the information in proposed § 201.407(b)(2)(iii) and (iv), concerning active ingredients and inactive ingredients, would need to appear on the same panel.

*a. Front panel.* The proposed rule would require the following information to be presented on the front panel of the OTC label for an approved or conditionally approved OTC new animal drug and in the following order (see proposed § 201.407(b)(1)). Unless otherwise indicated, this information would be the same as that required by proposed § 201.405(a) for full prescribing information for approved or conditionally approved OTC new animal drugs or proposed § 201.407(a) for full product information for approved or conditionally approved OTC new animal drugs.

*i. Drug product identification.* The proposed rule would require this section of the OTC label to include drug product identification (see § 201.407(b)(1)(i)). This information may help the user to identify the product quickly and correctly and distinguish it from other, similar products. The information included in this section of the OTC label would include the same information as that in the drug product identification section of full product information, as described in proposed § 201.407(a)(1), in addition to a statement that the drug product is sterile, if applicable. Full product information would require a drug product identification section and “Description” section. Full product information for sterile OTC new animal drugs would be required to identify in the “Description” section that the drug is sterile. However, due to space limitations, no “Description” section is proposed for the OTC label. Instead, the drug product identification section of the OTC label for sterile OTC new animal drugs would be required to state that the drug product is sterile. See proposed § 201.407(b)(1)(i).

*ii. Conditional approval statement.* For conditionally approved new animal drugs, the proposed rule would require this section of the OTC label to include a conditional approval statement, as described in proposed § 201.405(a)(3)) for full prescribing information for Rx new animal drugs (see proposed § 201.407(b)(1)(ii)).

*iii. “Uses.”* The proposed rule would require this section of the OTC label to have the heading “Uses,” followed by the “Uses” section, as described in proposed § 201.407(a)(3) for full product information. If there is insufficient space on the OTC label for the complete “Uses” section as described in proposed § 201.407(a)(3), then the proposed rule would require the sponsor to include in this section of the OTC label the statement required in proposed § 201.407(a)(3)(i), *i.e.*, “For [indication(s)] in [target animal(s)].” If there is insufficient space on the OTC label for the statement in proposed § 201.407(a)(3)(i), then an abbreviated version of the statement would be required: “For [abbreviated indication(s)] in [target animal(s)].” In either situation where there is insufficient space on the OTC label for the complete “Uses” section as specified in proposed § 201.407(a)(3), the required statement would be followed by one of the following statements: “See package insert for complete ‘Uses’” if full product information is provided on a package insert; or “See package labeling for

complete ‘Uses’” if full product information is provided on the secondary container labeling. See proposed § 201.407(b)(1)(iii). The complete “Uses” section as described in proposed § 201.407(a)(3) may exceed the available space on the OTC label if, for example, it includes specific conditions of use (proposed § 201.407(a)(3)(ii)), a statement describing the relative effectiveness of doses within the approved range of doses (proposed § 201.407(a)(3)(iii)), animals for which the new animal drug is not approved or conditionally approved (proposed § 201.407(a)(3)(iv)), and/or the indication(s) is lengthy and/or complex.

iv. *Extralabel use statement.* The proposed rule would require this section of the OTC label to include the extralabel use statement, as described in proposed § 201.407(a)(4) for full product information (see proposed § 201.407(b)(1)(iv)).

v. *Extralabel use prohibition statement.* For approved OTC new animal drugs prohibited from extralabel use, in accordance with § 530.41, the proposed rule would require this section of the OTC label to include the extralabel use prohibition statement, as described in proposed § 201.405(a)(5) for full prescribing information for Rx new animal drugs (see proposed § 201.407(b)(1)(v)).

vi. *“Withdrawal Periods and Residue Warnings” or “Withdrawal Periods.”* For new animal drugs approved or conditionally approved for use in food-producing animals, the proposed rule would require this section of the OTC label to have the heading “Withdrawal Periods and Residue Warnings” or “Withdrawal Periods,” followed by all human food safety warnings, including milk discard times, withdrawal periods, and residue warning statements, as described in proposed § 201.405(a)(10)(i) for full prescribing information for Rx new animal drugs. If there is insufficient space on the front panel of the OTC labels with only a front panel and one side or back panel, the proposed rule would require this section to be provided on the side or back panel of the OTC label immediately following the complete product information statement specified in proposed § 201.407(b)(2)(i). See proposed § 201.407(b)(1)(vi).

vii. *“Net Contents.”* The proposed rule would require this section of the OTC label to have the heading “Net Contents,” followed by the contents of the immediate container, in accordance with § 201.62 (see proposed § 201.407(b)(1)(vii)).

viii. *NADA/ANADA approval statement.* For approved new animal

drugs or approved generic new animal drugs, the proposed rule would require this section of the OTC label to include the NADA or ANADA approval statement, as described in proposed § 201.405(a)(21) for full prescribing information for Rx new animal drugs (see proposed § 201.407(b)(1)(viii)).

b. *Side or back panel.* The proposed rule would require the following information to be presented on the side or back panel of the OTC label for an approved or conditionally approved OTC new animal drug in the following order (see proposed § 201.407(b)(2)). Unless otherwise indicated, this information would be the same as that required by proposed § 201.405(a) for full prescribing information for approved or conditionally approved Rx new animal drugs or proposed § 201.407(a) for full product information for approved or conditionally approved OTC new animal drugs.

i. *Complete product information statement.* The proposed rule would require this section of the OTC label to include one of two statements (see proposed § 201.407(b)(2)(i)). If full product information is provided on the package insert, the following statement would be used: “Before using this drug, read package insert for complete product information.” If full product information is provided on the secondary container labeling, the following statement would be used: “Before using this drug, read package labeling for complete product information.” Because full product information would not be provided on the OTC label, the purpose of the statements would be to remind the user to read full product information before using the OTC new animal drug.

ii. *“Directions.”* The proposed rule would require this section of the OTC label to have the heading “Directions,” followed by the “Directions” section as described in proposed § 201.407(a)(10) for full product information. If there is insufficient space on the OTC label for the complete requirements as specified in § 201.407(a)(10), or if it is necessary for additional information provided in full product information that is not provided on the OTC label to be read before administering the drug (e.g., complete warnings and/or additional recommendations), then FDA may exclude this section from the OTC label (see proposed § 201.407(b)(2)(ii)). For example, if an OTC new animal drug is approved for multiple indications and/or target animals, there may be different target animal safety warnings or precautions associated with each indication and/or target animal. This information would be provided in full

product information for the OTC new animal drug (in the “Animal Safety Warnings” subsection and “Additional Recommendations” section, respectively), but there may be insufficient space for it on the OTC label. Excluding the “Directions” section from the OTC label in this situation helps to ensure that the user would read full product information, which would include the “Directions” section as well as the “Animal Safety Warnings” subsection and “Additional Recommendations” section, before treating the animal. The user would also be reminded to read full product information before using the drug via the complete product information statement that would be required in the previous section of the OTC label by proposed § 201.407(b)(2)(i).

iii. *“Active Ingredient” or “Active Ingredients.”* The proposed rule would require this section of the OTC label to have the heading “Active Ingredient” or “Active Ingredients,” followed by the established name and strength or concentration of each active ingredient (see proposed § 201.407(b)(2)(iii)).

iv. *“Inactive Ingredients.”* When inactive ingredients are provided on the OTC label, the proposed rule would require they be listed in the “Inactive Ingredients” section in decreasing order of predominance, by weight or concentration, as described in proposed § 201.405(a)(6)(viii) for full prescribing information for Rx new animal drugs (see proposed § 201.407(b)(2)(iv)).

v. *“Storage, Handling, and Disposal.”* The proposed rule would require this section of the OTC label to have the heading “Storage, Handling, and Disposal,” followed by drug storage, handling, and disposal information, as described in proposed § 201.405(a)(20) for full prescribing information for Rx new animal drugs (see proposed § 201.407(b)(2)(v)).

vi. *Name and place of business.* The proposed rule would require this section of the OTC label to identify the name and place of business of the manufacturer, packer, or distributor, as required in section 502(b) of the FD&C Act (see proposed § 201.407(b)(2)(vi)).

vii. *“Lot Number and Expiration Date” or “Lot Number.”* The proposed rule would require this section of the OTC label to have the heading “Lot Number and Expiration Date” or “Lot Number,” followed by the identifying lot or control number of the OTC new animal drug within the immediate container (see proposed § 201.407(b)(2)(vii)). A lot or control number would allow us more easily to identify and trace back a specific lot of a product should a problem be reported

to FDA. We would also require this section of the OTC label to include the expiration date of the OTC new animal drug within the immediate container, in accordance with § 201.17. An expiration date on the OTC label better ensures that the new animal drug would not be used after it expires. Alternatively, the proposed rule would allow for this section to refer to the location on the OTC label or immediate container where the lot or control number and expiration date are printed (see proposed § 201.407(b)(2)(vii)). As an example, if the lot number and expiration date are printed at the top of the immediate container, then the OTC label may state in this section, “See top of container for lot number and expiration date.” If the immediate container provides a single dose of the OTC new animal drug and is packaged individually in a secondary container that provides an expiration date on the secondary container labeling or secondary container, the proposed rule would not require an expiration date on the OTC label or immediate container, in accordance with § 201.17. Under such provision, this section of the OTC label would be required to be entitled “Lot Number.”

viii. “*Revision Date.*” The proposed rule would require the last section of the OTC label to have the heading “Revision Date,” followed by the date of the most recent revision of the OTC label, listing the month followed by the year (see proposed § 201.407(b)(2)(viii)).

### 3. OTC New Animal Drug Small Label (OTC Small Label) (Proposed § 201.407(c))

The proposed rule would establish content and format requirements for the small label for OTC new animal drugs (OTC small label) where the label does not provide full product information (see proposed § 201.407(c)).

Some immediate containers, such as blister packs, pre-filled syringes, and small vials, are so small that only a minimal amount of information can be included on their label. The proposed rule would establish requirements for OTC small labels for approved or conditionally approved OTC new animal drugs (see proposed § 201.407(c)). We recognize that the size of the label is dependent upon the size of the immediate container. If an immediate container lacks sufficient space to contain a label that accommodates all of the information required by proposed § 201.407(a) or (b), the requirements of proposed § 201.407(c) would instead apply. We would ordinarily make this determination during the review of the

new animal drug and its labeling, taking into consideration the readability and legibility of the information.

The proposed rule would require the following information to be presented on the OTC small label for an approved or conditionally approved OTC new animal drug and in the following order (see proposed § 201.407(c)).

*a. Proprietary name of the finished drug product.* The proposed rule would require this section of the OTC small label to include the proprietary name of the finished drug product (see proposed § 201.407(c)(1)). This requirement already exists for small labels for drugs in general in § 201.10(i)(1), but is repeated in these proposed regulations to include all requirements for labeling of approved or conditionally approved new animal drugs in proposed subpart H.

*b. Established name of the drug product.* The proposed rule would require this section of the OTC small label to include the established name of the drug product (see proposed § 201.407(c)(2)). This requirement already exists for small labels for drugs in general in § 201.10(i)(1), but is repeated in these proposed regulations to include all requirements for labeling of approved or conditionally approved new animal drugs in proposed subpart H.

*c. Active ingredient(s).* The proposed rule would require this section of the OTC small label to include the established name and strength or concentration of each active ingredient (see proposed § 201.407(c)(3)). This information should reduce the risk of miscalculating doses.

*d. “For [target animal(s)] only.”* The proposed rule would require this section of the OTC small label to include a brief listing of the approved target animal(s) as follows: “For [target animal(s)] only” (see proposed § 201.407(c)(4)). The brief listing of the approved target animal(s) is used in place of full “Uses” information because OTC small labels lack sufficient space. This listing would not require as much space on the OTC small label.

*e. Complete product information statement.* The proposed rule would require this section of the OTC small label to include one of two statements. If full product information is provided on the package insert, the following statement would be used: “Read package insert for complete product information”. If full product information is provided on the secondary container labeling, the following statement would be used: “Read package labeling for complete product information.” See proposed

§ 201.407(c)(5). Because full product information would not be provided on the OTC small label, the purpose of the statements would be to remind the user to read full product information before using the OTC new animal drug.

*f. “Net Contents.”* The proposed rule would require this section of the OTC small label to have the heading “Net Contents,” followed by the contents of the immediate container, in accordance with § 201.62 (see proposed § 201.407(c)(6)).

*g. Name and place of business.* The proposed rule would require this section of the OTC small label to identify the name and place of business of the manufacturer, packer, or distributor, as required in section 502(b) of the FD&C Act (see proposed § 201.407(c)(7)).

*h. “Lot, Exp. and Storage” or “Lot and Storage.”* The proposed rule would require this section of the OTC small label to have the heading “Lot, Exp. and Storage” or “Lot and Storage,” followed by the identifying lot or control number of the OTC new animal drug within the immediate container. A lot or control number would allow FDA more easily to identify and trace back a specific lot of a product should a problem be reported to FDA. The proposed rule would also require this section of the OTC small label to include the expiration date of the OTC new animal drug within the immediate container, in accordance with § 201.17. An expiration date on the OTC small label better ensures that the new animal drug would not be used after it expires.

The proposed rule would also require this section of the OTC small label to include and drug storage information for the new animal drug (see proposed § 201.407(c)(8)). Storage information is necessary to maintain potency of the drug before its expiration date. Requiring this information on the OTC small label is needed for safe and effective use of new animal drugs. If the immediate container provides a single dose of the OTC new animal drug and is packaged individually in a secondary container that provides an expiration date on the secondary container labeling or secondary container, the proposed rule would not require an expiration date on the immediate container or OTC small label, in accordance with § 201.17, in which case this section of the OTC small label would be required to be entitled “Lot and Storage.”

*i. “Revision Date.”* The proposed rule would require this section of the OTC small label to have the heading “Revision Date,” followed by the date of the most recent revision of the OTC small label, listing the month followed

by the year (see proposed § 201.407(c)(9)).

4. Labeling for Secondary Containers for OTC New Animal Drugs That Include a Package Insert (OTC Secondary Container Labeling) (Proposed § 201.407(d))

The proposed rule would establish content and format requirements for the information on the labeling for secondary containers of approved or conditionally approved OTC new animal drugs that include a package insert (OTC secondary container labeling) (see proposed § 201.407(d)). In this situation, the package insert would be required by the proposed regulations to include full product information as in proposed § 201.407(a)).

In accordance with section 201(k) of the FD&C Act, the OTC secondary container labeling could exclude any information described in proposed § 201.407(d) that would be required to appear on the OTC label or OTC small label (see proposed § 201.407(b) or (c), respectively) if such information on the OTC label or OTC small label was easily legible through the secondary container.

The OTC secondary container labeling to which proposed § 201.407(d) would apply may consist of a front panel and one side or back panel, or a front panel and multiple side and/or back panels. Proposed § 201.407(d) would provide for such OTC secondary container labeling designs. For OTC secondary container labeling with a front panel and one side or back panel, proposed § 201.407(d)(1) would provide required information for the front panel, and proposed § 201.407(d)(2) would provide required information for the side or back panel. For OTC secondary container labeling with a front panel and multiple side and/or back panels, the information identified in proposed § 201.407(d)(1) followed by the information identified in proposed § 201.407(d)(2) would be required in order, starting on the front panel, continuing on the panel immediately to the right of the front panel, and continuing to fill the panels to the right until all of the information in proposed § 201.407(d)(1) and (2) was presented. In all instances, the information proposed in § 201.407(d)(2)(iv) and (v), concerning active ingredients and inactive ingredients, would need to appear on the same panel.

*a. Front panel.* The proposed rule would require the following information to be presented on the front panel of the OTC secondary container labeling and in the following order (see proposed § 201.407(d)(1)). Unless otherwise indicated, this information would be the

same as that required by proposed § 201.405(a) for full prescribing information for approved or conditionally approved Rx new animal drugs or proposed § 201.407(a) for full product information for approved or conditionally approved OTC new animal drugs.

*i. Drug product identification.* The proposed rule would require this section of the OTC secondary container labeling to include drug product identification (see proposed § 201.407(d)(1)(i)). The information would be the same as that included in the drug product identification section for full product information, as described in proposed § 201.407(a)(1), and would also identify if the drug product is sterile. Full product information would require a drug product identification section and a “Description” section. Full product information for sterile OTC new animal drugs would be required to identify in the “Description” section that the drug is sterile. However, due to space limitations, no “Description” section would be required on the OTC secondary container labeling. Instead, the drug product identification section of the OTC secondary container labeling for sterile OTC new animal drugs would be required to state that the drug is sterile.

*ii. Conditional approval statement.* For conditionally approved OTC new animal drugs, the proposed rule would require this section of the OTC secondary container labeling to include a conditional approval statement, as described in proposed § 201.405(a)(3) for full prescribing information for Rx new animal drugs (see proposed § 201.407(d)(1)(ii)).

*iii. “Uses.”* The proposed rule would require this section of the OTC secondary container labeling to have the heading “Uses,” followed by the “Uses” section, as described in proposed § 201.407(a)(3) for full product information (see proposed § 201.407(d)(1)(iii)).

*iv. Extralabel use statement.* The proposed rule would require this section of the OTC secondary container labeling to include the extralabel use statement as described in proposed § 201.407(a)(4) for full product information (see proposed § 201.407(d)(1)(iv)).

*v. Extralabel use prohibition statement.* For approved new animal drugs prohibited from extralabel use, in accordance with § 530.41, the proposed rule would require this section of the OTC secondary container labeling to include the extralabel use prohibition statement, as described in proposed

§ 201.405(a)(5) for full prescribing information for Rx new animal drugs (see proposed § 201.407(d)(1)(v)).

*vi. “Net Contents.”* The proposed rule would require this section of the OTC secondary container labeling to have the heading “Net Contents,” followed by the contents of the secondary container (see proposed § 201.407(d)(1)(vi)).

*vii. NADA/ANADA approval statement.* For approved new animal drugs or approved generic new animal drugs, the proposed rule would require this section of the OTC secondary container labeling to include the NADA or ANADA approval statement, as described in proposed § 201.405(a)(21) for full prescribing information for Rx new animal drugs (see proposed § 201.407(d)(1)(vii)).

*b. Side or back panel.* The proposed rule would require the following information to be presented on the side or back panel of the OTC secondary container labeling and in the following order (see proposed § 201.407(d)(2)). Unless otherwise indicated, this information would be the same as that required by proposed § 201.405(a) for full prescribing information for approved or conditionally approved Rx new animal drugs or proposed § 201.407(a) for full product information for approved or conditionally OTC new animal drugs.

*i. Complete product information statement.* The proposed rule would require this section of the OTC secondary container labeling to include the statement, “Before using this drug, read package insert for complete product information” (see proposed § 201.407(d)(2)(i)). Because full product information would not be provided on the OTC secondary container labeling, the purpose of the Complete product information statement would be to remind the user to read full product information before using the OTC new animal drug.

*ii. “Directions.”* The proposed rule would require this section of the OTC secondary container labeling to have the heading “Directions,” followed by the “Directions” section, as described in proposed § 201.407(a)(10) for full product information (see proposed § 201.407(d)(2)(ii)).

*iii. “Warnings.”* The proposed rule would require this section of the OTC secondary container labeling to have the heading “Warnings,” followed by the “Warnings” section, as described in proposed § 201.407(a)(7) for full product information (see proposed § 201.407(d)(2)(iii)).

*iv. “Active Ingredient” or “Active Ingredients.”* The proposed rule would require this section of the OTC

secondary container labeling to have the heading "Active Ingredient" or "Active Ingredients," followed by the established name and strength or concentration of each active ingredient, as described in proposed § 201.407(b)(2)(iii) for the OTC label (see proposed § 201.407(d)(2)(iv)).

v. "Inactive Ingredients." When inactive ingredients are provided on the OTC secondary container labeling, the proposed rule would require they be listed in the "Inactive Ingredients" section by their established name in decreasing order of predominance, by weight or concentration, as described in proposed § 201.405(a)(6)(viii) (see proposed § 201.407(d)(2)(v)).

vi. "Storage, Handling, and Disposal." The proposed rule would require this section of the OTC secondary container labeling to have the heading "Storage, Handling, and Disposal," followed by drug storage, handling, and disposal information, as described in proposed § 201.405(a)(20) for full prescribing information for Rx animal drugs (see proposed § 201.407(d)(2)(vi)).

vii. *Name and place of business.* The proposed rule would require this section of the OTC secondary container labeling to identify the manufacturer, packer, or distributor, as described in proposed § 201.405(a)(22) for full prescribing information for Rx animal drugs (see proposed § 201.407(d)(2)(vii)).

viii. "Lot Number and Expiration Date." The proposed rule would require this section of the OTC secondary container labeling to have the heading "Lot Number and Expiration Date," followed by the identifying lot or control number of the OTC new animal drug within the secondary container. The proposed rule would also require this section of the OTC secondary container labeling to include the expiration date of the OTC new animal drug within the secondary container, in accordance with § 201.17. Alternatively, the proposed rule would allow for this section to refer to the location on the OTC secondary container labeling or secondary container where the lot or control number and expiration date are printed (see proposed § 201.407(d)(2)(viii)). As an example, if the lot number and expiration date are printed on the bottom flap of a secondary container, then the labeling may state in this section, "See carton bottom flap for lot number and expiration date." However, in accordance with § 201.17, the proposed rule would allow an expiration date to be excluded from the OTC secondary container labeling or secondary

container if the expiration date provided on the OTC label, OTC small label, or immediate container is easily legible through the secondary container.

ix. "Revision Date." The proposed rule would require this section of the OTC secondary container labeling to have the heading "Revision Date," followed by the date of the most recent revision of the OTC secondary container labeling, listing the month followed by the year (see proposed § 201.407(d)(2)(ix)).

#### 5. Shipping Labeling for OTC New Animal Drugs (OTC Shipping Labeling) (Proposed § 201.407(e))

The proposed rule would establish content and format requirements for the information on the shipping labeling for approved or conditionally approved OTC new animal drugs (OTC shipping labeling). As defined in proposed § 201.403, shipping labeling is associated with the outermost carton containing immediate containers, secondary containers, and/or multiple unit (multi-unit) cartons of a new animal drug and intended for shipment, but not display, of the product. The proposed rule would require the OTC shipping labeling to include, among additional information, drug product identity, the manufacturer, packer, or distributor, and drug storage and handling conditions. See proposed § 201.407(e).

The proposed rule would require the following information to be presented on the OTC shipping labeling and in the following order (see proposed § 201.407(e)). Unless otherwise indicated, this information would be the same as that required by proposed § 201.405(a) for full prescribing information for approved or conditionally approved Rx new animal drugs or proposed § 201.407(a) for full product information for approved or conditionally approved OTC new animal drugs.

a. *Proprietary name of the finished drug product.* The proposed rule would require this section of the OTC shipping labeling to include the proprietary name of the finished drug product (see proposed § 201.407(e)(1)).

b. *Established name of the drug product.* The proposed rule would require this section of the OTC shipping labeling to include the established name of the drug product (see proposed § 201.407(e)(2)).

c. *Established name and strength or concentration of each active ingredient.* The proposed rule would require this section of the OTC shipping labeling provide the established name and strength or concentration of each active

ingredient (see proposed § 201.407(e)(3)).

d. *Conditional approval statement.*

For conditionally approved OTC new animal drugs, the proposed rule would require this section of the OTC shipping labeling to include a conditional approval statement, as described in proposed § 201.405(a)(3) for full prescribing information for Rx new animal drugs (see proposed § 201.407(e)(4)).

e. "Net Contents." The proposed rule would require this section of the OTC shipping labeling to have the heading "Net Contents," followed by the contents of the shipping carton (see proposed § 201.407(e)(5)).

f. "Storage and Handling." The proposed rule would require this section of the OTC shipping labeling to have the heading "Storage and Handling," followed by drug storage information (see proposed § 201.407(e)(6)). Also, any handling information required for safe and effective use of the new animal drug would be included in this section. Information on disposal of the new animal drug would not be required to be included on the OTC shipping labeling.

g. *NADA/ANADA approval statement.* For approved new animal drugs or approved generic new animal drugs, the proposed rule would require this section of the OTC shipping labeling to include the NADA or ANADA approval statement, as described in proposed § 201.405(a)(21) for full prescribing information for Rx new animal drugs (see proposed § 201.407(e)(7)).

h. *Name and place of business.* The proposed rule would require this section of the OTC shipping labeling to identify the name and place of business of the manufacturer, packer, or distributor, as described in proposed § 201.405(a)(22) for full prescribing information for Rx new animal drugs (see proposed § 201.407(e)(8)).

i. "Lot Number and Expiration Date." The proposed rule would require this section of the OTC shipping labeling to have the heading "Lot Number and Expiration Date," followed by the identifying lot or control number(s) and the expiration date(s) of the OTC new animal drug within the shipping carton (see proposed § 201.407(e)(9)). The shipping carton may contain more than one lot of the OTC new animal drug, and therefore, more than one lot or control number and expiration date may be listed in this section of the OTC shipping labeling.

j. "Revision Date." The proposed rule would require the last section of the OTC shipping labeling to have the heading "Revision Date," followed by

the date of the most recent revision of the OTC shipping labeling, listing the month followed by the year (see proposed § 201.407(e)(10)).

6. Other Approved Labeling for OTC New Animal Drugs (OTC Other Approved Labeling) (Proposed § 201.407(f))

The proposed rule would establish content and format requirements for the information presented on other approved labeling for approved or conditionally approved OTC new animal drugs (OTC other approved labeling) (see proposed § 201.407(f)). OTC other approved labeling includes, but is not limited to, labeling on display cartons and multi-unit cartons (excluding shipping cartons), containing the immediate containers or the secondary containers of the OTC new animal drug.

The proposed rule would require the following information to be presented on the OTC other approved labeling and in the following order (see proposed § 201.407(f)). Unless otherwise indicated, this information would be the same as that required by proposed § 201.405(a) for full prescribing information for approved or conditionally approved Rx new animal drugs or proposed § 201.407(a) for full product information for approved or conditionally approved OTC new animal drugs.

*a. Proprietary name of the finished drug product.* The proposed rule would require this section of the OTC other approved labeling to include the proprietary name of the finished drug product (see proposed § 201.407(f)(1)).

*b. Established name of the drug product.* The proposed rule would require this section of the OTC other approved labeling to include the established name of the drug product (see proposed § 201.407(f)(2)).

*c. Established name and strength or concentration of each active ingredient.* The proposed rule would require this section of the OTC other approved labeling to provide the established name and strength or concentration of each active ingredient (see proposed § 201.407(f)(3)).

*d. Conditional approval statement.* For conditionally approved new animal drugs, the proposed rule would require this section of the OTC other approved labeling to include a conditional approval statement, as described in proposed § 201.405(a)(3) for full prescribing information for Rx animal drugs (see proposed § 201.407(f)(4)).

*e. Extralabel use statement.* The proposed rule would require this section of the OTC other approved

labeling to include the extralabel use statement as described in proposed § 201.407(a)(4) for full product information (see proposed § 201.407(f)(5)).

*f. Extralabel use prohibition statement.* For approved new animal drugs prohibited from extralabel use, in accordance with § 530.41, the proposed rule would require this section of the OTC other approved labeling to include the extralabel use prohibition statement, as described in proposed § 201.405(a)(5) for full prescribing information for Rx new animal drugs (see proposed § 201.407(f)(6)).

*g. "Net Contents."* The proposed rule would require this section of the OTC other approved labeling to have the heading "Net Contents," followed by the contents of the container to which the OTC other approved labeling applies (see proposed § 201.407(f)(7)).

*h. "Storage, Handling, and Disposal."* The proposed rule would require this section of the OTC other approved labeling to have the heading "Storage, Handling, and Disposal," followed by drug storage, handling, and disposal information, as described in proposed § 201.405(a)(20) for full prescribing information for Rx new animal drugs (see proposed § 201.407(f)(8)).

*i. NADA/ANADA approval statement.* For approved new animal drugs or approved generic new animal drugs, the proposed rule would require this section of the OTC other approved labeling to include the NADA or ANADA approval statement, as described in proposed § 201.405(a)(21) for full prescribing information for Rx new animal drugs (see proposed § 201.407(f)(9)).

*j. Name and place of business.* The proposed rule would require this section of the OTC other approved labeling to identify the name and place of business of the manufacturer, packer, or distributor, as described in proposed § 201.405(a)(22) for full prescribing information for Rx new animal drugs (see proposed § 201.407(f)(10)).

*k. "Lot Number and Expiration Date."* The proposed rule would require this section of the OTC other approved labeling to have the heading "Lot Number and Expiration Date," followed by the identifying lot or control number of the OTC new animal drug within the container to which the OTC other approved labeling applies. This section of the OTC other approved labeling would also be required to include the expiration date of the OTC new animal drug within the container to which the OTC other approved labeling applies, in accordance with § 201.17. In accordance with § 201.17, the proposed rule would

allow an expiration date to be excluded from the OTC other approved labeling if the expiration date provided on containers within or their labeling is easily legible through the container to which the OTC other approved labeling applies (see proposed § 201.407(f)(11)).

*l. "Revision Date."* The proposed rule would require the last section of the OTC other approved labeling to have the heading "Revision Date," followed by the date of the most recent revision of the OTC other approved labeling, listing the month followed by the year (see proposed § 201.405(f)(12)).

*F. Content and Format of Labeling for New Animal Drugs for Use in Animal Feeds—Overview (Proposed § 201.409)*

The proposed rule provides content and format requirements for all components of labeling for approved or conditionally approved new animal drugs for use in animal feeds and that are subject to part 558, including VFD drugs. New animal drugs for use in animal feeds are approved in accordance with section 512 of the FD&C Act or conditionally approved in accordance with section 571 of the FD&C Act (see proposed § 201.409). Most combination new animal drugs are currently approved for use in animal feeds or drinking water in accordance with section 512(d)(4) of the FD&C Act. The majority of new animal drugs approved or conditionally approved for use in animal feeds are intended for use in food-producing animals and to be fed to multiple animals at one time.

As described above, proposed § 201.405 ("Content and format for prescription (Rx) new animal drug labeling") would not apply to approved or conditionally approved new animal drugs intended for use in or on animal feeds under the professional supervision of a licensed veterinarian because, in accordance with section 504(a) of the FD&C Act, such drugs are approved or conditionally approved as VFD drugs. The proposed rule would establish the content and format requirements for all components of labeling for approved or conditionally approved new animal drugs intended for use in animal feeds that are subject to part 558, including VFD drugs (see proposed § 201.409).

The proposed rule would require that labeling sections or subsections that do not apply be omitted from the labeling for approved or conditionally approved new animal drugs for use in animal feeds (see proposed § 201.409). For example, new animal drugs approved or conditionally approved for use in animal feeds that are not VFD drugs would not require a VFD cautionary statement section.

FDA determines the final content of each applicable section of labeling during the review of each new animal drug as part of the approval process.

Sponsors of new animal drugs for use in animal feeds often submit an application for approval or conditional approval of a "Type A medicated article," which is a concentrated form of the drug intended solely for use in the manufacture of another Type A medicated article or medicated feeds (*i.e.*, "Type B medicated feeds" and/or "Type C medicated feeds," see below). The Type A medicated article consists of a new animal drug(s), with or without a carrier, with or without inactive ingredients (see § 558.3(b)(2) (21 CFR 558.3(b)(2))).

Type B medicated feed is intended solely for the manufacture of other medicated feeds (Type B or Type C). It serves as an intermediate medicated feed not approved for feeding to the target animals. It is manufactured by diluting a Type A medicated article or another Type B medicated feed with non-medicated feed, and at least 25 percent of its weight is from nutritional ingredients (see § 558.3(b)(3)). The maximum approvable concentrations of new animal drugs in Type B medicated feeds must be established in accordance with § 558.3(b)(3). The specific maximum concentrations for approved new animal drugs in Type B medicated feeds are listed in § 558.4(d).

Type C medicated feed is fed directly to target animals. It may also be used in the manufacture of another Type C medicated feed. When fed directly to target animals, it is intended to be the animals' complete feed or part of their total diet. It is manufactured by diluting a Type A medicated article, a Type B medicated feed, or another Type C medicated feed with non-medicated feed, and it contains a substantial quantity of nutritional ingredients (see § 558.3(b)(4)).

Labeling for new animal drugs intended for use in feed must be included in the new animal drug application (see § 514.1(b)(3)(v)). Such labeling may include a Type A medicated article label, representative labeling for Type B and Type C medicated feeds containing the new animal drug, proprietary labeling for Type B or Type C medicated feeds, and/or other approved labeling associated with the Type A medicated article.

Proposed § 201.409(a) identifies the information that would be required to be included on Type A medicated article labels. A Type A medicated article label is on the immediate container, which is typically a bag. The Type A medicated article label provides

all information necessary for the safe and effective use of the new animal drug.

Similar to the labeling of other approved or conditionally approved new animal drugs, the Type A medicated article label includes product and manufacturer, packer or distributor identification, approved or conditionally approved indications for use, warnings, and directions for use. In addition, the directions for use for a Type A medicated article must include mixing directions for the manufacture of medicated feeds from the Type A medicated article, as well as feeding directions for the finished Type C medicated feeds manufactured from the Type A medicated article (see § 514.1(b)(3)(v)(a)).

Proposed § 201.409(b) and (c) identify the information that would be required to be included on representative Type B medicated feed labeling and representative Type C medicated feed labeling, respectively. Sponsors of a Type A medicated article must include in their application representative labeling proposed for use in manufacturing Type B and Type C medicated feeds containing the new animal drug (see § 514.1(b)(3)(v)(b)). FDA approves or conditionally approves the use of the Type A medicated article to manufacture Type B and Type C medicated feeds and also approves or conditionally approves the Type A medicated article label and the representative labeling for the Type B and Type C medicated feeds.

Representative Type B and Type C medicated feed labeling is template labeling approved by FDA as part of an NADA or CNADA for a Type A medicated article. Representative Type B and Type C medicated feed labeling approved in the NADA or CNADA provide feed mills the minimal information that must be included on the final printed labels prepared for the respective Type B and Type C medicated feeds manufactured containing the Type A medicated article to provide for safe and effective use of the new animal drug for its approved or conditionally approved indication(s) for use. FDA also uses the term "Blue Bird labels" to refer to representative Type B and Type C medicated feed labeling (see 64 FR 63195 at 63197, November 19, 1999).

Because the approved or conditionally approved Type C medicated feeds will be used as part of the diet, or as the complete diet, of the target animals, the representative Type B and Type C medicated labeling also provide for the nutritional requirements

or content to be specified in the final printed labels for the medicated feed.

If a final printed label for a Type B or Type C medicated feed fails to conform to the approved representative Type B or Type C medicated feed labeling, the medicated feed will be deemed unsafe, in accordance with section 512(a)(2) of the FD&C Act, and adulterated, in accordance with section 501(a)(6) of the FD&C Act.

If Type A medicated article(s) are approved or conditionally approved for more than one indication and/or target animal, the concentration of the new animal drug(s) may differ in the medicated feed approved or conditionally approved for these indication(s) and/or target animal(s). Also, the nutritional requirements or content specified in the representative labeling for the medicated feeds may vary for different target animals. These applications for Type A medicated articles may include representative Type B medicated feed labeling and representative Type C medicated feed labeling for each of the approved uses.

Some Type A medicated articles are approved or conditionally approved to be manufactured only directly into Type C medicated feeds. In addition to the Type A medicated article label, the applications for these Type A medicated articles must provide representative labeling only for Type C medicated feeds.

If new animal drugs for use in animal feeds or drinking water are approved for combination use, in accordance with section 512(d)(4) of the FD&C Act, these "combination new animal drugs" generally provide for more than one approved Type A medicated article to be mixed into medicated feed or drinking water for the approved target animal. The only labeling approved for such combination new animal drugs is representative labeling for the medicated feeds that combines information from the representative labeling of each individual Type A medicated article. Combination new animal drugs exclude conditionally approved drugs subject to section 571 of the FD&C Act. Section 512(d)(4) of the FD&C Act was amended as part of the MUMS Act of 2004 to clarify that only products approved under section 512(b)(1) of the FD&C Act can be used in new animal drug combinations.

Proposed § 201.409(f) identifies the information that would be required to be included on other approved labeling for Type A medicated articles. Other approved labeling for Type A medicated articles may include shipping labeling associated with shipment of bags of the Type A medicated article.

Proposed § 201.409(d) identifies the information that would be required to be included on proprietary Type B medicated feed labels. In addition to approving or conditionally approving applications for Type A medicated articles, FDA may also approve or conditionally approve applications for proprietary final formulations of Type B medicated feeds. A proprietary Type B medicated feed is intended solely for the manufacture of Type C medicated feeds or other Type B medicated feeds and is not approved or conditionally approved for feeding to the target animals. For some proprietary Type B medicated feeds, the formulation and labeling are approved in an NADA or CNADA. In other situations, the underlying data and labeling for the proprietary Type B medicated feed to support the approved uses are maintained in a VMF. For example, this would include situations in which a proprietary Type B medicated feed is manufactured via modification to an approved formulation published in the CFR or where a feed manufacturer creates its own proprietary formulation. The application for a proprietary Type B medicated feed will include the proprietary label for the final Type B medicated feed and representative Type C medicated feed labeling that directs the preparation of final printed labels for Type C medicated feeds manufactured from the proprietary Type B medicated feed. Applications for proprietary final formulations of Type B medicated feeds will not include a Type A medicated article label.

Proposed § 201.409(e) identifies the information that would be required to be included on proprietary Type C medicated feed labels. FDA may also approve or conditionally approve applications for proprietary final formulations of Type C medicated feeds. For some proprietary Type C medicated feeds, the formulation and labeling are approved in an NADA or CNADA. In other situations, the underlying data and labeling for the proprietary Type C medicated feed to support the approved uses are maintained in a VMF. For example, this would include situations in which a proprietary Type C medicated feed is manufactured via modification to an approved formulation published in the CFR or where a feed manufacturer creates its own proprietary formulation. The application for a proprietary Type C medicated feed will include the proprietary label for the final Type C medicated feed.

Prior to the enactment of the ADAA, new animal drugs for use in animal feeds were approved almost exclusively

for OTC use. The ADAA allowed for approval or conditional approval of a new type of new animal drugs for use in or on animal feeds called the “veterinary feed directive drug” (VFD drug). Although not identical, the use of VFD drugs shares similar requirements to the use of Rx new animal drugs.

A veterinarian may only issue a VFD for use in animals under his or her supervision or oversight in the course of his or her professional practice, and in compliance with all applicable veterinary licensing and practice requirements (see § 558.6(b) (21 CFR 558.6(b))). Information that must be included in a VFD is in § 558.6(b).

In accordance with § 558.6(a)(6), the following cautionary statement must appear on all labeling and advertising associated with a VFD drug: “Caution: Federal law restricts medicated feed containing this veterinary feed directive (VFD) drug to use by or on the order of a licensed veterinarian.”

Some sections of proposed § 201.409 are patterned after sections of proposed § 201.405 for labeling of Rx new animal drugs or proposed § 201.407 for labeling of OTC new animal drugs. These sections include the conditional approval statement or NADA/ANADA approval statement, indications for use, warnings, and other information associated with the effects of the new animal drug. Other sections of proposed § 201.409 are uniquely associated with medicated articles and feeds, such as mixing directions, feeding directions, and information on nutritional content.

The labeling sections and subsections for new animal drugs for use in animal feeds would not be numbered. Headings of sections and subsections that would be required to appear verbatim on labeling are identified in the proposed regulations in quotations. Similarly, certain other labeling text would be required to appear verbatim on labeling; this text is also identified in the proposed regulations in quotations.

The proposed rule would require the labeling of approved or conditionally approved new animal drugs for use in animal feeds and that are subject to part 558 of this chapter to comply with other applicable requirements in proposed subpart H (see proposed § 201.409).

#### 1. Type A Medicated Article Label (Proposed § 201.409(a))

The proposed rule would establish content and format requirements for the Type A medicated article label for new animal drugs approved or conditionally approved for use in animal feeds (see proposed § 201.409(a)). A Type A medicated article is a concentrated form of the new animal drug intended solely

for use in the manufacture of another Type A medicated article or Type B medicated feeds and/or Type C medicated feeds. As defined in § 558.3(b)(2), a Type A medicated article consists of a new animal drug(s), with or without a carrier, with or without inactive ingredients. A Type A medicated article label is on the immediate container, which is typically a bag.

The Type A medicated article label provides all information necessary for the safe and effective use of the new animal drug.

The proposed rule would require the following information to be presented on the Type A medicated article label for an approved or conditionally approved new animal drug and in the following order (see proposed § 201.409(a)). Unless otherwise indicated, this information would be the same as that required by proposed § 201.405(a) for full prescribing information for approved or conditionally approved Rx new animal drugs or proposed § 201.407(a) for full product information for approved or conditionally approved OTC new animal drugs.

*a. Type A medicated article identification.* The proposed rule would require this section of the Type A medicated article label to include the proprietary name, the established name of the Type A medicated article, and the phrase “Type A medicated article” or “Type A liquid medicated article,” as applicable, if not included as part of the established name of the Type A medicated article (see proposed § 201.409(a)(1)).

*b. VFD cautionary statement.* For VFD new animal drugs, the proposed rule would require this section of the Type A medicated article label to include the following cautionary statement, in accordance with § 558.6(a)(6): “Caution: Federal law restricts medicated feed containing this veterinary feed directive (VFD) drug to use by or on the order of a licensed veterinarian.” This statement would be required to be displayed prominently and conspicuously on the Type A medicated article label (see proposed § 201.409(a)(2)).

*c. “For further manufacturing only.”* The proposed rule would require this section of the Type A medicated article label to include the statement, “For further manufacturing only” (see proposed § 201.409(a)(3)). This statement would indicate that the Type A medicated article can only be used to manufacture another Type A medicated article or a medicated feed. A Type A medicated article cannot be fed directly to animals.

*d. Conditional approval statement.*

For conditionally approved new animal drugs, the proposed rule would require this section of the Type A medicated article label to include a conditional approval statement, as described in proposed § 201.405(a)(3) for full prescribing information for conditionally approved Rx new animal drugs (see proposed § 201.409(a)(4)).

*e. "Indications for Use."* The proposed rule would require this section of the Type A medicated article label to have the heading "Indications for Use," followed by the approved or conditionally approved indication(s) and target animal(s), as described in proposed § 201.407(a)(3) for full product information for OTC new animal drugs, with the exception of the heading of the section (see proposed § 201.409(a)(5)).

*f. Extralabel use statement.* The proposed rule would require this section of the Type A medicated article label to include an extralabel use statement (see proposed § 201.409(a)(6)). Extralabel use of an approved new animal drug or human drug in or on an animal feed is not permitted (see section 512(a)(4) of the FD&C Act and part 530). The required statement would be: "It is a violation of Federal law to use other than as directed in the labeling." It is important for the layperson and veterinarian to know that it is a violation of Federal law to use new animal drugs in or on animal feeds in an extralabel manner.

*g. "Active Ingredient" or "Active Ingredients."* The proposed rule would require this section of the Type A medicated article label to have the heading "Active Ingredient" or "Active Ingredients," followed by the established name and concentration of each active ingredient in the Type A medicated article (see proposed § 201.409(a)(7)). If the Type A medicated article contains one active ingredient, the proposed rule would require this section of the Type A medicated article label to be entitled "Active Ingredient." If the Type A medicated article contains more than one active ingredient, the proposed rule would require this section of the Type A medicated article label to be entitled "Active Ingredients." Including the concentration of the active ingredient(s) is critical so that feed manufacturers can properly mix Type B and C medicated feeds from the Type A medicated article with the approved concentration(s) of the active ingredient(s).

*h. "Inactive Ingredients."* When inactive ingredients are provided on the Type A medicated article label, the proposed rule would require they be listed in the "Inactive Ingredients"

section in decreasing order of predominance, by weight or concentration, as described in proposed § 201.405(a)(6)(viii) for full prescribing information for Rx new animal drugs (see proposed § 201.409(a)(8)).

*i. "Directions."* The proposed rule would require this section of the Type A medicated article label to have the heading "Directions," followed by the directions for use of the Type A medicated article (see proposed § 201.409(a)(9)). The "Directions" section of the Type A medicated article label would include three subsections.

*i. "Approved Concentration(s) of [Active Ingredient or Active Moiety] in Type C Medicated Feeds."* The proposed rule would require the first subsection of the "Directions" section of the Type A medicated article label to have the heading "Approved Concentration(s) of [Active Ingredient or Active Moiety] in Type C Medicated Feeds," followed by the approved concentration(s) of each active ingredient in Type C medicated feed(s) to be manufactured from the Type A medicated article for the approved or conditionally approved indications for use (see proposed § 201.409(a)(9)(i)). If an active ingredient is a salt or other noncovalent derivative, its concentration in the Type A medicated article in the "Active Ingredient" or "Active Ingredients" section (see proposed § 201.409(a)(7)) may be expressed on the basis of the full active ingredient (*i.e.*, including the salt or other noncovalent derivative) or the active moiety. If an active ingredient is a salt or other noncovalent derivative and its concentration in the Type A medicated article was expressed in the "Active Ingredient" or "Active Ingredients" section based on the active moiety, the proposed rule would require the approved concentration(s) in the Type C medicated feeds to also be expressed based on the active moiety, and the title of this subsection would be required to include the name of the active moiety instead of the active ingredient (see proposed § 201.409(a)(9)(i)). Consistent expression of the concentrations of active ingredients on the Type A medicated article label may reduce the risk of mixing errors when manufacturing medicated feeds from the Type A medicated article.

Multiple Type C medicated feeds may be approved or conditionally approved for a Type A medicated article. Also, different concentrations, or ranges of concentrations, of the active ingredient may be approved or conditionally approved for different indications for use. This subsection of the Type A

medicated article label would clarify this information for manufacturers of medicated feeds manufactured from the Type A medicated article.

*ii. "Mixing Directions."* The proposed rule would require this subsection of the "Directions" section of the Type A medicated article label to have the heading "Mixing Directions," followed by the approved mixing directions for the manufacture of approved medicated feeds from the Type A medicated article for each approved or conditionally approved indication for use (see proposed § 201.409(a)(9)(ii)). An intermediate mixing step (called preblend step) is sometimes required to manufacture medicated feeds from the Type A medicated article. For example, the Type A medicated article may need to be preblended with a small amount of one or more feed ingredients before being added to the rest of the feed ingredients to increase the uniformity of the drug distribution in the finished medicated feed. The directions for such a preblend step would also be required to be included in this subsection of the Type A medicated article label.

*iii. "Feeding Directions."* The proposed rule would require the last subsection in the "Directions" section of the Type A medicated article label to have the heading "Feeding Directions," followed by the approved feeding directions for each approved or conditionally approved indication for use for Type C medicated feeds approved or conditionally approved to be manufactured from the Type A medicated article (see proposed § 201.409(a)(9)(iii)).

*j. "Warnings."* The proposed rule would require this section of the Type A medicated article label for all approved or conditionally approved Type A medicated articles, and it would have the heading "Warnings," followed by all warnings (see proposed § 201.409(a)(10)). This section of the Type A medicated article label would have the same subsections as described in § 201.405(a)(10) in full prescribing information for Rx new animal drugs, except that the "Animal Safety Warnings" subsection would be the same as described in proposed § 201.407(a)(7)(iii) for full product information for OTC new animal drugs.

*k. "Additional Recommendations."* For new animal drugs having precautions, the proposed rule would require this section of the Type A medicated article label to have the heading "Additional Recommendations," followed by all precautions (see proposed § 201.409(a)(11)). This section of the Type A medicated article label would be

the same as described in proposed § 201.407(a)(8) for full product information for OTC new animal drugs. For VFD new animal drugs, this section would include precautions directed to veterinarians as well as the layperson.

*l. "Other Effects You May Notice."* For new animal drugs that have effects on the target animal(s) that are not considered contraindications, target animal safety warnings, adverse reactions, or post-approval adverse drug experiences, and FDA determines that these effects are required to be described on labeling, the proposed rule would require this section of the Type A medicated article label to have the heading "Other Effects You May Notice," followed by a description of the effects (see proposed § 201.409(a)(12)). This section of the Type A medicated article label would be the same as described in proposed § 201.407(a)(9) for full product information for OTC new animal drugs.

*m. "Net Weight."* The proposed rule would require this section of the Type A medicated article label to have the heading "Net Weight," followed by the net weight of the Type A medicated article in the immediate container (see proposed § 201.409(a)(13)).

*n. "Storage, Handling, and Disposal."* The proposed rule would require this section of the Type A medicated article label to have the heading "Storage, Handling, and Disposal," followed by storage information for the Type A medicated article, as well as any required handling and disposal information (see proposed § 201.409(a)(14)). This section of the Type A medicated article label would be the same as described in proposed § 201.405(a)(20) for full prescribing information for Rx new animal drugs.

*o. "Questions/Comments?"* The proposed rule would require this section of the Type A medicated article label to have the heading "Questions/Comments?," followed by the sponsor's contact information for feed manufacturers or other users of the Type A medicated article to facilitate requesting additional information or to report suspected adverse drug experiences. FDA's contact information for voluntary reporting of adverse drug experiences for animal drugs would also be required (see proposed § 201.409(a)(15)). The "Questions/Comments?" section of the Type A medicated article label would be similar to the "Questions/Comments?" section in proposed § 201.407(a)(14) for full product information for OTC new animal drugs.

The sponsor's contact information would be the name of the manufacturer,

packer, or distributor, whichever is identified in the "Name and place of business" section of the Type A medicated article label (see proposed § 201.409(a)(17)). If more than one business is identified in the "Name and place of business" section of the Type A medicated article label, the drug sponsor would select the most appropriate of these businesses to use in the "Questions/Comments?" section to provide additional information about the Type A medicated article and to contact regarding suspected adverse drug experiences.

The statements in this section of the Type A medicated article label would be required to be structured as follows: "Contact [insert name of business] at [insert business telephone number] or [insert business web address]. To report side effects, contact [insert name of business] at [insert business telephone number]. For additional information about reporting side effects for animal drugs, contact FDA at [insert current FDA telephone number for voluntary reporting of adverse drug experiences] or [insert current FDA web address for voluntary reporting of adverse drug experiences]." Sponsors can search FDA's website or contact FDA by telephone to find the current FDA telephone number or web address for voluntary reporting of adverse drug experiences for animal drug.

*p. NADA/ANADA approval statement.* For approved or generic approved Type A medicated articles, the proposed rule would require this section of the Type A medicated article label to include an "NADA approval statement" or "ANADA approval statement," respectively (see proposed § 201.409(a)(16)). This section of the Type A medicated article label would be the same as described in proposed § 201.405(a)(21) for full prescribing information for Rx new animal drugs.

*q. Name and place of business.* The proposed rule would require this section of the Type A medicated article label to identify the name and place of business of the manufacturer, packer, or distributor (see proposed § 201.409(a)(17)). This section of the Type A medicated article label would be the same as described in proposed § 201.405(a)(22) for full prescribing information for Rx new animal drugs.

*r. "Lot Number and Expiration Date."* The proposed rule would require this section of the Type A medicated article label to have the heading "Lot Number and Expiration Date," followed by the identifying lot or control number of the Type A medicated article within the immediate container. A lot or control number would help us to more easily

identify and trace back a specific lot of a Type A medicated article should a problem be reported to FDA (see proposed § 201.409(a)(18)). In accordance with § 226.58(d) of this chapter, the proposed rule would also require this section of the Type A medicated article label to include the expiration date of the Type A medicated article within the immediate container. An expiration date is important to ensure the safe and effective use of products.

Alternatively, the proposed rule would allow for this section of the Type A medicated article label to refer to the location on the Type A medicated article label or immediate container where the lot or control number and expiration date are printed (see proposed § 201.409(a)(18)). As an example, if the lot number and expiration date are printed on the bottom half of the back of the bag containing the Type A medicated article, then the Type A medicated article label may state in this section, "See bottom back half of bag for lot number and expiration date."

*s. "Revision Date."* The proposed rule would require this section of the Type A medicated article label to have the heading "Revision Date," followed by the date of the most recent revision of the Type A medicated article label, listing the month followed by the year (see proposed § 201.409(a)(19)). This information is important to ensure that the most current approved version of the Type A medicated article label is being used.

## 2. Representative Type B Medicated Feed Labeling (Proposed § 201.409(b))

The proposed rule would establish content and format requirements for representative Type B medicated feed labeling for new animal drugs approved or conditionally approved for use in animal feeds (see proposed § 201.409(b)). A Type B medicated feed is intended solely for the manufacture of other medicated feeds (Type B or Type C). It serves as an intermediate medicated feed not approved for feeding to the target animals. It is manufactured by diluting a Type A medicated article or another Type B medicated feed with non-medicated feed, and at least 25 percent of its weight is from nutritional ingredients (see § 558.3(b)(3)). Representative Type B medicated feed labeling is template labeling approved by FDA as part of an NADA or CNADA for a Type A medicated article.

Representative Type B medicated feed labeling approved in the NADA or CNADA provide feed mills the minimal information that must be included on

the final printed labels prepared for the Type B medicated feeds manufactured containing the Type A medicated article to provide for safe and effective use of the new animal drug for its approved or conditionally approved indication(s) for use.

The proposed rule would require the following information to be presented on the representative Type B medicated feed labeling for an approved or conditionally approved new animal drug and in the following order (see proposed § 201.409(b)). Unless otherwise indicated, this information would be the same as that required by proposed § 201.405(a) for full prescribing information for approved or conditionally approved Rx new animal drugs, proposed § 201.407(a) for full product information for approved or conditionally approved OTC new animal drugs, or proposed § 201.409(a) for the Type A medicated article label.

*a. Description of the Type B medicated feed.* The proposed rule would require this section of the representative Type B medicated feed labeling to provide a description of the Type B medicated feed (see proposed § 201.409(b)(1)). This section of the representative Type B medicated feed labeling would serve as a placeholder for the proprietary name of the final Type B medicated feed to be added by the feed manufacturer to the label of the final Type B medicated feed manufactured in accordance with the approved representative Type B labeling.

Representative Type B medicated labeling may be approved or conditionally approved for multiple Type B medicated feeds within an application. The proposed rule would require the description of each approved Type B medicated feed to distinguish it from any other Type B medicated feeds approved or conditionally approved within the same application (see proposed § 201.409(b)(1)(i)). Distinguishing information may include the animals and/or indications for use for which Type C medicated feeds manufactured from the Type B medicated feed are approved or conditionally approved and/or other characteristics of the Type B medicated feeds.

The proposed rule would require that the description of the approved Type B medicated feed not include the proprietary name of a Type A medicated article (see proposed § 201.409(b)(1)(ii)). The proprietary name of a Type A medicated article is specific to the Type A medicated article; use of that proprietary name in the description of a Type B medicated feed may incorrectly

imply that the Type B medicated feed is a Type A medicated article.

*b. Established name of the Type B medicated feed.* The proposed rule would require this section of the representative Type B medicated feed labeling to include the established name of the Type B medicated feed. The established name of the Type B medicated feed would include the active moiety or active ingredient of each new animal drug, as determined by FDA, followed by an identifying statement of either “Type B medicated feed” or “Type B liquid medicated feed,” as applicable (see proposed § 201.409(b)(2)). The identifying statements also clearly designate the medicated feeds as Type B (as opposed to a Type C) medicated feeds. The identifying statements also distinguish Type B liquid medicated feeds from other Type B medicated feeds, which is important because Type B liquid medicated feeds have unique approval and labeling requirements (see § 558.5 (21 CFR 558.5)).

*c. VFD cautionary statement.* For VFD new animal drugs, the proposed rule would require this section of the representative Type B medicated feed labeling to provide the VFD cautionary statement, in accordance with § 558.6(a)(6), as described in proposed § 201.409(a)(2) for the Type A medicated article label (see proposed § 201.409(b)(3)).

*d. “Do Not Feed Undiluted.”* The proposed rule would require this section of the representative Type B medicated feed labeling to state, “Do Not Feed Undiluted” (see proposed § 201.409(b)(4)). This statement would remind users that the Type B medicated feed is not to be fed directly to animals.

*e. Conditional approval statement.* For conditionally approved new animal drugs, the proposed rule would require this section of the representative Type B medicated feed labeling to include a conditional approval statement, as described in proposed § 201.405(a)(3) for full prescribing information for Rx new animal drugs (see proposed § 201.409(b)(5)).

*f. “Indications for Use.”* The proposed rule would require this section of the representative Type B medicated feed labeling to have the heading “Indications for Use,” followed by the approved or conditionally approved indications(s) and target animal(s), as described in proposed § 201.407(a)(3) for full product information for OTC new animal drugs, with the exception of the heading. In addition, this section of the representative Type B medicated feed labeling would include only the indications for use applicable to the

specific Type B medicated feed to which the representative labeling applies (see proposed § 201.409(b)(6)).

*g. Extralabel use statement.* The proposed rule would require this section of the representative Type B medicated feed labeling to include an extralabel use statement, as described in proposed § 201.409(a)(6) for the Type A medicated article label (see proposed § 201.409(b)(7)).

*h. “Active Ingredient” or “Active Ingredients.”* The proposed rule would require this section of the representative Type B medicated feed labeling to have the heading “Active Ingredient” or “Active Ingredients,” followed by the established name and approved concentration(s) of each active ingredient (see proposed § 201.409(b)(8)). If the Type B medicated feed contains one active ingredient, the proposed rule would require this section of the representative Type B medicated feed labeling to be titled “Active Ingredient.” If the Type B medicated feed contains more than one active ingredient, the proposed rule would require this section of the representative Type B medicated feed labeling to be titled “Active Ingredients.” FDA approves a single concentration or a range of concentrations of each active ingredient for Type B medicated feeds and their representative Type B medicated feed labeling. However, the final Type B medicated feed label would only include a single concentration of each active ingredient. If a range of concentrations of the active ingredient(s) is approved or conditionally approved for Type B medicated feeds, the representative Type B medicated feed labeling would be required to include a footnote, placed at the bottom of the page of the representative Type B medicated feed labeling containing the “Active Ingredient” or “Active Ingredients” section, which instructs feed manufacturers that the final printed Type B medicated feed label must only include a single concentration for each active ingredient.

*i. “Guaranteed Analysis.”* The proposed rule would require this section of the representative Type B medicated feed labeling to have the heading “Guaranteed Analysis,” followed by the nutritional content guarantees of the Type B medicated feed appropriate for the approved target animals in addition to any other required specifications (see proposed § 201.409(b)(9)). The Type B medicated feed will be used to make a Type C medicated feed that will be included as part of the target animals’ diet or serve

as their complete diet. Therefore, the feed manufacturer and user must be aware of the nutritional content of the Type B medicated feed to properly balance the nutritional content of the diet of the target animal. Without this nutritional content information being made available to the manufacturer and user of the medicated feed, the animals' diet may be imbalanced, e.g., either under- or over-feeding critical nutrients, which could be harmful to the health of the target animals. For this reason, information of this type may be considered material under section 201(n) of the FD&C Act such that it would be required to be disclosed on the representative Type B feed labeling.

Additional specifications may also be required in this section of the representative Type B medicated feed labeling, such as the range of pH and/or range of percent dry matter. For example, the pH and/or ratio of dry matter to moisture (expressed as percent dry matter) of a liquid medicated feed may affect the stability of the new animal drug(s) it contains, such that a specific Type B liquid medicated feed would be approved only within a specific range of pH and/or percent dry matter (see § 558.5(d)(1) and (2)).

*j. "Ingredients."* The proposed rule would require this section of the representative Type B medicated feed labeling to have the heading "Ingredients," followed by information relative to feed ingredients (see proposed § 201.409(b)(10)). This information would include a statement that the feed ingredients must be listed on each final printed Type B medicated feed label by their common or usual names in descending order of predominance by weight, in accordance with § 501.4(a) (21 CFR 501.4(a)), including their collective names where permitted, in accordance with § 501.4(b)(13). Also included would be a statement that spices, flavorings, colorings, and chemical preservatives, if used, must be declared on each final printed Type B medicated feed label, in accordance with § 501.22 (21 CFR 501.22).

*k. "Mixing Directions."* The proposed rule would require this section of the representative Type B medicated feed labeling to have the heading "Mixing Directions," followed by approved mixing directions for the manufacture of a Type C medicated feed(s) or another Type B medicated feed(s), as applicable, from the Type B medicated feed for which the representative Type B medicated feed labeling applies (see proposed § 201.409(b)(11)).

*l. "Warnings."* The proposed rule would require this section of the

representative Type B medicated feed labeling to have the heading "Warnings," followed by the "Warnings" section, as described in proposed § 201.409(a)(10) for the Type A medicated article label. In addition, this section of the representative Type B medicated feed labeling would include only the warnings applicable to the specific Type B medicated feed to which the representative labeling applies (see proposed § 201.409(b)(12)).

*m. "Additional Recommendations."* For new animal drugs having precautions, the proposed rule would require this section of the representative Type B medicated feed labeling to have the heading "Additional Recommendations," followed by the precautions, as described in proposed § 201.407(a)(8) for full product information for OTC new animal drugs. In addition, this section of the representative Type B medicated feed labeling would include only the precautions applicable to the specific Type B medicated feed to which the representative labeling applies (see proposed § 201.409(b)(13)).

*n. "Other Effects You May Notice."* For new animal drugs that have effects on the target animal(s) that are not considered contraindications, target animal safety warnings, adverse reactions, or post-approval adverse drug experiences, and FDA determines that these effects are required to be described on labeling, the proposed rule would require this section of the representative Type B medicated feed labeling to have the heading "Other Effects You May Notice," followed by a description of the effects. This section of the representative Type B medicated feed labeling would be the same as described in proposed § 201.407(a)(9) for full product information for OTC new animal drugs. In addition, this section of the representative Type B medicated feed labeling would include only statements of other effects applicable to the specific Type B medicated feed to which the representative Type B medicated feed labeling applies (see proposed § 201.409(b)(14)).

*o. Name and place of business.* The proposed rule would require this section of the representative Type B medicated feed labeling to provide for identification of the name and place of business of the manufacturer, packer, or distributor of the final Type B medicated feed on the final printed Type B medicated feed label, in accordance with § 501.5 (see proposed § 201.409(b)(15)).

*p. "Net Weight."* The proposed rule would require this section of the representative Type B medicated feed

labeling to have the heading "Net Weight," followed by space to provide for a statement on the final printed Type B medicated feed label of the net weight of the Type B medicated feed in the immediate container (see proposed § 201.409(b)(16)).

*q. "Storage, Handling, and Disposal."* The proposed rule would require this section of the representative Type B medicated feed labeling to have the heading "Storage, Handling, and Disposal," followed by storage information for the Type B medicated feed, as well as any required handling and disposal information, as described in proposed § 201.405(a)(20) for full prescribing information for Rx new animal drugs (see proposed § 201.409(b)(17)).

*r. "Questions/Comments?"* The proposed rule would require this section of the representative Type B medicated feed labeling to have the heading "Questions/Comments?," followed by statements providing contact information for use by feed manufacturers or other users of the final Type B medicated feed to request additional information on the product and/or to report problems with the medicated feed (see proposed § 201.409(b)(18)). The first statement would provide placeholders for the name and contact information of the business of the manufacturer, packer, or distributor of the final Type B medicated feed to later be inserted by the business. The second statement would provide FDA contact information for reporting adverse drug experiences for animal drugs and would be required to be inserted by the sponsor of the new animal drug application.

*s. "Lot, Batch, or Control Number."* The proposed rule would require this section of the representative Type B medicated feed labeling to have the heading "Lot, Batch, or Control Number," followed by space to provide for an identifying lot, batch, or control number on the final printed Type B medicated feed label (see proposed § 201.409(b)(19)).

*t. "Expiration Date."* For Type B medicated feeds requiring an expiration date, in accordance with § 514.1(b)(5)(x), the proposed rule would require this section of the representative Type B medicated feed labeling to have the heading "Expiration Date," followed by space to provide for the expiration date to be printed on the final printed Type B medicated feed label. In addition, the approved expiration period would need to be included in this section of the representative Type B medicated feed labeling (see proposed § 201.409(b)(20)).

*u. "Revision Date."* The proposed rule would require this section of the representative Type B medicated feed labeling to have the heading "Revision Date," followed by the date of the most recent revision of the representative Type B medicated feed labeling, listing the month followed by the year (see proposed § 201.409(b)(21)). This information is important to ensure that the most current approved version of the representative Type B medicated feed labeling is being used.

### 3. Representative Type C Medicated Feed Labeling (Proposed § 201.409(c))

The proposed rule would establish content and format requirements for representative Type C medicated feed labeling for new animal drugs approved or conditionally approved for use in animal feeds (see proposed § 201.409(c)). Type C medicated feed is fed directly to target animals. It may also be used in the manufacture of another Type C medicated feed. When fed directly to target animals, it is intended to be the animals' complete feed or part of their total diet. It is manufactured by diluting a Type A medicated article, a Type B medicated feed, or another Type C medicated feed with non-medicated feed, and it contains a substantial quantity of nutritional ingredients (see § 558.3(b)(4)).

Representative Type C medicated feed labeling approved in the NADA or CNADA provide feed mills the minimal information that must be included on the final printed labels prepared for the Type C medicated feeds manufactured containing the Type A medicated article to provide for safe and effective use of the new animal drug for its approved or conditionally approved indication(s) for use.

The proposed rule would require the following information to be presented on the representative Type C medicated feed labeling for an approved or conditionally approved new animal drug and in the following order (see proposed § 201.409(c)). Unless otherwise indicated, this information would be the same as that required by proposed § 201.405(a) for full prescribing information for approved or conditionally approved Rx new animal drugs, proposed § 201.407(a) for full product information for approved or conditionally approved OTC new animal drugs, proposed § 201.409(a) for the Type A medicated article label, or proposed § 201.409(b) for representative Type B medicated feed labeling.

*a. Description of the Type C medicated feed.* The proposed rule would require this section of the

representative Type C medicated feed labeling to provide a description of the Type C medicated feed (see proposed § 201.409(c)(1)). This section of the representative Type C medicated feed labeling would serve as a placeholder for the proprietary name of the final Type C medicated feed to be added by the feed manufacturer to the label of the final Type C medicated feed manufactured in accordance with the approved representative Type C labeling.

Representative Type C medicated labeling may be approved or conditionally approved for multiple Type C medicated feeds within an application. The proposed rule would require the description of each approved Type C medicated feed to distinguish it from any other Type C medicated feeds approved or conditionally approved within the same application (see proposed § 201.409(c)(1)(i)). Distinguishing information may include the animals and/or indications for use for which Type C medicated feeds are approved or conditionally approved and/or other characteristics of the Type C medicated feeds.

The proposed rule would require that the description of the approved Type C medicated feed not include the proprietary name of a Type A medicated article (see proposed § 201.409(c)(1)(ii)). The proprietary name of a Type A medicated article is specific to the Type A medicated article; use of that proprietary name in the description of a Type C medicated feed may incorrectly imply that the Type C medicated feed is a Type A medicated article.

*b. Established name of the Type C medicated feed.* The proposed rule would require this section of the representative Type C medicated feed labeling to include the established name of the Type C medicated. The established name of the Type C medicated feed would include the active moiety or active ingredient of each new animal drug, as determined by FDA, followed by an identifying statement of, "Type C medicated feed," "Type C liquid medicated feed," "Type C top-dress medicated feed," "Type C free-choice medicated feed," or "Type C liquid free-choice medicated feed," as applicable (see proposed § 201.409(c)(2)). The identifying statements also clearly designate the medicated feeds as Type C (as opposed to a Type B) medicated feeds. The identifying statements also distinguish Type C liquid medicated feeds from other Type C medicated feeds, which is important because Type C liquid medicated feeds have unique approval and labeling requirements (see § 558.5).

Similarly, Type C free-choice medicated feeds have specific requirements for their approval (see § 510.455 (21 CFR 510.455)).

*c. VFD cautionary statement.* For VFD new animal drugs, the proposed rule would require this section of the representative Type C medicated feed labeling to provide the VFD cautionary statement, in accordance with § 558.6(a)(6), as described in proposed § 201.409(a)(2) for the Type A medicated article label (see proposed § 201.409(c)(3)).

*d. Conditional approval statement.* For conditionally approved new animal drugs, the proposed rule would require this section of the representative Type C medicated feed labeling to include a conditional approval statement, as described in proposed § 201.405(a)(3) for full prescribing information for Rx new animal drugs (see proposed § 201.409(c)(4)).

*e. "Indications for Use."* The proposed rule would require this section of the representative Type C medicated feed labeling to have the heading "Indications for Use," followed by the approved or conditionally approved indications(s) and target animal(s), as described in proposed § 201.407(a)(3) for full product information for OTC new animal drugs, with the exception of the heading. In addition, this section of the representative Type C medicated feed labeling would include only the indications for use applicable to the specific Type C medicated feed to which the representative labeling applies (see proposed § 201.409(c)(5)).

*f. Extralabel use statement.* The proposed rule would require this section of the representative Type C medicated feed labeling to include an extralabel use statement, as described in proposed § 201.409(a)(6) for the Type A medicated article label (see proposed § 201.409(c)(6)).

*g. "Active Ingredient" or "Active Ingredients."* The proposed rule would require this section of the representative Type C medicated feed labeling to have the heading "Active Ingredient" or "Active Ingredients," followed by the established name and approved concentration(s) of each active ingredient (see proposed § 201.409(c)(7)). If the Type C medicated feed contains one active ingredient, the proposed rule would require this section of the representative Type C medicated feed labeling to be entitled "Active Ingredient." If the Type C medicated feed contains more than one active ingredient, the proposed rule would require this section of the representative Type C medicated feed

labeling to be entitled “Active Ingredients.” We approve a single concentration or a range of concentrations of each active ingredient for Type C medicated feeds and their representative Type C medicated feed labeling. However, the final Type C medicated feed label would only include a single concentration of each active ingredient. If a range of concentrations of the active ingredient(s) is approved or conditionally approved for Type C medicated feeds, the representative Type C medicated feed labeling would be required to include a footnote, placed at the bottom of the page of the representative Type C medicated feed labeling containing the “Active Ingredient” or “Active Ingredients” section, which instructs feed manufacturers that the final printed Type C medicated feed label must include only a single concentration for each active ingredient.

*h. “Guaranteed Analysis.”* The proposed rule would require this section of the representative Type C medicated feed labeling to have the heading “Guaranteed Analysis,” followed by the nutritional content guarantees of the Type C medicated feed and any other required specifications, as described in proposed § 201.409(b)(9) for representative Type B medicated feed labeling (see proposed § 201.409(c)(8)).

*i. “Ingredients.”* The proposed rule would require this section of the representative Type C medicated feed labeling to have the heading “Ingredients,” followed by information relative to feed ingredients (see proposed § 201.409(c)(9)).

For Type C medicated feeds that are not Type C free-choice medicated feeds, proposed § 201.409(b)(9)(i) would require the heading to be followed by a statement that the feed ingredients must be listed on each final printed Type C medicated feed label by their common or usual names in descending order of predominance by weight, in accordance with § 501.4(a), including their collective names where permitted, in accordance with § 501.4(b)(13). Also included would be a statement that spices, flavorings, colorings, and chemical preservatives, if used, must be declared on the final printed Type C medicated feed label, in accordance with § 501.22.

For Type C free-choice medicated feeds, the proposed rule would require the heading to be followed by a listing of the feed ingredients and their inclusion rates, including the drug concentrations exactly as they appear in the approved non-proprietary formula

published for the specific new animal drug in part 558 (see proposed § 201.409(b)(9)(ii)).

*j. “Feeding Directions.”* The proposed rule would require this section of the representative Type C medicated feed labeling to have the heading “Feeding Directions,” followed by the approved feeding directions (see proposed § 201.409(c)(10)). This section of representative Type C medicated feed labeling would include only the feeding directions applicable to the specific Type C medicated feed to which the representative Type C medicated feed labeling applies.

*k. “Warnings.”* The proposed rule would require this section of the representative Type C medicated feed labeling to have the heading “Warnings,” followed by the “Warnings” section, as described in proposed § 201.409(a)(10) for the Type A medicated article label. In addition, this section of the representative Type C medicated feed labeling would include only the warnings applicable to the specific Type C medicated feed to which the representative labeling applies (see proposed § 201.409(c)(11)).

*l. “Additional Recommendations.”* For new animal drugs having precautions, the proposed rule would require this section of the representative Type C medicated feed labeling to have the heading “Additional Recommendations,” followed by the precautions, as described in proposed § 201.407(a)(8) for full product information for OTC new animal drugs. In addition, this section of the representative Type C medicated feed labeling would include only the precautions applicable to the specific Type C medicated feed to which the representative labeling applies (see proposed § 201.409(c)(12)).

*m. “Other Effects You May Notice.”* For new animal drugs that have effects on the target animal(s) that are not considered contraindications, target animal safety warnings, adverse reactions, or post-approval adverse drug experiences, and FDA determines that these effects are required to be described on labeling, the proposed rule would require this section of the representative Type C medicated feed labeling to have the heading “Other Effects You May Notice,” followed by a description of the effects. This section of the representative Type C medicated feed labeling would be the same as described in proposed § 201.407(a)(9) for full product information for OTC new animal drugs. In addition, this section of the representative Type C medicated feed labeling would include only statements of other effects applicable to

the specific Type C medicated feed to which the representative Type C labeling applies (see proposed § 201.409(c)(13)).

*n. Name and place of business.* The proposed rule would require this section of the representative Type C medicated feed labeling to provide for identification of the name and place of business of the manufacturer, packer, or distributor of the final Type C medicated feed on the final printed Type C medicated feed label, in accordance with § 501.5 (see proposed § 201.409(c)(14)).

*o. “Net Weight.”* The proposed rule would require this section of the representative Type C medicated feed labeling to have the heading “Net Weight,” followed by space to provide for a statement on the final printed Type C medicated feed label of the net weight of the Type C medicated feed in the immediate container (see proposed § 201.409(c)(15)).

*p. “Storage, Handling, and Disposal.”* The proposed rule would require this section of the representative Type C medicated feed labeling to have the heading “Storage, Handling, and Disposal,” followed by storage information for the Type C medicated feed, as well as any required, handling and disposal information, as described in proposed § 201.405(a)(20) for full prescribing information for Rx new animal drugs (see proposed § 201.409(c)(16)).

*q. “Questions/Comments?”* The proposed rule would require this section of the representative Type C medicated feed labeling to have the heading “Questions/Comments?” followed by statements providing contact information for use by feed manufacturers or other users of the final Type C medicated feed to request additional information on the product and/or to report problems with the medicated feed (see proposed § 201.409(c)(17)). The first statement would provide placeholders for the name and contact information of the business of the manufacturer, packer, or distributor of the final Type C medicated feed to later be inserted by the business. The second statement would provide FDA contact information for reporting adverse drug experiences for animal drugs and would be required to be inserted by the sponsor of the new animal drug application.

*r. “Lot, Batch, or Control Number.”* The proposed rule would require this section of the representative Type C medicated feed labeling to have the heading “Lot, Batch, or Control Number,” followed by space to provide for an identifying lot, batch, or control

number on the final printed Type C medicated feed label (see proposed § 201.409(c)(19)).

*s. "Expiration Date."* For Type C medicated feeds requiring an expiration date, in accordance with § 514.1(b)(5)(x), the proposed rule would require this section of the representative Type C medicated feed labeling to have the heading "Expiration Date," followed by space to provide for the expiration date to be printed on the final printed Type C medicated feed label. In addition, the approved expiration period would need to be included in this section of the representative Type C medicated feed labeling (see proposed § 201.409(c)(19)).

*t. "Revision Date."* The proposed rule would require this section of the representative Type C medicated feed labeling to have the heading "Revision Date," followed by the date of the most recent revision of the representative Type C medicated feed labeling, listing the month followed by the year (see proposed § 201.409(c)(20)). This information is important to ensure that the most current approved version of the representative Type C medicated feed labeling is being used.

#### 4. Proprietary Type B Medicated Feed Label (Proposed § 201.409(d))

The proposed rule would establish content and format requirements for a proprietary Type B medicated feed label for new animal drugs approved or conditionally approved for use in animal feeds (see proposed § 201.409(d)). A proprietary Type B medicated feed is intended solely for the manufacture of Type C medicated feeds or other Type B medicated feeds and is not approved or conditionally approved for feeding to the target animals. For some proprietary Type B medicated feeds, the formulation and labeling are approved in an NADA. In other situations, the underlying data and labeling for the proprietary Type B medicated feed to support the approved uses are maintained in a VMF. For example, this would include situations in which a proprietary Type B medicated feed is manufactured via modification to an approved formulation published in the CFR or where a feed manufacturer creates its own proprietary formulation. The application for a proprietary Type B medicated feed will include the proprietary label for the final Type B medicated feed and representative Type C medicated feed labeling that directs the preparation of final printed labels for Type C medicated feeds manufactured from the proprietary Type B medicated feed. A proprietary Type B

medicated feed label is on the immediate container, which is typically a bag or bulk container.

The proposed rule would require the following information to be presented on the proprietary Type B medicated feed label for an approved or conditionally approved new animal drug and in the following order (see proposed § 201.409(d)). Unless otherwise indicated, this information would be the same as that required by proposed § 201.405(a) for full prescribing information for approved or conditionally approved Rx new animal drugs, proposed § 201.407(a) for full product information for approved or conditionally approved OTC new animal drugs, or proposed § 201.409(a) for the Type A medicated article label.

*a. Proprietary Type B medicated feed identification.* The proposed rule would require this section of the proprietary Type B medicated feed label to identify the Type B medicated feed (see proposed § 201.409(d)(1)). This section of the proprietary Type B medicated feed label would be required to include the following components in order:

*i. Proprietary name of the Type B medicated feed.* The proposed rule require this subsection of the proprietary Type B medicated feed label to include the proprietary name of the Type B medicated feed (see proposed § 201.409(d)(1)(i)).

*ii. Established name of the Type B medicated feed.* The proposed rule would require this subsection of the proprietary Type B medicated feed label to include the established name of the Type B medicated feed. The established name of the Type B medicated feed would include the active moiety or active ingredient of each new animal drug, as determined by FDA, followed by an identifying statement of either "Type B medicated feed" or "Type B liquid medicated feed," as applicable (see proposed § 201.409(d)(1)(ii)). The identifying statements also clearly designate the medicated feed as a Type B (as opposed to a Type C) medicated feed. The identifying statements also distinguish Type B liquid medicated feeds from other Type B medicated feeds, which is important because Type B liquid medicated feeds have unique approval and labeling requirements (see § 558.5).

*b. VFD cautionary statement.* For VFD new animal drugs, the proposed rule would require this section of the proprietary Type B medicated feed label to provide the VFD cautionary statement, in accordance with § 558.6(a)(6), as described in proposed § 201.409(a)(2) for the Type A

medicated article label (see proposed § 201.409(d)(2)).

*c. "Do Not Feed Undiluted."* The proposed rule would require this section of the proprietary Type B medicated feed label to state, "Do Not Feed Undiluted" (see proposed § 201.409(d)(3)). This statement would remind users that the Type B medicated feed is not to be fed directly to animals.

*d. Conditional approval statement.* For conditionally approved new animal drugs, the proposed rule would require this section of the proprietary Type B medicated feed label to include a conditional approval statement, as described in proposed § 201.405(a)(3) for full prescribing information for Rx new animal drugs (see proposed § 201.409(d)(4)).

*e. "Indications for Use."* The proposed rule would require this section of the proprietary Type B medicated feed label to have the heading "Indications for Use," followed by the approved or conditionally approved indications(s) and target animal(s), as described in proposed § 201.407(a)(3) for full product information for OTC new animal drugs, with the exception of the heading (see proposed § 201.409(d)(5)).

*f. Extralabel use statement.* The proposed rule would require this section of the proprietary Type B medicated feed label to include an extralabel use statement, as described in proposed § 201.409(a)(6) for the Type A medicated article label (see proposed § 201.409(d)(6)).

*g. "Active Ingredient" or "Active Ingredients."* The proposed rule would require this section of the proprietary Type B medicated feed label to have the heading "Active Ingredient" or "Active Ingredients," followed by the established name and approved concentration of each active ingredient (see proposed § 201.409(d)(7)). If the proprietary Type B medicated feed contains one active ingredient, the proposed rule would require this section of the proprietary Type B medicated feed label to be entitled "Active Ingredient." If the proprietary Type B medicated feed contains more than one active ingredient, the proposed rule would require this section of the proprietary Type B medicated feed label to be entitled "Active Ingredients." Because the proprietary Type B medicated feed label applies to a final Type B medicated feed, a single concentration would be required for each active ingredient rather than a range.

*h. "Guaranteed Analysis."* The proposed rule would require this section of the proprietary Type B

medicated feed label to have the heading “Guaranteed Analysis,” followed by the nutritional content guarantees and any other required specifications for the proprietary Type B medicated feed (see proposed § 201.409(d)(8)).

*i. “Ingredients.”* The proposed rule would require this section of the proprietary Type B medicated feed label to have the heading “Ingredients,” followed by a listing of the feed ingredients in the proprietary Type B medicated feed. The feed ingredients would be required to be listed by their common or usual names in descending order of predominance by weight, in accordance with § 501.4(a), including their collective names where permitted, in accordance with § 501.4(b)(13) (see proposed § 201.409(d)(9)(i)). Spices, flavorings, colorings, and chemical preservatives, if used, would be required to be declared, in accordance with § 501.22 (see proposed § 201.409(d)(9)(ii)).

*j. “Mixing Directions.”* The proposed rule would require this section of the proprietary Type B medicated feed label to have the heading “Mixing Directions,” followed by the approved mixing directions for the manufacture of a Type C medicated feed(s) or another Type B medicated feed(s), if applicable, from the proprietary Type B medicated feed (see proposed § 201.409(d)(10)).

*k. “Warnings.”* The proposed rule would require this section of the proprietary Type B medicated feed label to have the heading “Warnings,” followed by the “Warnings” section, as described in proposed § 201.409(a)(10) for the Type A medicated article label (see proposed § 201.409(d)(11)).

*l. “Additional Recommendations.”* For new animal drugs having precautions, the proposed rule would require this section of the proprietary Type B medicated feed label to have the heading “Additional Recommendations,” followed by all precautions, as described in proposed § 201.407(a)(8) for full product information for OTC new animal drugs (see proposed § 201.409(d)(12)).

*m. “Other Effects You May Notice.”* For new animal drugs that have effects on the target animal(s) that are not considered contraindications, target animal safety warnings, adverse reactions, or post-approval adverse drug experiences, and FDA determines that these effects are required to be described on labeling, the proposed rule would require this section of the proprietary Type B medicated feed label to have the heading “Other Effects You May Notice,” followed by a description of the effects. This section of the

proprietary Type B medicated feed label would be the same as described in proposed § 201.407(a)(9) for full product information for OTC new animal drugs (see proposed § 201.409(d)(13)).

*n. “Net Weight.”* The proposed rule would require this section of the proprietary Type B medicated feed label to have the heading “Net Weight,” followed by the net weight of the Type B medicated feed in the immediate container (see proposed § 201.409(d)(14)).

*o. “Storage, Handling, and Disposal.”* The proposed rule would require this section of the proprietary Type B medicated feed label to have the heading “Storage, Handling, and Disposal,” followed by storage information for the Type B medicated feed, as well as any required handling and disposal information, as described in proposed § 201.405(a)(20) for full prescribing information for Rx new animal drugs (see proposed § 201.409(d)(15)).

*p. “Questions/Comments?”* The proposed rule would require this section of the proprietary Type B medicated feed label to have the heading “Questions/Comments?,” followed by the sponsor’s contact information for feed manufacturers or other users of the Type B medicated feed to facilitate requesting additional information on the product or to report suspected adverse drug experiences. FDA’s contact information for voluntary reporting of adverse drug experiences for animal drugs would also be required (see proposed § 201.409(d)(16)).

The sponsor’s contact information would be the name of the manufacturer, packer, or distributor, whichever is identified in the “Name and place of business” section of the Type B medicated feed (see proposed § 201.409(d)(18)). If more than one business is identified in the “Name and place of business” section of the proprietary Type B medicated feed label, the drug sponsor would select the most appropriate of these businesses to use in the “Questions/Comments?” section to provide additional information about the Type B medicated feed and to contact regarding suspected adverse drug experiences.

The statements in this section of the proprietary Type B medicated feed label would be required to be structured as follows: “Contact [insert name of business] at [insert business telephone number] or [insert business web address]. To report side effects, contact [insert name of business] at [insert business telephone number]. For additional information about reporting problems with medicated feeds, contact

FDA at [insert current FDA telephone number for voluntary reporting of adverse drug experiences] or [insert current FDA web address for voluntary reporting of adverse drug experiences].” Sponsors can search FDA’s website or contact FDA by telephone to find the current FDA telephone number or web address for voluntary reporting of adverse drug experiences for animal drug.

*q. NADA/ANADA approval statement.* For approved or generic approved proprietary Type B medicated feeds, the proposed rule would require this section of the proprietary Type B medicated feed label to include an “NADA approval statement” or “ANADA approval statement,” respectively, as described in proposed § 201.405(a)(21) for full prescribing information for Rx new animal drugs (see proposed § 201.409(d)(17)).

*r. Name and place of business.* The proposed rule would require this section of the proprietary Type B medicated feed label to identify name and place of business of the manufacturer, packer, or distributor, as described in proposed § 201.405(a)(22) for full prescribing information for Rx new animal drugs (see proposed § 201.409(d)(18)).

*s. “Lot, Batch, or Control Number.”* The proposed rule would require this section of the proprietary Type B medicated feed label to have the heading “Lot, Batch, or Control Number,” followed by the identifying lot, batch, or control number of the Type B medicated feed. Alternatively, the proposed rule would allow for this section of the proprietary Type B medicated feed label to refer to the location on the proprietary Type B medicated feed label or immediate container where the lot, batch, or control number is printed (see proposed § 201.409(d)(19)).

*t. “Expiration Date.”* For Type B medicated feeds requiring an expiration date, in accordance with § 514.1(b)(5)(x), the proposed rule would require this section of the proprietary Type B medicated feed label to have the heading “Expiration Date,” followed by the expiration date of the proprietary Type B medicated feed. Alternatively, the proposed rule would allow for this section of the proprietary Type B medicated feed label to refer to the location on the proprietary Type B medicated feed label or immediate container where the expiration date is printed (see proposed § 201.409(d)(20)).

*u. “Revision Date.”* The proposed rule would require this section of the proprietary Type B medicated feed label to have the heading “Revision Date,”

followed by the date of the most recent revision of the proprietary Type B medicated feed label, listing the month followed by the year (see proposed § 201.409(d)(21)). This information is important to ensure that the most current approved version of the proprietary Type B medicated feed label is being used.

#### 5. Proprietary Type C Medicated Feed Label (Proposed § 201.409(e))

The proposed rule would establish content and format requirements for a proprietary Type C medicated feed label for new animal drugs approved or conditionally approved for use in animal feeds (see proposed § 201.409(e)). FDA may approve or conditionally approve applications for proprietary final formulations of Type C medicated feeds. For some proprietary Type C medicated feeds, the formulation and labeling are approved in an NADA. In other situations, the underlying data and labeling for the proprietary Type C medicated feed to support the approved uses are maintained in a VMF. For example, this would include situations in which a proprietary Type C medicated feed is manufactured via modification to an approved formulation published in the CFR or where a feed manufacturer creates its own proprietary formulation. The application for a proprietary Type C medicated feed will include the proprietary label for the final Type C medicated feed. A proprietary Type C medicated feed label is on the immediate container, which is typically a bag or bulk container.

The proposed rule would require the following information to be presented on the proprietary Type C medicated feed label for an approved or conditionally approved new animal drug and in the following order (see proposed § 201.409(e)). Unless otherwise indicated, this information would be the same as that required by proposed § 201.405(a) for full prescribing information for approved or conditionally approved Rx new animal drugs, proposed § 201.407(a) for full product information for approved or conditionally approved OTC new animal drugs, proposed § 201.409(a) for the Type A medicated article label, or proposed § 201.409(d) for the proprietary Type B medicated feed label.

*a. Proprietary Type C medicated feed identification.* The proposed rule would require this section of the proprietary Type C medicated feed label to identify the Type C medicated feed (see proposed § 201.409(e)(1)). This section of the proprietary Type C medicated

feed label would be required to include the following components in order:

*i. Proprietary name of the Type C medicated feed.* The proposed rule would require this subsection of the proprietary Type C medicated feed label to include the proprietary name of the Type C medicated feed (see proposed § 201.409(e)(1)(i)).

*ii. Established name of the Type C medicated feed.* The proposed rule would require this subsection of the proprietary Type C medicated feed label to include the established name of the Type C medicated feed. The established name of the proprietary Type C medicated feed would include the active moiety or active ingredient of each new animal drug, as determined by FDA, followed by an identifying statement of, “Type C medicated feed,” “Type C liquid medicated feed,” “Type C top-dress medicated feed,” “Type C free-choice medicated feed,” or “Type C liquid free-choice medicated feed,” as applicable (see proposed § 201.409(e)(1)(ii)). The identifying statements also clearly designate the medicated feeds as Type C (as opposed to a Type B) medicated feeds. The identifying statements also distinguish Type C liquid medicated feeds from other Type C medicated feeds, which is important because Type C liquid medicated feeds have unique approval and labeling requirements (see § 558.5). Similarly, Type C free-choice medicated feeds have specific requirements for their approval (see § 510.455).

*b. VFD cautionary statement.* For VFD new animal drugs, the proposed rule would require this section of the proprietary Type C medicated feed label to provide the VFD cautionary statement, in accordance with § 558.6(a)(6), as described in proposed § 201.409(a)(2) for the Type A medicated article label (see proposed § 201.409(e)(2)).

*c. Conditional approval statement.* For conditionally approved new animal drugs, the proposed rule would require this section of the proprietary Type C medicated feed label to include a conditional approval statement, as described in proposed § 201.405(a)(3) for full prescribing information for Rx new animal drugs (see proposed § 201.409(e)(3)).

*d. “Indications for Use.”* The proposed rule would require this section of the proprietary Type C medicated feed label to have the heading “Indications for Use,” followed by the approved or conditionally approved indications(s) and target animal(s), as described in proposed § 201.407(a)(3) for full product information for OTC new animal drugs,

with the exception of the heading (see proposed § 201.409(e)(4)).

*e. Extralabel use statement.* The proposed rule would require this section of the proprietary Type C medicated feed label to include an extralabel use statement, as described in proposed § 201.409(a)(6) for the Type A medicated article label (see proposed § 201.409(e)(5)).

*f. “Active Ingredient” or “Active Ingredients.”* The proposed rule would require this section of the proprietary Type C medicated feed label to have the heading “Active Ingredient,” or “Active Ingredients,” followed by the established name and approved concentration of each active ingredient (see proposed § 201.409(e)(6)). If the proprietary Type C medicated feed contains one active ingredient, the proposed rule would require this section of the proprietary Type C medicated feed label to be entitled “Active Ingredient.” If the proprietary Type C medicated feed contains more than one active ingredient, the proposed rule would require this section of the proprietary Type C medicated feed label to be entitled “Active Ingredients.” Because the proprietary Type C medicated feed label applies to a final Type C medicated feed, a single concentration would be required for each active ingredient rather than a range.

*g. “Guaranteed Analysis.”* The proposed rule would require this section of the proprietary Type C medicated feed label to have the heading “Guaranteed Analysis,” followed by the nutritional content guarantees and other required specifications for the final proprietary Type C medicated feed, as described in § 201.409(d)(8) for the proprietary Type B medicated feed label (see proposed § 201.409(e)(7)).

*h. “Ingredients.”* The proposed rule would require this section of the proprietary Type C medicated label to have the heading “Ingredients,” followed by a listing of the feed ingredients in the proprietary Type C medicated feed, as described in § 201.409(d)(9) for the proprietary Type B medicated feed label (see proposed § 201.409(e)(8)).

*i. “Feeding Directions.”* The proposed rule would require this section of the proprietary Type C medicated feed label to have the heading “Feeding Directions,” followed by the approved feeding directions (see proposed § 201.409(e)(9)).

*j. “Warnings.”* The proposed rule would require this section of the proprietary Type C medicated feed label to have the heading “Warnings,”

followed by the “Warnings” section, as described in proposed § 201.409(a)(10) for the Type A medicated article label (see proposed § 201.409(e)(10)).

*k. “Additional Recommendations.”* For new animal drugs having precautions, the proposed rule would require this section of the proprietary Type C medicated feed label to have the heading “Additional Recommendations,” followed by all precautions, as described in proposed § 201.407(a)(8) for full product information for OTC new animal drugs (see proposed § 201.409(e)(11)).

*l. “Other Effects You May Notice.”* For new animal drugs that have effects on the target animal(s) that are not considered contraindications, target animal safety warnings, adverse reactions, or post-approval adverse drug experiences, and FDA determines that these effects are required to be described on labeling, the proposed rule would require this section of the proprietary Type C medicated feed label to have the heading “Other Effects You May Notice,” followed by a description of the effects. This section of the proprietary Type C label would be the same as described in proposed § 201.407(a)(9) for full product information for OTC new animal drugs (see proposed § 201.409(e)(12)).

*m. “Net Weight.”* The proposed rule would require this section of the proprietary Type C medicated feed label to have the heading “Net Weight,” followed by the net weight of the Type C medicated feed in the immediate container (see proposed § 201.409(e)(13)).

*n. “Storage, Handling, and Disposal.”* The proposed rule would require this section of the proprietary Type C medicated feed label to have the heading “Storage, Handling, and Disposal,” followed by storage information for the Type C medicated feed, as well as any required handling, and disposal information, as described in proposed § 201.405(a)(20) for full prescribing information for Rx new animal drugs (see proposed § 201.409(e)(14)).

*o. “Questions/Comments?”* The proposed rule would require this section of the proprietary Type C medicated feed label to have the heading “Questions/Comments?,” followed by the sponsor’s contact information for users of the Type C medicated feed to facilitate requesting additional information on the product or to report suspected adverse drug experiences. FDA’s contact information for voluntary reporting of adverse drug experiences for animal drugs would also

be required (see proposed § 201.409(e)(15)).

The sponsor’s contact information would be the name of the manufacturer, packer, or distributor, whichever is identified in the “Name and place of business” section of the Type C medicated feed (see proposed § 201.409(e)(17)). If more than one business is identified in the “Name and place of business” section of the proprietary Type C medicated feed label, the drug sponsor would select the most appropriate of these businesses to use in the “Questions/Comments?” section to provide additional information about the Type C medicated feed and to contact regarding suspected adverse drug experiences.

The statements in this section of the proprietary Type C medicated feed label would be required to be structured as follows: “Contact [insert name of business] at [insert business telephone number] or [insert business web address]. To report side effects, contact [insert name of business] at [insert business telephone number]. For additional information about reporting side effects or other problems with medicated feeds, contact FDA at [insert current FDA telephone number for voluntary reporting of adverse drug experiences] or [insert current FDA web address for voluntary reporting of adverse drug experiences].” Sponsors can search FDA’s website or contact FDA by telephone to find the current FDA telephone number or web address for voluntary reporting of adverse drug experiences for animal drugs.

*p. NADA/ANADA approval statement.* For approved or generic approved proprietary Type C medicated feeds, the proposed rule would require this section of the proprietary Type C medicated feed label to include an “NADA approval statement” or “ANADA approval statement,” respectively, as described in proposed § 201.405(a)(21) for full prescribing information for Rx new animal drugs (see proposed § 201.409(e)(16)).

*q. Name and place of business.* The proposed rule would require this section of the proprietary Type C medicated feed label to identify name and place of business of the manufacturer, packer, or distributor, as described in proposed § 201.405(a)(22) for full prescribing information for Rx new animal drugs (see proposed § 201.409(e)(17)).

*r. “Lot, Batch, or Control Number.”* The proposed rule would require this section of the proprietary Type C medicated feed label to have the heading “Lot, Batch, or Control Number,” followed by the identifying

lot, batch, or control number of the Type C medicated feed. Alternatively, the proposed rule would allow for this section of the proprietary Type C medicated feed label to refer to the location on the proprietary Type C medicated feed label or immediate container where the lot, batch, or control number is printed (see proposed § 201.409(e)(18)).

*s. “Expiration Date.”* For Type C medicated feeds requiring an expiration date, in accordance with § 514.1(b)(5)(x), the proposed rule would require this section of the proprietary Type C medicated feed label to have the heading “Expiration Date,” followed by the expiration date of the proprietary Type C medicated feed. Alternatively, the proposed rule would allow for this section of the proprietary Type C medicated feed label to refer to the location on the proprietary Type C medicated feed label or immediate container where the expiration date is printed (see proposed § 201.409(e)(19)).

*t. “Revision Date.”* The proposed rule would require this section of the proprietary Type C medicated feed label to have the heading “Revision Date,” followed by the date of the most recent revision of the proprietary Type C medicated feed label, listing the month followed by the year (see proposed § 201.409(e)(20)).

#### 6. Other Approved Labeling for Type A Medicated Articles (Proposed § 201.409(f))

The proposed rule would establish content and format requirements for the information presented on other approved labeling for Type A medicated articles approved or conditionally approved for use in animal feeds. Other approved labeling for Type A medicated articles includes, but is not limited to, labeling on shipping cartons containing bags of Type A medicated articles (see proposed § 201.409(f)).

The proposed rule would require the following information to be presented on other approved labeling for Type A medicated articles and in the following order (see proposed § 201.409(f)). Unless otherwise indicated, this information would be the same as that required by proposed § 201.405(a) for full prescribing information for approved or conditionally approved Rx new animal drugs, or proposed § 201.409(a) for a Type A medicated article label.

*a. Type A medicated article identification.* The proposed rule would require this section of the other approved labeling for Type A medicated articles to include, in order, the proprietary name and the established

name of the Type A medicated article (see proposed § 201.409(f)(1)).

*b. VFD cautionary statement.* For VFD new animal drugs, the proposed rule would require this section of the other approved labeling for Type A medicated articles to provide the VFD cautionary statement, in accordance with § 558.6(a)(6), as described in proposed § 201.409(a)(2) for the Type A medicated article label (see proposed § 201.409(f)(2)).

*c. "Active Ingredient" or "Active Ingredients."* The proposed rule would require this section of the other approved labeling for Type A medicated articles to have the heading "Active Ingredient" or "Active Ingredients," followed by the established name and concentration of each active ingredient in the Type A medicated article. If the Type A medicated article contains one active ingredient, the proposed rule would require this section of the other approved labeling for Type A medicated articles to be entitled "Active Ingredient." If the Type A medicated article contains more than one active ingredient, the proposed rule would require this section of the other approved labeling for Type A medicated articles to be entitled "Active Ingredients" (see proposed § 201.409(f)(3)).

*d. Conditional approval statement.* For conditionally approved new animal drugs, the proposed rule would require this section of the other approved labeling for Type A medicated articles to include a conditional approval statement, as described in proposed § 201.405(a)(3) for full prescribing information for Rx new animal drugs (see proposed § 201.409(f)(4)).

*e. "Net Contents."* The proposed rule would require this section of the other approved labeling for Type A medicated articles to have the heading "Net Contents," followed by the contents of the container to which the other approved labeling for Type A medicated articles applies (see proposed § 201.409(f)(5)).

*f. "Storage and Handling."* The proposed rule would require this section of the other approved labeling for Type A medicated articles to have the heading "Storage and Handling," followed by storage information for the Type A medicated article (see proposed § 201.409(f)(6)). Also, any handling information required for safe and effective use of the Type A medicated article would be included in this section. Information on disposal of the Type A medicated article would not be required to be included on other approved labeling for Type A medicated articles.

*g. NADA/ANADA approval statement.* For approved or generic approved proprietary Type A medicated articles, the proposed rule would require this section of the other approved labeling for Type A medicated articles to include an "NADA approval statement" or "ANADA approval statement," respectively, as described in proposed § 201.405(a)(21) for full prescribing information for Rx new animal drugs (see proposed § 201.409(f)(7)).

*h. Name and place of business.* The proposed rule would require this section of the other approved labeling for Type A medicated articles to identify name and place of business of the manufacturer, packer, or distributor, as described in proposed § 201.405(a)(22) for full prescribing information for Rx new animal drugs (see proposed § 201.409(f)(8)).

*i. "Lot Number and Expiration Date."* The proposed rule would require this section of the other approved labeling for Type A medicated articles to have the heading "Lot Number and Expiration Date," followed by the identifying lot or control number(s) and the expiration date(s) of the Type A medicated article within the container (see proposed § 201.409(f)(9)). The container may include more than one lot of the Type A medicated article, and therefore, more than one lot or control number and expiration date may be listed in this section of other approved labeling for Type A medicated articles.

*j. "Revision Date."* The proposed rule would require this section of the other approved labeling for Type A medicated articles to have the heading "Revision Date," followed by the date of the most recent revision of the other approved labeling for Type A medicated articles, listing the month followed by the year (see proposed § 201.409(f)(10)).

*G. Exemptions From Labeling Requirements for Approved or Conditionally Approved New Animal Drugs (Proposed § 201.411)*

FDA would provide sponsors the opportunity to request an exemption from one or more specific requirements set forth in this proposed subpart on the basis that the requirements are not appropriate for the specific approved or conditionally approved new animal drug (see proposed § 201.411).

An exemption request would be required to be submitted to the corresponding application or investigational new animal drug file (INAD) for the new animal drug. A separate request would be required to be submitted for each new animal drug for which an exemption is sought. Requests for exemptions would be granted or

denied by the Director of FDA's Center for Veterinary Medicine or the Director's designee (see proposed § 201.411(a)). The sponsor seeking an exemption would be required to: (1) describe why the particular requirement for which the exemption is requested was not appropriate for the new animal drug; (2) describe why granting the exemption would not adversely impact the safety or effectiveness of the use of the new animal drugs; and (3) include copies of all draft labeling proposed to be used for the new animal drug (see proposed § 201.411(b)). We anticipate that such exemptions would be rare.

*H. Labeling Requirements for Certain Approved or Conditionally Approved New Animal Drugs (Proposed § 201.413)*

This section of the proposed regulations would consolidate, and where appropriate, update existing labeling requirements pertaining to certain approved or conditionally approved new animal drugs that would continue to apply in addition to the other labeling requirements in proposed subpart H. Currently, the labeling requirements for these new animal drugs are dispersed throughout the regulations. It would be helpful to new animal drug sponsors and FDA reviewers if the proposed rule were to consolidate, and where appropriate, update the additional labeling requirements for these specific new animal drugs in the same subpart of the CFR as general labeling requirements for approved or conditionally approved new animal drugs.

This section also proposes a new labeling provision for all new animal drugs approved or conditionally approved for use in horses and anthelmintic new animal drugs for certain species of animals.

We may propose to amend § 201.413 in the future to include additional labeling requirements for certain specific new animal drugs as appropriate.

**1. Approved or Conditionally Approved Corticosteroid-Containing New Animal Drugs for Oral, Injectable, and/or Ophthalmic Use**

The proposed rule would move labeling requirements currently provided in § 510.410 relating to corticosteroid-containing new animal drugs intended for oral, injectable, and/or ophthalmic use to proposed § 201.413(a). We also propose a conforming amendment to remove current § 510.410.

Section 510.410 was originally issued by FDA in 1970 as § 135.101 (35 FR 11556, July 18, 1970) and provided

background information and established certain labeling requirements for corticosteroid animal drugs administered orally or parenterally. The regulation stated that such corticosteroid animal drugs must bear the veterinary prescription legend and meet the labeling requirements in § 201.105 for prescription new animal drugs. The regulation also required the labeling of these products to bear a warning statement regarding potential adverse reproductive effects to the treated animals when these drugs are administered during the last trimester of pregnancy, specifically premature parturition followed by dystocia, fetal death, retained placenta, and metritis. The regulation was subsequently revised in 1972 (37 FR 24343, November 16, 1972) to address corticosteroid animal drugs for oral, injectable, and intramammary use. In 1984, FDA amended the regulation on labeling requirements for use of corticosteroid animal drugs again to add ophthalmic products, delete intramammary products, and to include an additional warning concerning certain potential congenital/teratogenic effects (49 FR 48535, December 13, 1984). Ophthalmic products were added to the regulation based on the results of a published study supporting the need for these warning statements for ophthalmic use corticosteroid drugs. Intramammary corticosteroid animal drugs were removed from the regulation because intramammary products no longer included steroids in their formulations.

The proposed rule would redesignate § 510.410 as proposed § 201.413(a) and revise its contents to remove some of the background information because we believe it is now well understood. Furthermore, we propose to update some of the warning statements to use more concise language. These animal drug products would continue to be subject to the labeling requirements for prescription new animal drugs. However, because the labeling requirements for approved or conditionally approved prescription new animal drugs would no longer be in § 201.105, we would update the citation to refer to the labeling requirements for prescription new animal drugs in proposed subpart H.

The proposed rule would require the warning statements for adverse reproductive effects to be included in the “Animal Safety Warnings and Precautions” subsection of labeling for approved or conditionally approved corticosteroid new animal drugs for oral, and/or injectable use (see proposed § 201.413(a)). For corticosteroid new animal drugs approved or conditionally

approved for ophthalmic use, per this proposal, we may require these statements to also be included in the “Animal Safety Warnings and Precautions” subsection of labeling. For example, the warning statements might not be necessary for ophthalmic corticosteroid new animal drugs if data are provided to us that demonstrate the intended use is not associated with adverse reproductive effects in the treated animal.

## 2. Anthelmintic New Animal Drugs

The proposed rule would move labeling requirements currently provided in § 500.25 for approved or conditionally approved OTC anthelmintic new animal drugs to proposed § 201.413(b)(1). Labeling requirements currently provided in § 500.25 for OTC anthelmintic new animal drugs that are indexed would be moved to § 516.155 (21 CFR 516.155), “Labeling of indexed drugs”. We also propose a conforming amendment to remove current § 500.25. Furthermore, the proposed rule would require that all approved or conditionally approved anthelmintic new animal drugs for use in sheep, goats, cattle, horses, swine, and/or poultry include statements on labeling on appropriate use of these drugs to minimize anthelmintic resistance development (see proposed § 201.413(b)(2)).

Section 500.25 was originally issued by FDA in 1974 as § 135.111 (39 FR 7165 at 7166, February 25, 1974) and required that labeling for anthelmintic animal drugs not carrying the prescription statement bear the following statement “Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.” Labeling of approved anthelmintic animal drugs not carrying the prescription statement were to be revised accordingly by February 25, 1975, and labeling of all subsequently approved non-prescription anthelmintic new animal drugs were to bear the statement. In 2007, § 500.25 was amended to add the labeling requirement for indexed non-prescription anthelmintic new animal drugs (72 FR 69108 at 69120, December 6, 2007).

The proposed rule would redesignate portions of § 500.25 for approved or conditionally approved OTC anthelmintic new animal drugs, including OTC anthelmintic new animal drugs for use in animal feeds, as proposed § 201.413(b)(1) and update some of its contents. VFD anthelmintic new animal drugs for use in or on animal feeds would be excluded from this requirement. The labeling statement

would be required to be placed in the “Additional Recommendations” section of labeling. Reference to being able to revise labeling without prior approval would be removed because the labeling statement would be required for approval or conditional approval. Reference to an effective date of February 25, 1975 would be removed.

Portions of § 500.25 for indexed OTC anthelmintic new animal drugs would be redesignated as paragraph (c) in § 516.155, “Labeling of indexed drugs”. Reference to an effective date of February 25, 1975 would be removed. The current § 516.155(c) would be redesignated as § 516.155(d).

The proposed rule would also require all approved or conditionally approved anthelmintic new animal drugs for use in sheep, goats, cattle, horses, swine, and/or poultry to include statements on their labeling providing information to end users on appropriate use of these drugs to minimize anthelmintic resistance development. FDA’s Center for Veterinary Medicine held a public meeting on antiparasitic drug use and resistance in ruminants and equines on March 5 and 6, 2012. During that meeting, a panel of veterinary parasitology experts discussed the emerging problem of anthelmintic resistance cattle, horses, and especially small ruminants in the United States, contributing factors to resistance development, strategies to detect and manage anthelmintic resistance, and the importance of educating both veterinarians and other end users about how to detect and manage anthelmintic resistance. Since this meeting, published reports in the United States continue to support that anthelmintic resistance is spreading and is particularly concerning in grazing species (cattle, sheep, goats, and horses), but is also becoming a problem in swine and poultry.

It is in the interest of animal health to take a proactive approach to ensure that anthelmintics are used appropriately to help maintain the effectiveness of these drugs. Therefore, the proposed rule would require that all approved or conditionally approved anthelmintic new animal drugs for use in sheep, goats, cattle, horses, swine, and/or poultry include statements on their labeling providing information to end users on appropriate use of these drugs to minimize antiparasitic resistance development. These statements would include information on appropriate dosing, anthelmintic drug selection, effectiveness monitoring, the integration of anthelmintic drug use with other parasite management practices, and other information as needed (see

proposed § 201.413(b)(2)). The statements would be required in the “Other Warnings” subsection of labeling, and if applicable, additional statements may be required in the “Dosage and Administration” section of labeling for Rx anthelmintic new animal drugs, the “Directions” section of labeling for OTC anthelmintic new animal drugs, or the “Feeding Directions” section or subsection of labeling for anthelmintic new animal drugs for use in animal feeds. We would determine specific statements during review of the new animal drug and its labeling as part of the approval process and/or via guidance developed by FDA.

### 3. Approved or Conditionally Approved New Animal Drugs for Use in Horses

The proposed rule would require that all approved or conditionally approved new animal drugs for use in horses include in the “Other Warnings” subsection of labeling a statement advising against the use of the drug in certain horses (see proposed § 201.413(c)). Historically, drugs approved or conditionally approved for use in horses do not have tolerance levels established because FDA does not consider horses to be food-producing animals. Therefore, FDA currently does not require a human food safety evaluation of new animal drugs intended for use in horses. Because there is no human food safety evaluation of the new animal drug, FDA does not have the data needed to ensure that horses that have been treated with the drugs could safely be used for human consumption and sponsors may not label their drugs as appropriate for use in horses intended for use as human food. Proposed § 201.413(c) would require that all new animal drugs approved or conditionally approved for use in horses include a statement in the “Other Warnings” subsection of labeling advising against use of the drug in horses intended for human consumption.

#### I. Proposed Conforming Amendments

We also propose to amend the following sections:

- § 201.15 pertaining to foreign translations of labeling,
- § 201.100 pertaining to prescription drugs for human use,
- § 201.105 pertaining to prescription drugs for animal use,
- part 501 pertaining to animal food labeling,
- § 514.1 pertaining to new animal drug applications, and
- § 516.155 pertaining to labeling of indexed drugs.

Also, we propose to remove the following sections and incorporate their requirements in proposed new subpart H:

- § 500.25 pertaining to OTC anthelmintic drug use in animals, and
- § 510.410 pertaining to corticosteroids for oral, injectable, and ophthalmic use in animals.

We propose to remove the following sections:

- § 500.55 pertaining to the exemption of certain drug-labeling requirements, and
- §§ 510.105 and 510.106 pertaining to labeling of drugs for use in milk-producing animals.

The proposed rule would establish translation requirements for approved or conditionally approved new animal drug labeling that contains any representation of a foreign language in proposed § 201.404(i) and (j). Therefore, we propose a change to § 201.15, “Drugs; prominence of required label statements.” We propose adding paragraph (4) to § 201.15(c). Proposed paragraph (c)(4) would exempt approved or conditionally approved new animal drugs from the requirements established in § 201.15(c) and state that foreign translations of the labeling for approved or conditionally approved new animal drugs must comply with § 201.404(i) and (j).

The proposed rule would amend § 201.100, “Prescription drugs for human use,” in paragraph (d) to remove the words, “and § 201.105(b)(2)” from the introductory text. This conforming amendment would be in conjunction with conforming amendments proposed for § 201.105, “Veterinary drugs” (see discussion below), which includes the removal of § 201.105(f). Paragraph (f) provides labeling requirements for prescription drugs intended for both human and veterinary use.

Current § 201.105, entitled “Veterinary drugs,” provides requirements, including labeling requirements, for drugs subject to section 503(f)(1) of the FD&C Act, which are prescription drugs for animal use. These drugs include approved or conditionally approved prescription new animal drugs, prescription new animal drugs listed in the index of legally marketed unapproved new animal drugs for minor species, and prescription animal drugs not subject to an approved or conditionally approved application or index listing. Section 201.100, “Prescription drugs for human use,” serves a similar purpose for prescription human drugs. The proposed rule would revise the title of § 201.105 to read “Prescription drugs for animal use.” This would clarify the

scope of the section and be consistent with the title of its counterpart for human prescription drugs in § 201.100.

We propose minor editorial changes to update § 201.105(a), which provides requirements, other than labeling requirements, for prescription animal drugs.

To accommodate the proposed content and format requirements in proposed subpart H for labeling authorized in approved or conditionally approved new animal drug applications, the proposed rule would change § 201.105 to provide the labeling requirements for approved or conditionally approved prescription new animal drugs separately from the labeling requirements for prescription new animal drugs listed in the index of legally marketed unapproved new animal drugs for minor species, and prescription animal drugs not subject to an approved or conditionally approved application or index listing.

Accordingly, we propose to insert a new paragraph § 201.105(b) that would provide labeling requirements for prescription new animal drugs approved under section 512 of the FD&C Act or conditionally approved under section 571 of the FD&C Act. The provisions in the proposed paragraph § 201.105(c) would apply to prescription new animal drugs listed in the index of legally marketed unapproved new animal drugs for minor species established under section 572 of the FD&C Act, and prescription animal drugs not subject to an approved or conditionally approved application or index listing.

The proposed rule would provide requirements for the labeling components for approved or conditionally approved prescription new animal drugs identified in proposed § 201.405 (see proposed § 201.105(b)(1)), which include labeling providing full prescribing information, labels, small labels, labeling for secondary containers that include a package insert, shipping labeling, and other approved labeling for prescription new animal drugs. Such labeling would be required to contain adequate information for use of the drug, including indications for use, dosages, routes of administration, frequency and duration of administration, and any relevant contraindications, warnings, precautions, and adverse reactions, under which veterinarians licensed by law to administer the drug can use the drug safely and for the purposes for which it is intended, including all purposes for which it is advertised or represented (see proposed § 201.105(b)(1)(i)). The labeling

components identified in proposed § 201.405 also would be required to be the labeling authorized by the approved new animal drug application or conditionally approved new animal drug application for the prescription new animal drug (see proposed § 201.105(b)(1)(ii)).

These requirements for the labeling components identified in proposed § 201.405 would be consistent with requirements in current paragraph § 201.105(c) for labeling on or within the package from which the approved or conditionally approved prescription new animal drugs is dispensed. We also propose editorial revisions to use more current terminology regarding the types of information required to provide adequate information for use of the drug by veterinarians. These labeling components also would be required to comply with the applicable content and format requirements of proposed subpart H (see proposed § 201.105(b)(1)(iii)).

The exemption currently provided in § 201.105(c)(2) permits, upon written request to the Commissioner of Food and Drugs, the labeling information required by § 201.105(c)(1) (*i.e.*, adequate information for use) to be omitted from the dispensing container of prescription animal drugs for which the directions, hazards, warnings, and use information are commonly known to licensed veterinarians. Providing an exemption from the requirement that all prescription animal drugs must provide labeling that bears adequate information for use by veterinarians does not ensure safe and effective use of these drugs and is no longer warranted. Additional risks relating to the use of an animal drug may become known long after the drug is first marketed, even when veterinarians have become familiar with the directions, hazards, and warnings concerning its use. Moreover, in some cases, labeling may need to be revised to include additional safety information. Therefore, the proposed rule would revoke the exemption provided in current § 201.105(c)(2). As discussed below, we also propose to remove § 500.55, which lists the animal drugs to which this exemption has been applied.

The proposed rule would set forth requirements for any labeling, as defined in section 201(m) of the FD&C Act, for approved or conditionally approved prescription new animal drugs, distributed by or on behalf of the manufacturer, packer, or distributor of the drug, that provides or purports to provide information for use or prescribes, recommends, or suggests a dosage for use of the drug (see proposed § 201.105(b)(2)), consistent with the

requirements in current § 201.105(d) for such prescription new animal drugs. Labeling, as defined in section 201(m) of the FD&C Act, means “all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article.” Thus, labeling includes material such as promotional labeling, in addition to the labeling authorized in the approved new animal drug application or the conditionally approved new animal drug application. Such labeling that provides or purports to provide information or a dosage for the drug’s use would be required to contain adequate information to ensure licensed veterinarians can use the drug safely and for the purposes for which the drug is intended, including all conditions for which the drug is advertised or represented. For the labeling of the approved or conditionally approved prescription animal drug to contain adequate information for use by veterinarians, proposed § 201.105(b)(2) would require such labeling to include the indications for use, dosages, routes of administration, frequency and duration of administration, and any relevant contraindications, warnings, precautions, and adverse reactions, and information relevant to compliance with the new animal drug provisions of the FD&C Act. It would also require the labeling components providing such information for use to be the same in language and emphasis as the labeling authorized by the approved or conditionally approved new animal drug application, and any other labeling components would have to be consistent with and not contrary to such authorized labeling (see proposed § 201.105(b)(2)(i)). The labeling would be required to contain the same information concerning the ingredients of the drug as appears on the labeling authorized by the approved new animal drug application or the conditionally approved new animal drug application (see proposed § 201.105(b)(2)(ii)).

We propose requirements for the label of prescription new animal drugs listed in the index of legally marketed unapproved new animal drugs for minor species established under section 572 of the FD&C Act, and prescription animal drugs not subject to an approved or conditionally approved application or index listing, that are consistent with those currently provided in § 201.105(b) (see proposed § 201.105(c)(1)). The proposed rule includes requirements for the labeling on or within the package from which such drugs are to be dispensed that are consistent with the

requirements currently provided in § 201.105(c) (see proposed § 201.105(c)(2)). In addition, the proposed rule includes editorial revisions to use more current terminology to identify the types of information that would need to be included on the labeling on or within the dispensing container in order to provide adequate information for use of such drugs by veterinarians (see proposed § 201.105(c)(2)). The proposed rule would revoke the exemption provided in current § 201.105(c)(2) for the reasons described previously.

Proposed § 201.105(c)(3) would require that any labeling, as defined in section 201(m) of the FD&C Act, for prescription new animal drugs listed in the index of legally marketed unapproved new animal drugs for minor species, or prescription animal drugs not subject to an approved or conditionally approved application or an index listing, that is distributed by or on behalf of the manufacturer, packer, or distributor of the drug, that provides information for use or a dosage for use of the drug contain adequate information for use of the drug by licensed veterinarians. This provision is consistent with the requirements currently provided in § 201.105(d) for these prescription animal drugs. In addition, all labeling for such prescription animal drugs, except labels and cartons, that contain information for use of the drug would be required to include the date of the issuance or latest revision of such labeling, consistent with the requirements currently provided in § 201.105(e) (see proposed § 201.105(c)(4)).

The proposed rule would replace the current proviso language in § 201.105(d)(2) relating to prescription animal drug *reminder-piece labeling* with a provision that is similar to the *reminder labeling* provision at § 201.100(f) (21 CFR 201.100(f)) for human prescription drugs (see proposed § 201.105(d)). Specifically, the proposed provision would replace the term *reminder-piece labeling* with the term *reminder labeling* and define *reminder labeling* for prescription animal drugs in a manner similar to how that term is defined for prescription human drugs. In the past, we have relied on the definition for reminder labeling in § 201.100(f) as a guide when reviewing such labeling because the current proviso language in § 201.105 lacks such a detailed definition. We propose to modify the definition for reminder labeling found at § 201.100(f) to establish a similar definition for prescription animal drugs. The proposed use of the term *reminder*

labeling for prescription animal drugs and the proposed inclusion of a definition for this term that is similar to the definition in § 201.100(f) is clearer and more accurate than the current definition for reminder-piece labeling (see proposed § 201.105(d)).

Current § 201.105(f) provides labeling requirements for prescription drugs intended for both human and veterinary use. The proposed rule would remove this provision, which was established in 1960 (as § 1.106(c)(6)); 25 FR 12592) and is now obsolete. In 1968, section 512 of the FD&C Act established separate approval requirements for new animal drugs, including their labeling.

The proposed rule would remove § 500.25, which contains labeling requirements for OTC anthelmintic new animal drugs. The requirements for the labeling of approved or conditionally approved OTC anthelmintic new animal drugs contained in current § 500.25 would be moved to proposed § 201.413(b)(1), “Labeling requirements for certain approved or conditionally approved new animal drugs.” This would further consolidate regulations pertaining to labeling of approved or conditionally approved new animal drugs. The requirements for the labeling of indexed OTC anthelmintic new animal drugs contained in current § 500.25 would be moved to § 516.155, “Labeling of indexed drugs.”

To ensure the safe and effective use of new animal drugs, the proposed rule would remove from the provision found at § 500.55, “Exemption from certain drug-labeling requirements,” and proviso language at § 201.105(c)(2) that permits animal drug sponsors to receive an exemption from including certain labeling information required by § 201.105(c)(1) on the dispensing package for their products where the Commissioner of Food and Drugs has determined that such information is already commonly known to veterinarians. Under § 201.105(c)(1) of this Agency’s regulations, the labeling on or within the dispensing package of prescription new animal drugs must have adequate information for its use, including indications, effects, dosages, routes, methods, and frequency and duration of administration, and any relevant hazards, contraindications, side effects, and precautions, under which veterinarians licensed by law to administer the drug can use it safely and for the purposes for which the drug is intended, including all purposes for which the drug is advertised or represented. Section 201.105(c)(2) contains certain proviso language that permits the “full disclosure” labeling required by § 201.105(c)(1) to be omitted

from the dispensing package of prescription new animal drugs if the directions, hazards, warnings, and use information are commonly known to veterinarians. The Commissioner of Food and Drugs has, upon written request, offered an opinion that such information may be omitted from the dispensing package for the prescription animal drugs listed in § 500.55. Only eight animal drugs have received such an exemption from providing the full disclosure labeling information otherwise required by § 201.105(c)(1).

The list of unapproved prescription animal drugs currently in § 500.55 that have received an exemption from providing full disclosure labeling meeting the requirements of § 201.105(c)(1) on their dispensing package was initially created in 1962. This list was added to a then-existing provision at 21 CFR 3.515 that permitted full disclosure labeling to be omitted from the dispensing package of certain prescription drugs for human use in cases where the Commissioner of Food and Drugs determined that directions, hazards, warnings, and use information for such drugs was commonly known to physicians (27 FR 5428, June 8, 1962). In 1971, when FDA issued regulations implementing the Animal Drug Amendments of 1968, the human and animal drug provisions were recodified in separate sections of FDA’s regulations. As a result, the list of animal drugs exempt from the requirement to have full disclosure labeling on their dispensing package was moved to § 135.107 and the list of human prescription drugs exempt from similar labeling requirements was moved to § 201.160. In the mid-1970s, as part of the Agency’s reorganization of its regulations, the animal drug list was moved again to § 500.55.

In 1979, FDA removed § 201.160, the human drug provision similar to § 500.55, because the Agency’s experience had shown that risks from the use of a drug may be uncovered long after the drug is first marketed, even for long-used drugs for which physicians had become familiar with the directions, hazards, and warnings concerning their use. FDA concluded that current full disclosure labeling should be provided for all human prescription drugs to ensure that physicians have the information they need to use these drugs safely. For similar reasons, full disclosure labeling is needed for all prescription new animal drugs to ensure veterinarians are able to use these products safely and effectively. In addition, none of the eight products listed in § 500.55 received FDA approval for the uses in animals for

which they were generally employed by veterinarians at the time the list of exempt drugs was initially established in 1962, and several are no longer used in veterinary medicine. Therefore, we propose to remove § 500.55 and the proviso language at § 201.105(c)(2).

In part 501 subpart A, we propose to add a new section, § 501.19, “Animal food; labeling of animal food containing new animal drugs.” Proposed § 501.19 would require labeling of animal food containing an approved or conditionally approved new animal drug to comply with proposed § 201.409. The requirements in part 501 would apply only as specified in proposed § 201.409.

The proposed rule would remove § 510.105, “Labeling of drugs for use in milk-producing animals”, and § 510.106, “Labeling of antibiotic and antibiotic-containing drugs intended for use in milk-producing animals”, which provide statements required to appear on the labeling of such drugs for use in milk-producing animals. The requirements in proposed § 201.405(a)(10)(i), 201.407(a)(7)(i), and 201.409(a)(10)(i) would supersede the requirements in §§ 510.105 and 510.106.

Section 510.105 was originally issued by FDA in 1960 as 21 CFR 3.18 (25 FR 8321, August 31, 1960) and was recodified as § 135.103 (21 CFR 135.103) in 1971 (36 FR 18375 at 18393, September 14, 1971). In 1975 § 135.103 was redesignated as § 510.105 (40 FR 13802, March 27, 1975).

Section 510.106 was originally issued by FDA in 1960 as § 146.14 (21 CFR 146.14) (25 FR 8321 at 8322, August 31, 1960). In 1964, § 146.14 was redesignated as § 148.5 (21 CFR 148.5) (29 FR 15672, November 21, 1964) and subsequently amended in 1965 (30 FR 7040 at 7041, May 26, 1965) to update the warning statements. In 1975 § 148.5 was redesignated as § 510.106 (40 FR 13802, March 27, 1975).

Both §§ 510.105 and 510.106 were amended in 1998 to update the warning statements in those provisions to reflect current practices in the dairy industry (63 FR 32978, June 17, 1998).

The proposed rule would remove §§ 510.105 and 510.106 because the labeling requirements proposed for the subsection entitled “Withdrawal Periods and Residue Warnings” or “Withdrawal Periods” would supersede such requirements in §§ 510.105 and 510.106. The labeling requirements for the proposed “Withdrawal Periods and Residue Warnings” or “Withdrawal Periods” subsection would provide flexibility to have more targeted and informative statements with respect to human food safety warnings, including

milk discard times, withdrawal periods, and residue warning statements for the labeling of all new animal drugs intended for use in food-producing animals (see proposed §§ 201.405(a)(10)(i), 201.407(a)(7)(i), and 201.409(a)(10)(i)).

The proposed rule would remove § 510.410. The requirements in current § 510.410 would be moved to proposed § 201.413, “Labeling requirements for certain approved or conditionally approved new animal drugs.” The warning language would be clarified and updated in proposed § 201.413(a). This would further consolidate regulations pertaining to labeling of approved or conditionally approved new animal drugs.

The proposed rule would amend § 514.1, which describes the requirements for applications for new animal drugs. Current § 514.1(b)(3) describes the labeling that must be included in a new animal drug application. Paragraphs (ii) through (vi) of current § 514.1(b)(3) describe the labeling required in a new animal drug application for prescription and nonprescription new animal drugs and new animal drugs intended for use in the manufacture of medicated feeds.

The proposed rule would insert a paragraph after § 514.1(b)(3)(i) to indicate that the content and format of all proposed labeling must comply with subpart H of part 201 of this chapter.

Paragraphs (ii) through (vi) of § 514.1(b)(3) would be redesignated as paragraphs (iii) through (vii). The current text “prescription veterinary drugs” in redesignated paragraphs (iv) and (vii) would be changed to “prescription new animal drugs” to be consistent with the text used in proposed subpart H.

#### **VI. Proposed Effective/Compliance Dates**

If finalized, sponsors of new animal drugs would need to comply with these proposed regulations within 6 years of the effective date of the final rule, according to the compliance schedule provided in the General Requirements section of this proposed rule, discussed in section V.C. The compliance schedule is based on application number, 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. The 6-year compliance period would begin on the effective date of the final rule (see proposed § 201.404(a)(4)).

#### **VII. Preliminary Economic Analysis of Impacts**

We have examined the impacts of the proposed rule under Executive Order 12866, Executive Order 13563, Executive Order 14094, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104–4).

Executive Orders 12866, 13563, and 14094 direct us to assess all benefits, costs, and transfers of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). Rules are “significant” under Executive Order 12866 Section 3(f)(1) (as amended by Executive Order 14094) if they “have an annual effect on the economy of \$200 million or more (adjusted every 3 years by the Administrator of [the Office of Information and Regulatory Affairs (OIRA)] for changes in gross domestic product); or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, territorial, or tribal governments or communities.” OIRA has determined that this proposed rule is not a significant regulatory action as defined by Executive Order 12866 Section 3(f)(1).

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because net annualized compliance costs of the proposed rule are less than 2 percent of average annual revenues for the smallest firms in the industry, we propose to certify that the proposed rule will not have a significant economic impact on a substantial number of small entities.

The Unfunded Mandates Reform Act of 1995 (section 202(a)) requires us to prepare a written statement, which includes an assessment of anticipated impacts, before proposing “any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any one year.” The current threshold after adjustment for inflation is \$177 million, using the most current (2022) Implicit Price Deflator for the Gross Domestic Product. This proposed rule would not result in an expenditure in

any year that meets or exceeds this amount.

The proposed rule, if finalized, would require that sponsors follow specific content and format requirements for labeling of approved or conditionally approved new animal drugs. A comprehensive set of standardized requirements for the content and format of information on labeling of such drugs currently does not exist. Veterinarians, pet owners, livestock owners, and other users of new animal drugs may more easily locate the information they need with standardized labeling.

We quantify potential cost savings to industry and FDA from a reduction in the quantity and time burden of new animal drug labeling amendments and informal communications related to new animal drug labeling. There may be additional benefits to users of approved or conditionally approved new animal drugs from greater predictability and ease of reading new animal drug labeling in the form of time saved searching for content, which we are unable to quantify. Additionally, animal or human health benefits may result from reductions in medication errors or improvements in adverse event reporting, which we cannot quantify.

We expect that new animal drug sponsors would incur one-time costs to read and understand the rule, revise standard operating procedures (SOPs) related to labeling, and train employees on the revised SOPs. New animal drug sponsors would also bear costs to update labeling and prepare supplemental labeling applications to conform to the proposed requirements. FDA would incur costs to review these supplemental applications.

We summarize the quantified benefits and costs in table 2. We estimate that the annualized benefits over 10 years would range from \$0.143 million to \$0.243 million at a 2 percent discount rate, with a primary estimate of \$0.193 million. The annualized costs would range from \$2.16 million to \$2.77 million at a 2 percent discount rate, with a primary estimate of \$2.45 million.

The present value of total benefits over 10 years would range from \$1.31 million to \$2.23 million at a 2 percent discount rate, with a primary estimate of \$1.77 million. At a 2 percent discount rate, the present value of total costs would range from \$19.78 million to \$25.38 million, with a primary estimate of \$22.48 million.

TABLE 2—SUMMARY OF BENEFITS, COSTS, AND DISTRIBUTIONAL EFFECTS OF THE PROPOSED RULE  
[Millions of 2022 dollars]

Category	Primary estimate	Low estimate	High estimate	Dollar year	Discount rate	Time horizon	Notes (e.g., Risk assumptions; source citations; whether inclusion of capital effects differs across low, primary, high estimates; etc.)
<b>Benefits:</b>							
Annualized monetized benefits .....	\$0.193	\$0.143	\$0.243	2022	2	10	Cost savings to industry and FDA.
Annualized quantified, but non-monetized, benefits .....							
Unquantified benefits .....	Information search cost savings to users of new animal drugs and potential benefits to animal or human health.						
<b>COSTS:</b>							
Annualized monetized costs .....	2.45	2.16	2.77	2022	2	10	
Annualized quantified, but non-monetized, costs .....							
Unquantified costs .....							
<b>Transfers:</b>							
Annualized monetized Federal budgetary transfers .....							
Bearers of transfer gain and loss? .....							
Other annualized monetized transfers .....							
Bearers of transfer gain and loss? .....							
<b>Net Benefits:</b>							
Annualized monetized net benefits .....	-2.26	-2.02	-2.53	2022	2	10	
<b>Category</b>	<b>Effects</b>			<b>Notes</b>			
Effects on State, local, or Tribal governments .....	None.						
Effects on small businesses .....	Quantified effects of less than 2 percent of average annual revenues for the smallest firms.						
Effects on wages .....	None.						
Effects on growth .....	None.						

We have developed a comprehensive Preliminary Economic Analysis of Impacts that assesses the impacts of the proposed rule. The full preliminary analysis of economic impacts is available in the docket for this proposed rule (Ref. 2) and at <https://www.fda.gov/about-fda/economics-staff/regulatory-impact-analyses-ria>.

**VIII. Analysis of Environmental Impact**

The Agency has determined under § 25.30(k) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

**IX. Paperwork Reduction Act of 1995**

This proposed rule contains information collection provisions that are subject to review by the OMB under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3521). A description of these provisions is given in the *Description* section of this document with an estimate of the annual reporting

burden. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

FDA invites comments on these topics: (1) whether the proposed collection of information is necessary for the proper performance of FDA’s functions, including whether the information will have practical utility; (2) the accuracy of FDA’s estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

*Title:* Reporting Associated With New Animal Drug Applications and Veterinary Master Files; OMB control number 0910–0032—Revision.

*Description:* The proposed rule, if finalized, would revise the existing requirements for the content and format of labeling for approved or conditionally approved new animal drugs that sponsors submit as part of NADAs or CNADAs, respectively. The proposed rule would also place labeling requirements that are specific to approved or conditionally approved new animal drugs in a single location in the CFR. The proposed rule would apply to the labeling of both Rx and OTC new animal drugs, as well as new animal drugs for use in animal feeds.

The proposed regulations would provide the following for the content and format elements of labeling for approved or conditionally approved new animal drugs:

*Description of Respondents:* Respondents include persons developing, manufacturing, and/or researching new animal drugs, commonly referred to as new animal drug sponsors.

We estimate the burden of the information collection as follows:

TABLE 3—ESTIMATED ONE-TIME REPORTING BURDEN

21 CFR section; activity	Number of respondents	Number of responses per respondent	Total responses	Average burden per response	Total hours
514.8 and 514.8(c)(2); supplements and changes to an approved application .....	66	<sup>1</sup> 12.55	<sup>2</sup> 828	20	16,560

<sup>1</sup> Decimal rounded up.  
<sup>2</sup> Decimal rounded down.

To ease the burden of the information collection on respondents, we have established a 6-year implementation period. We estimate 828 supplemental labeling applications of approved and marketed new animal drugs over the course of 6 years to comply with the labeling regulations, if finalized. Based

on internal data, there were 78 unique firms with an approved or conditionally approved new animal drug application (sponsors) in September 2023. Sixty-six of these sponsors currently had an approved and marketed new animal drug. We assume 828 submissions regarding supplements and changes to

an application for an approved and marketed new animal drug, for an average of 12.55 submissions per respondent. We further assume it takes an average of 20 hours to prepare each submission for a total of 16,560 hours.

TABLE 4—ESTIMATED ONE-TIME RECORDKEEPING BURDEN

Activity	Number of Recordkeepers	Number of records per recordkeeper	Total annual records	Average burden per recordkeeping	Total hours
Reading and understanding the rule .....	156	1	156	6	936
Writing new labeling SOPs .....	156	1	156	2.14	1 334
Training .....	156	1	156	0.89	1 139
Total .....					1,409

<sup>1</sup> Decimal rounded up.

We estimate that approved new animal drug sponsors will incur one-time burden attributable to reading and understanding the rule, revising SOPs related to labeling, and training employees on the revised SOPs. We estimate the average time to read and understand the proposed rule is 6 hours (156 × 6 = 936 hours). We estimate that small businesses will spend 4 hours and large business will spend 8 hours revising SOPs related to labeling. Based on data from the 2017 Statistics of U.S. Businesses, there are 72 small business entities and 6 large business entities. ((72 × 4) + (6 × 8) ÷ 156 = 2.14 hours per record). We also estimate that small businesses will spend 1 hour and large businesses will spend 12 hours to train employees on the revised SOPs ((72 × 1) + (6 × 12) ÷ 156 = 0.89 hours per record). We assume at least two recordkeepers per drug sponsor.

To ensure that comments on information collection are received, OMB recommends that written comments be submitted through *reginfo.gov* (see **ADDRESSES**). All comments should be identified with the title of the information collection.

In compliance with the Paperwork Reduction Act of 1995 (44 U.S.C. 3407(d)), we have submitted the information collection provisions of this proposed rule to OMB for review. These

information collection requirements will not be effective until FDA publishes a final rule, OMB approves the information collection requirements, and the rule goes into effect. FDA will announce OMB approval of these requirements in the **Federal Register**.

**X. Federalism**

We have analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132: Federalism. The Order requires Federal Agencies to examine actions carefully to determine if they contain policies that have federalism implications or that preempt State law. As defined in the Order, “policies that have federalism implications” refers to regulations, legislative comments or proposed legislation, and other policy statements or actions that have substantial direct effects on the States, on the relationship between the Federal Government and the States, or on the distribution of power and responsibilities among the various levels of government.

Section 4(a) of the Order requires Agencies to “construe . . . a Federal statute to preempt State law only where the statute contains an express preemption provision or there is some other clear evidence that the Congress intended preemption of State law, or where the exercise of State authority

conflicts with the exercise of Federal authority under the Federal statute.” The sole statutory provision giving preemptive effect to this proposed rule is section 751 of the FD&C Act (21 U.S.C. 379r), which would apply only with respect to nonprescription animal drugs. There are no express preemption provisions of the FD&C Act applicable to prescription animal drugs.

We have complied with all of the applicable requirements under the Executive order and have determined that the preemptive effect of this proposed rule, if finalized, would be consistent with Executive Order 13132. Through publication of this proposed rule, we are providing notice and an opportunity for State and local officials to comment on this rulemaking.

**XI. Consultation and Coordination With Indian Tribal Governments**

We have analyzed this proposed rule in accordance with the principles set forth in Executive Order 13175. We have tentatively determined that the rule does not contain policies that would have a substantial direct effect on one or more Indian Tribes, on the relationship between the Federal Government and Indian Tribes, or on the distribution of power and responsibilities between the Federal Government and Indian Tribes. The

Agency solicits comments from tribal officials on any potential impact on Indian Tribes from this proposed action.

## XII. References

The following references are on display in the Dockets Management Staff (see **ADDRESSES**) and are available for viewing by interested persons between 9 a.m. and 4 p.m. Monday through Friday; they are also available electronically at <https://www.regulations.gov>. Although FDA has verified the website addresses in this document, please note that websites are subject to change over time.

1. FDA, Preliminary Regulatory Impact, Initial Regulatory Flexibility, and Unfunded Mandates Reform Act Analyses, 2023; Docket No. FDA-2023-N-5160; <https://www.fda.gov/about-fda/economics-staff/regulatory-impact-analyses-ria>.

## List of Subjects

### 21 CFR Part 201

Drugs, Labeling, Reporting and Recordkeeping requirements.

### 21 CFR Part 500

Animal drugs, Animal feeds, Cancer, Labeling, Packaging and containers, Polychlorinated biphenyls (PCB's).

### 21 CFR Part 501

Animal foods, Packaging and containers, Reporting and recordkeeping requirements.

### 21 CFR Part 510

Administrative practice and procedure, Animal drugs, Labeling, Reporting and recordkeeping requirements.

### 21 CFR Parts 514 and 516

Administrative practice and procedure, Animal drugs, Confidential business information, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, we propose that 21 CFR parts 201, 500, 501, 510, 514, and 516 be amended as follows:

## PART 201—LABELING

- 1. The authority citation for part 201 is revised to read as follows:

**Authority:** 21 U.S.C. 321, 331, 343, 351, 352, 353, 354, 355, 358, 360, 360b, 360ccc, 360ccc-1, 360ee, 360gg-360ss, 371, 374, 379e; 42 U.S.C. 216, 241, 262, 264.

- 2. In § 201.15, add paragraph (c)(4) to read as follows:

### § 201.15 Drugs; prominence of required label statements.

\* \* \* \* \*

(c) \* \* \*

(4) Approved or conditionally approved new animal drugs are exempted from the requirements in paragraph (c). Foreign language translations of the labeling for approved or conditionally approved new animal drugs must comply with § 201.404(i) and (j).

### § 201.100 [Amended].

- 3. In § 201.100, in paragraph (d) introductory text remove the words, “and § 201.105(b)(2)”.

- 4. Revise § 201.105 to read as follows:

### § 201.105 Prescription drugs for animal use.

A drug subject to the requirements of section 503(f)(1) of the Federal Food, Drug, and Cosmetic Act is exempt from section 502(f)(1) of the Federal Food, Drug, and Cosmetic Act if all the following conditions are met:

(a) The prescription animal drug is:

(1)(i) In the possession of a person, or the person's agents or employees, regularly and lawfully engaged in the manufacture, transportation, storage, or wholesale distribution of drugs that are to be used only by or on the prescription or other order of a licensed veterinarian; or

(ii) In the possession of a retail, hospital, or clinic pharmacy, or other person authorized under State law to dispense prescription animal drugs, who is regularly and lawfully engaged in dispensing drugs that are to be used only by or on the prescription or other order of a licensed veterinarian; or

(iii) In the possession of a licensed veterinarian for use in the course of his or her professional practice; and

(2) To be dispensed in accordance with section 503(f) of the Federal Food, Drug, and Cosmetic Act.

(b) For prescription new animal drugs approved under section 512 of the Federal Food, Drug, and Cosmetic Act or conditionally approved under section 571 of the Federal Food, Drug, and Cosmetic Act:

(1) The labeling components identified in § 201.405 for the prescription new animal drug:

(i) Contain adequate information for its use, including indications for use, dosages, routes of administration, frequency and duration of administration, and any relevant contraindications, warnings, precautions, and adverse reactions, under which veterinarians licensed by law to administer the drug can use the drug safely and for the purposes for

which it is intended, including all purposes for which it is advertised or represented;

(ii) Are authorized by the approved new animal drug application or the conditionally approved new animal drug application for the prescription new animal drug; and

(iii) Comply with the applicable content and format requirements of subpart H of this part.

(2) Any labeling, as defined in section 201(m) of the Federal Food, Drug, and Cosmetic Act, for the approved or conditionally approved prescription new animal drug, distributed by or on behalf of the manufacturer, packer, or distributor of the drug, that provides or purports to provide information for its use or a dosage for its use contains:

(i) Adequate information for such use, including indications for use, dosages, routes of administration, frequency and duration of administration, and any relevant contraindications, warnings, precautions, and adverse reactions, and information relevant to compliance with the new animal drug provisions of the Federal Food, Drug, and Cosmetic Act, under which veterinarians licensed by law to administer the drug can use the drug safely and for the purposes for which it is intended, including all conditions for which it is advertised or represented, and the labeling components providing such information for use are the same in language and emphasis as labeling authorized by the approved new animal drug application or the conditionally approved new animal drug application, and any other labeling components are consistent with and not contrary to such authorized labeling; and

(ii) The same information concerning the ingredients of the drug as appears on the labeling authorized by the approved new animal drug application or the conditionally approved new animal drug application.

(c) For prescription new animal drugs listed in the index of legally marketed unapproved new animal drugs for minor species established under section 572 of the Federal Food, Drug, and Cosmetic Act, or prescription animal drugs not subject to an approved or conditionally approved application or indexed listing:

(1) The label of the drug bears:

(i) The statement, “Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian”;

(ii) The recommended or usual dosage;

(iii) The route of administration, if it is not for oral use;

(iv) The quantity or proportion of each active ingredient as well as the information required by section 502(e)

of the Federal Food, Drug, and Cosmetic Act; and

(v) If it is for other than oral use, the names of all inactive ingredients, except that:

(A) Flavorings and perfumes may be designated as such without naming their components;

(B) Color additives may be designated as coloring without naming specific color components unless the naming of such components is required by a color additive regulation prescribed in subchapter A of this chapter; and

(C) Trace amounts of harmless substances added solely for individual product identification need not be named.

(vi) If it is intended for administration by parenteral injection, the quantity or proportion of all inactive ingredients, except that ingredients added to adjust the pH or to make the drug isotonic may be declared by name and a statement of their effect; and if the vehicle is water for injection, it need not be named.

(vii) An identifying lot or control number from which it is possible to determine the complete manufacturing history of the package of the drug.

(viii) In the case of containers too small or otherwise unable to accommodate a label with sufficient space to bear all of the information required by paragraph (c)(1) of this section, but which are packaged within an outer container from which they are removed for dispensing or use, the information required by paragraphs (c)(1)(ii), (iii), (v), and (vi) of this section may be contained in other labeling on or within the package from which the drug is to be so dispensed, and the information referred to in paragraph (c)(1)(i) of this section may be placed on such outer container only, and the information required by paragraph (c)(1)(vii) of this section may be placed on the crimp of the dispensing tube.

(2) The labeling on or within the package from which the drug is to be dispensed:

(i) Bears adequate information for its use, including indications for use, dosages, routes of administration, frequency and duration of administration, and any relevant contraindications, warnings, precautions, and adverse reactions, under which veterinarians licensed by law to administer the drug can use the drug safely and for the purposes for which it is advertised or represented; and

(ii) For prescription new animal drugs listed in the index of legally marketed unapproved new animal drugs for minor species established under section 572 of

the Federal Food, Drug, and Cosmetic Act, the labeling bearing such information is the labeling contained in the index listing.

(3) Any labeling, as defined in section 201(m) of the Federal Food, Drug, and Cosmetic Act, whether or not it is on or within a package from which the drug is to be dispensed, distributed by or on behalf of the manufacturer, packer, or distributor of the drug, that provides or purports to provide information for use or which prescribes, recommends, or suggests a dosage for the use of the drug (other than dose information required by paragraph (c)(1)(ii) of this section) contains:

(i) Adequate information for such use, including indications for use, dosages, routes of administration, frequency and duration of administration, and any relevant contraindications, warnings, precautions, and adverse reactions, including information relevant to compliance with the new animal drug provisions of the Federal Food, Drug, and Cosmetic Act, under which veterinarians licensed by law to administer the drug can use the drug safely and for the purposes for which it is intended, including all conditions for which it is advertised or represented; for prescription new animal drugs listed in the index of legally marketed unapproved new animal drugs for minor species established under section 572 of the Federal Food, Drug, and Cosmetic Act, the labeling components providing such information are the same in language and emphasis as labeling indexed under the provisions of section 572 of the Federal Food, Drug, and Cosmetic Act, and any other labeling components are consistent with and not contrary to such indexed labeling; and

(ii) The same information concerning the ingredients of the drug as appears on the label and labeling on or within the package from which the drug is to be dispensed.

(4) All labeling, except labels and cartons, bearing information for use of the drug also bears the date of the issuance or the date of the latest revision of such labeling.

(d) Reminder labeling, which calls attention to the name of the prescription animal drug product but does not include indications or dosage recommendations for use of the drug product, is exempted from the provisions of paragraphs (b) and (c) of this section. This reminder labeling must contain only the proprietary name of the drug product, if any; the established name of the drug product, if any; the established name of each active ingredient in the drug product; and, optionally, information relating to

quantitative ingredient statements, dosage form, quantity of package contents, price, the name and address of the manufacturer, packer, or distributor or other written, printed, or graphic matter containing no representation or suggestion relating to the drug product. If the Commissioner finds that there is evidence of significant incidence of fatalities or serious injury associated with the use of a particular prescription animal drug, the Commissioner may withdraw this exemption by so notifying the manufacturer, packer, or distributor of the drug by letter. Reminder labeling, other than price lists and catalogs solely intended to convey price information, is not permitted for a prescription animal drug product whose labeling contains a boxed warning relating to a serious hazard associated with the use of the drug product.

■ 5. Add subpart H, consisting of §§ 201.401 through 201.413, to read as follows:

**Subpart H—Labeling Requirements for Approved or Conditionally Approved New Animal Drugs**

Sec.

- 201.401 Scope.
- 201.403 Definitions.
- 201.404 General requirements.
- 201.405 Content and format for prescription new animal drug labeling.
- 201.407 Content and format for over-the-counter (OTC) new animal drug labeling.
- 201.409 Content and format of labeling for new animal drugs for use in animal feeds.
- 201.411 Exemptions from labeling requirements for approved or conditionally approved new animal drugs.
- 201.413 Labeling requirements for certain approved or conditionally approved new animal drugs.

**Subpart H—Labeling Requirements for Approved or Conditionally Approved New Animal Drugs**

**§ 201.401 Scope.**

(a) This subpart establishes requirements for content and format of labeling for the following categories of prescription (Rx) new animal drugs, over-the-counter (OTC) new animal drugs other than those for use in animal feeds in accordance with part 558 of this chapter, and new animal drugs for use in animal feeds that are subject to part 558 of this chapter, including veterinary feed directive (VFD) drugs:

(1) New animal drugs that are the subject of a new animal drug application (NADA) approved or submitted pursuant to section 512 of the Federal Food, Drug, and Cosmetic Act;

(2) New animal drugs that are the subject of an application for conditional

approval (CNADA) conditionally approved or submitted pursuant to section 571 of the Federal Food, Drug, and Cosmetic Act;

(3) Generic new animal drugs that are the subject of an abbreviated new animal drug application (ANADA) approved or submitted pursuant to section 512(n) of the Federal Food, Drug, and Cosmetic Act that references a new animal drug for which the NADA has been voluntarily withdrawn for reasons other than safety or effectiveness, or that references a new animal drug for which the NADA has been withdrawn on the basis of one or more of the grounds included under section 512(e) of the Federal Food, Drug, and Cosmetic Act and for which the generic new animal drug's approval was not affected by the withdrawal; and

(4) New animal drugs for use in proprietary medicated feeds for which the labeling is maintained in a Veterinary Master File (VMF). Proprietary medicated feeds for which the labeling is maintained in a NADA or CNADA are included within the categories of drugs described in paragraphs (a)(1) and (2) of this section.

(b) The provisions of this subpart apply to the applications described in paragraphs (a)(1) through (4) of this section for new animal drugs that are approved before the [EFFECTIVE DATE OF THE FINAL RULE], pending on the [EFFECTIVE DATE OF THE FINAL RULE], or submitted on or after the [EFFECTIVE DATE OF THE FINAL RULE], in accordance with the schedule in § 201.404(a)(4).

(c) Any new animal drug subject to this subpart that does not fully comply with the applicable requirements of this subpart in accordance with the schedule in § 201.404(a)(4) is deemed to be misbranded under section 502 of the Federal Food, Drug, and Cosmetic Act and, if that drug is a VFD drug, also under section 504(b) of the Federal Food, Drug, and Cosmetic Act.

(d) The provisions of this subpart do 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;

(2) Heritable intentional genomic alterations in animals; and

(3) Promotional labeling or advertising.

#### § 201.403 Definitions.

The following definitions apply to this subpart H.

*Active ingredient* has the same meaning as given in § 210.3(b)(7) of this chapter.

*Active moiety* means the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance.

*Adverse drug experience* has the same meaning as given in § 514.3 of this chapter.

*Adverse reaction* means an undesirable effect, reasonably associated with the use of the drug product, that may occur as part of the pharmacological action of the drug or that may be unpredictable in occurrence.

*ANADA* has the same meaning as given in § 514.3 of this chapter.

*Boxed warning* means certain contraindications or serious warnings, particularly those that may lead to death or serious injury to animals or humans that must be presented in a box on labeling. The box and its contents must be bolded. The boxed warning is ordinarily based on data from the target animal, but data from other species may also be used.

*Contraindication* means any situation in which the new animal drug should not be used because the risk of use (e.g., certain potentially fatal adverse reactions) clearly outweighs any possible benefit to the animal. Those situations may include use of the drug in animals that, because of their particular species, class, breed, age, sex, concomitant therapy, disease state, or other condition such as pregnancy or lactation, have a substantial risk of being harmed by the drug and for which no potential benefit makes the risk acceptable. Contraindications include only known hazards.

*Drug product* has the same meaning as given in § 210.3(b)(4) of this chapter.

*Environmental warning* means a warning that identifies any potential hazard to the human environment associated with the use of the new animal drug.

*Established name* has the same meaning as given in section 502(e)(3) of the Federal Food, Drug, and Cosmetic Act.

*Extralabel use* has the same meaning as given in § 530.3(a) of this chapter.

*Field study* means a type of adequate and well-controlled study designed to assess the effectiveness and/or safety of a new animal drug in the target animal under conditions that closely approximate the actual conditions of use.

*Free-choice medicated feed* has the same meaning as given in § 510.455(a) of this chapter.

*Full prescribing information* means all information necessary for the safe and effective use of a Rx new animal drug.

*Full product information* means all information necessary for the safe and effective use of an OTC new animal drug.

*Immediate container* means the container in contact with the new animal drug. The term "immediate container" does not include package liners (section 201(l) of the Federal Food, Drug, and Cosmetic Act).

*Inactive ingredient* has the same meaning as given in § 210.3(b)(8) of this chapter.

*Indication* means the use for which the new animal drug is approved or conditionally approved.

*Label* has the same meaning as given in section 201(k) of the Federal Food, Drug, and Cosmetic Act.

*Labeling* has the same meaning as given in section 201(m) of the Federal Food, Drug, and Cosmetic Act.

*Lot number, control number, or batch number* has the same meaning as given in § 210.3(b)(11) of this chapter.

*Milk discard time* means the interval between the time of the last administration of a new animal drug and the time when the milk can be safely consumed.

*NADA* has the same meaning as given in § 514.3 of this chapter.

*New animal drug* has the same meaning as given in section 201(v) of the Federal Food, Drug, and Cosmetic Act.

*Package insert* means a labeling component that contains full prescribing information for Rx new animal drugs or full product information for OTC new animal drugs and is included with the immediate container or secondary container or is attached to the label.

*Precaution* means any special care to be exercised for safe and effective use of the new animal drug. This may include recommended screening, monitoring, or diagnostic tests.

*Representative Type B medicated feed labeling* means template labeling (also known as "Blue Bird labels," 64 FR 63197, November 19, 1999) approved by FDA as part of the new animal drug application or an application for conditional approval for a Type A medicated article for the preparation of final printed labels (for medicated feed bags) or labeling (accompanying bulk medicated feed) for Type B medicated feeds containing the new animal drug. Representative Type B medicated feed labeling provides the minimum

information that must be included on the final printed labels or labeling for Type B medicated feeds.

*Representative Type C medicated feed labeling* means template labeling (also known as “Blue Bird labels,” 64 FR 63197, November 19, 1999) approved by FDA as part of the new animal drug application or an application for conditional approval for a Type A medicated article or proprietary Type B medicated feed for the preparation of final printed labels (for medicated feed bags) or labeling (accompanying bulk medicated feed) for Type C medicated feeds containing the new animal drug. Representative Type C medicated feed labeling provides the minimum information that must be included on the final printed labels or labeling for Type C medicated feeds.

*Residue warning statement* means a statement that warns against the use of the new animal drug in animals for which the withdrawal period and/or milk discard time has not been determined, and/or provides other information to prevent illegal drug residues in food products from animals treated with the new animal drug.

*Secondary container* means the packaging that surrounds the immediate container for a new animal drug.

*Shipping labeling* means labeling associated with the outermost carton containing immediate containers, secondary containers, and/or multiple unit (multi-unit) cartons of a new

animal drug and intended for shipment, but not display, of the product.

*Small label* means a label on an immediate container for a new animal drug that has insufficient space to accommodate the information required for a label by § 201.405(b) for Rx new animal drugs or § 201.407(b) for OTC new animal drugs.

*Sponsor* has the same meaning as given in § 510.3(k) of this chapter.

*Strength* has the same meaning as given in § 210.3(b)(16) of this chapter.

*Target animal* means the species, or collection of species, of animals, and, if applicable, the specific subset(s) of animals (e.g., life stage, production class, age, gender) for which the new animal drug is approved or conditionally approved.

*Type A medicated article* has the same meaning as given in § 558.3(b)(2) of this chapter.

*Type B medicated feed* has the same meaning as given in § 558.3(b)(3) of this chapter.

*Type C medicated feed* has the same meaning as given in § 558.3(b)(4) of this chapter.

*User safety warning* means a warning that identifies any serious adverse reaction or potential hazard to human health associated with human exposure during use of a new animal drug via contact, inhalation, ingestion, injection, or by other means.

*Veterinary feed directive (VFD)* has the same meaning as given in § 558.3(b)(7) of this chapter.

*VFD drug* has the same meaning as given in § 558.3(b)(6) of this chapter.

*Warning* means any serious adverse reaction or potential hazard associated with the use of the new animal drug.

*Withdrawal period* means the interval between the time of the last administration of a new animal drug and the time when the animal can be safely slaughtered for food.

**§ 201.404 General requirements.**

(a) The labeling of a new animal drug subject to these regulations as identified in § 201.401(a):

(1) Must conform to an application approved under section 512 of the Federal Food, Drug, and Cosmetic Act or conditionally approved under section 571 of the Federal Food, Drug, and Cosmetic Act.

(2) Must be informative and accurate and neither promotional in tone nor false or misleading in any particular.

(3) Must be updated if new information becomes available that causes the labeling to become inaccurate, false, or misleading, in accordance with § 514.8 of this chapter.

(4) Must conform to this subpart in accordance with the earliest applicable compliance date provided in the following schedule, unless paragraphs (b), (c), or (d) of this section are applicable.

TABLE 1 TO PARAGRAPH (a)(4)

Application No. and/or status	All conforming labeling must be submitted:
(i) NADA, CNADA, or a supplement to an NADA or CNADA subject to § 514.8(c)(2) submitted after [effective date of the final rule plus 180 days].	As part of the application or supplemental application.
(ii) NADA, CNADA, or a supplement to an NADA or CNADA subject to § 514.8(c)(2) pending on [effective date of the final rule] or submitted between [effective date of the final rule] and [effective date of the final rule plus 180 days].	As part of the application or supplemental application; or, as a supplement to an approved application or supplemental application no later than 180 days after the approval date of the application or supplemental application.
(iii) NADA number 141–300 or greater and originally approved before [effective date of the final rule]; or ANADA that references an NADA (1) voluntarily withdrawn for reasons other than safety and effectiveness, or (2) withdrawn under section 512(e) of the Federal Food, Drug, and Cosmetic Act and the ANADA’s approval was not affected by the withdrawal.	As a supplement to an approved application between [effective date of the final rule plus 1 year] and [effective date of the final rule plus 2 years].
(iv) NADA number 141–000 to 141–299 .....	As a supplement to an approved application between [effective date of the final rule plus 2 years] and [effective date of the final rule plus 3 years].
(v) NADA number 115–000 to 140–999 .....	As a supplement to an approved application between [effective date of the final rule plus 3 years] and [effective date of the final rule plus 4 years].
(vi) NADA number 45–000 to 114–999 .....	As a supplement to an approved application between [effective date of the final rule plus 4 years] and [effective date of the final rule plus 5 years].
(vii) NADA number 1 to 44–999 .....	As a supplement to an approved application between [effective date of the final rule plus 5 years] and [effective date of the final rule plus 6 years].

(b) For proprietary Type B or Type C medicated feeds in which the underlying data and labeling are maintained in a VMF, a submission containing the conforming labeling must be made to the VMF within 180 days after all conforming labeling has been approved for the NADA or CNADA that is the approved or conditionally approved source of the new animal drug used to manufacture the proprietary medicated feed.

(c) Unless a supplement subject to § 514.8(c)(2) of this chapter is submitted to a CNADA after the [effective date of the final rule], new animal drugs conditionally approved before [effective date of the final rule] are not required to conform to this subpart until an application for full approval is submitted.

(d) For combination new animal drugs subject to section 512(d)(4) of the Federal Food, Drug, and Cosmetic Act that are approved for use in animal feed or drinking water on or before [effective date of the final rule], a supplement containing the conforming labeling for the combination new animal drug must be submitted within 180 days after all conforming labeling has been approved for the individual new animal drugs in the combination.

(e) In those circumstances where it may not be clear how a requirement in this subpart applies to a particular new animal drug, or whether it applies, the final determination will be made by FDA.

(f) When submitting labeling for the purposes of conforming to the requirements of subpart H according to the schedule in paragraph (a)(4) of this section, all labeling components for the approved or conditionally approved new animal drug must be provided in one submission. FDA will refuse to file labeling submissions intended to conform to this subpart if they are incomplete.

(g) All labeling for an approved or conditionally approved new animal drug must comply with the general formatting requirements described in this paragraph in addition to all content and formatting requirements described in this subpart.

(1) Placement of the established name relative to the proprietary name on labeling for approved or conditionally approved Rx new animal drugs must comply with § 201.10(g)(1). Size and prominence of the established name relative to the proprietary name must comply with section 502(e)(1)(B) of the Federal Food, Drug, and Cosmetic Act and § 201.10(g)(2).

(2) Placement, size, and prominence of the established name relative to the

proprietary name on the labeling for approved or conditionally approved OTC new animal drugs and the labeling for approved or conditionally approved new animal drugs for use in animal feeds (Type A medicated article label, proprietary Type B medicated feed label, proprietary Type C medicated feed label, other approved labeling associated with a Type A medicated article), excluding representative Type B and Type C medicated feed labeling, must comply with the following requirements:

(i) The proprietary name of the new animal drug must be accompanied by the established name each time the proprietary name is featured on the labeling, except in running text. Running text includes detailed information such as found in warnings and directions. On any panel or page of a component of labeling in which the proprietary name is not featured elsewhere but is used in the running text, the established name must be placed in conjunction with the proprietary name at least with the first presentation of the proprietary name in running text.

(ii) Where the established name accompanies the proprietary name, it must be placed directly to the right of, or directly below, the proprietary name. Except for trademark symbols associated with the proprietary name, the proprietary name and the established name must not be separated by placement of intervening matter that, in any way, detracts from, obfuscates, or de-emphasizes the established name of the product, or obscures the relationship between the proprietary name and the established name. The established name must be presented entirely within parentheses.

(iii) Except in running text, where the established name accompanies the proprietary name, the smallest letter of the established name (upper or lower case letters) must be printed in letters at least half the size of the largest letter of the proprietary name (upper or lower case letters). Within running text, the established name accompanying the proprietary name must be printed in letters the same size of the letters in the proprietary name (upper and lower case letters). The prominence of the established name must be consistent with the prominence of the proprietary name, taking into account all pertinent factors including typography, layout, contrast, and other printing features.

(3) For representative Type B and Type C medicated feed labeling for approved or conditionally approved new animal drugs for use in animal feeds, the established name of the Type

B or Type C medicated feed presented below the description of the Type B or Type C medicated feed must comply with the following requirements:

(i) The established name must be presented directly below the description of the Type B or Type C medicated feed and must not be separated by placement of intervening matter.

(ii) The established name must be printed in lower case letters except for "Type B" or "Type C".

(iii) The established name must be printed in non-bold font of the same size letters as the name of the Type B or Type C medicated feed (upper and lower case letters).

(iv) The established name must be presented entirely within parentheses.

(4) All labeling text and type style must be easy to read, and letters must not touch.

(5) Running text, section headings, and subsection headings on package inserts and representative Type B and Type C medicated feed labeling must be in black and on a white background and use a single type style. For other labeling components, other color combinations may be used if there is sufficient contrast between text and the background colors to ensure readability of the text.

(6) Representative Type B and Type C medicated feed labeling must not contain any logos, graphics, or designs other than illustrations or tables that FDA determines are necessary for proper use of the medicated feed. For other labeling components for approved or conditionally approved new animal drugs, in accordance with § 201.15(b)(1), graphics or designs associated with the labeling must not take up space needed for information required by this subpart. In accordance with paragraph (a)(2) of this section, graphics or diagrams must not be promotional in tone. If graphics are incorporated into the background, for any text appearing over the graphics, there must be sufficient contrast between the text and the graphics colors to ensure readability of the text. The use of compressed arrows on labeling is limited to the subsection entitled either "Withdrawal Periods and Residue Warnings" or "Withdrawal Periods," in accordance with paragraph (g)(8)(iii) of this section.

(7) The following minimum letter height or type size must be used for specific components of labeling, subject to the provisions of paragraph (g)(2) of this section:

(i) Immediate container label, secondary container labeling, package inserts, and labeling of multiple unit cartons and display cartons: 8 points.

(ii) Small label: 6 points.

(iii) Type A medicated article label, representative Type B medicated feed labeling, representative Type C medicated feed labeling, proprietary Type B medicated feed label, and proprietary Type C medicated feed label: 10 points.

(iv) Additional labeling for Rx new animal drugs that is to be provided to the animal owner: 12 points.

(v) Shipping labeling for Rx and OTC new animal drugs and other approved labeling for Type A medicated articles: 16 points.

(8) Section headings and subsection headings must be formatted as follows:

(i) All section headings and subsection headings must be in bold type that prominently distinguishes them from other approved labeling information.

(ii) Section headings must be either left justified or centered.

(iii) For the subsection entitled either "Withdrawal Periods and Residue Warnings" or "Withdrawal Periods," the subsection heading, and the contents of the subsection, must be centered within compressed arrows.

(iv) All other subsection headings must be left justified.

(h) If the National Drug Code (NDC) is included on labeling, it must appear in accordance with § 207.33 of this chapter.

(i) All words, statements, and other information required on the labeling for approved or conditionally approved new animal drugs must appear in the English language. Additional translations of labeling for approved or conditionally approved new animal drugs into foreign languages must comply with the following requirements:

(1) For approved or conditionally approved Rx new animal drugs, if a labeling component contains any section or wording translated into a foreign language, then the entire full prescribing information must be translated into the foreign language and must comply with the format and content requirements in § 201.405(a). FDA also may require additional wording on other labeling components for the Rx new animal drug to be translated into the foreign language when necessary to ensure its safe and effective use.

(2) For approved or conditionally approved OTC new animal drugs other than new animal drugs for use in animal feeds, if a labeling component contains any section or wording translated into a foreign language, then the entire full product information must be translated into the foreign language and must comply with the format and content

requirements in § 201.407(a). FDA also may require additional wording on other labeling components for the OTC new animal drug to be translated into the foreign language when necessary to ensure its safe and effective use.

(3) For approved or conditionally approved new animal drugs for use in animal feeds, if the labeling contains any section or wording translated into a foreign language, then all labeling must be translated into the foreign language and must comply with the format and content requirements in § 201.409.

(4) FDA may limit the number of languages into which labeling information is translated to ensure clarity of information and the safe and effective use of the new animal drug.

(j) For approved or conditionally approved new animal drugs distributed solely in the Commonwealth of Puerto Rico or in a Territory where the predominant language is other than English, the predominant language may be substituted for English. Such new animal drugs may be exempt from paragraph (i) of this section.

#### **§ 201.405 Content and format for prescription (Rx) new animal drug labeling.**

This section describes specific content and format requirements for the labeling of approved or conditionally approved Rx new animal drugs. This section does not apply to new animal drugs approved or conditionally approved as veterinary feed directive (VFD) drugs. See § 201.409 for content and format requirements for the labeling of approved or conditionally approved new animal drugs for use in animal feeds that are subject to part 558 of this chapter, including VFD drugs. Omit labeling sections or subsections that do not apply to the Rx new animal drug. The final content of each applicable component and section of labeling is determined by FDA. In addition to the content and format requirements in this section, the labeling of approved or conditionally approved Rx new animal drugs must comply with other applicable requirements in this subpart.

(a) *Labeling providing full prescribing information.* All approved or conditionally approved Rx new animal drugs must provide full prescribing information as described in this paragraph. The package insert must include full prescribing information. If no package insert is provided, a secondary container is required, and its labeling must include full prescribing information as described in this paragraph. The following information, as applicable, must appear in the order listed on the labeling component providing full prescribing information.

If full prescribing information is provided on the secondary container labeling, in accordance with section 201(k) of the Federal Food, Drug, and Cosmetic Act, the secondary container labeling may exclude any of the information described in this subsection that is required by paragraphs (b) or (c) of this section to appear on the label if such information is easily legible through the secondary container. Section headings, subsection headings, and other text presented in quotations in this paragraph must appear verbatim on the labeling providing full prescribing information. Sections and subsections are not numbered on full prescribing information.

(1) *Drug product identification.* This section of full prescribing information must include:

(i) The proprietary name of the finished drug product;

(ii) The established name of the drug product;

(iii) The route(s) of administration, if not included as part of the established name of the drug product;

(iv) The dosage form of the finished drug product, if not included as part of the established name of the drug product;

(v) The established name and strength or concentration of each active ingredient, except that the strength or concentration may be excluded from full prescribing information provided on a package insert that applies to multiple strengths or concentrations;

(vi) The pharmacological class of the new animal drug, if required to facilitate the drug's safe and effective use; and

(vii) For controlled substances, the required controlled substance symbol, in accordance with part 1302 of this title designating the schedule for the drug substance.

(2) *Prescription statement.* This section of full prescribing information must include the following statement: "Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian".

(3) *Conditional approval statement.* All conditionally approved new animal drugs must include the following statement in this section of full prescribing information in accordance with section 571(f)(1)(A) of the Federal Food, Drug, and Cosmetic Act: "conditionally approved by FDA pending a full demonstration of effectiveness under application number [insert number]". This statement must be prominent and conspicuous.

(4) *Boxed warnings.* All Rx new animal drugs with boxed warnings must include the boxed warning in this section of full prescribing information.

The box must contain, in upper case letters, the heading “WARNING”. The contents of the box must briefly explain the risk and, if appropriate, refer to more detailed information in other sections of full prescribing information. The box, heading, and contents must be bolded.

(5) *Extralabel use prohibition statement.* An approved new animal drug that is prohibited from extralabel use as listed under § 530.41 of this chapter must include in this section of full prescribing information an extralabel use prohibition statement that begins with the phrase: “Federal law prohibits the extralabel use of this drug . . .” and concludes with a description of the prohibition as described in § 530.41 of this chapter.

(6) *“Description”.* This section of full prescribing information must include:

- (i) The proprietary name of the finished drug product;
- (ii) The established name of the drug product;
- (iii) The route(s) of administration, if not included as part of the established name of the drug product;
- (iv) The dosage form of the finished drug product, if not included as part of the established name of the drug product;
- (v) A description of the identifying characteristics of the dosage form, such as color, shape, coating, scoring, and imprinting;
- (vi) The established name and strength or concentration of each active ingredient, including all available strengths or concentrations to which full prescribing information applies;
- (vii) If applicable, a statement that the product is sterile; and
- (viii) The established name of each inactive ingredient presented in decreasing order of predominance, by weight or concentration.

(A) If exemption from listing one or more inactive ingredients is granted, in accordance with § 201.411, to avoid disclosure of trade secret information, this section of full prescribing information must also state the following: “Certain inactive ingredients are not listed to avoid disclosing trade secret information.”

(B) If exemption from listing one or more inactive ingredients is granted, in accordance with § 201.411, because their listing would be impracticable, this section of full prescribing information must also state the following: “Certain inactive ingredients are not listed because their listing would be impracticable.”

(7) *“Indications for Use”.* Include the following information in this section of full prescribing information in order:

(i) The approved or conditionally approved indication(s) and target animal(s) in the following format: “For [indication(s)] in [target animal(s)]”;

(ii) A statement indicating that the new animal drug is approved or conditionally approved for use only under specific conditions, if applicable; and

(iii) A statement(s) indicating animals for which the new animal drug is not approved or conditionally approved, if FDA determines such a statement(s) is required for safety and/or effectiveness reasons.

(8) *“Dosage and Administration”.*

This section of full prescribing information must include for each indication and target animal:

- (i) The statement, “Always provide [additional labeling] with each prescription” for Rx new animal drugs requiring additional labeling, in accordance with paragraph (a)(14) of this section, inserting the title of the additional labeling in the location indicated by the bracketed text;
- (ii) The route(s) of administration, and specific site(s) of administration, if applicable;
- (iii) The dose (or dose range);
- (iv) The intervals between doses, if applicable;
- (v) The duration of treatment;
- (vi) The maximum volume per injection site, if required to facilitate the drug’s safe and effective use;
- (vii) Any modification of the information required in paragraphs (a)(8)(i) through (vi) of this section that is needed for special animal populations (e.g., neonatal, reproducing, lactating, geriatric, or those with specific disease states); and
- (viii) Other information regarding dosage and administration, if required to facilitate the drug’s safe and effective use.

(9) *“Contraindications”.* All Rx new animal drugs with contraindications must include the contraindications in this section of full prescribing information.

(10) *“Warnings and Precautions”.* This section of full prescribing information is required for all approved or conditionally approved Rx new animal drugs. Include in the following order all applicable subsections, headings, and information:

(i) *“Withdrawal Periods and Residue Warnings”* or *“Withdrawal Periods”.* This subsection of full prescribing information is required for all new animal drugs approved or conditionally approved for use in food-producing animals and must include all human food safety warnings, including milk discard times, withdrawal periods, and

residue warning statements, as applicable. The order of the human food safety warnings in this subsection of full prescribing information must be as described in paragraphs (a)(10)(i)(B) through (G) of this section, as applicable.

(A) If there is a residue warning statement(s), this subsection of full prescribing information must be entitled “Withdrawal Periods and Residue Warnings”. If there is no residue warning statement, this subsection of full prescribing information must be entitled “Withdrawal Periods”. The title of this subsection and all information in this subsection of full prescribing information must be centered and placed entirely within compressed arrows, in accordance with § 201.404(g)(8). The compressed arrows must be black for package inserts or a color that clearly contrasts from background colors for other approved labeling.

(B) If the new animal drug is approved or conditionally approved for use in food-producing animals excluding female animals that produce milk for human consumption, include in this subsection of full prescribing information the withdrawal period(s) followed by any residue warning statements.

(C) If the new animal drug is approved or conditionally approved for use in food-producing animals excluding female animals that produce milk for human consumption and there is no withdrawal period, include in this subsection of full prescribing information the statement “No withdrawal period is required when used according to labeling.”, followed by any residue warning statements.

(D) If the new animal drug is approved or conditionally approved for use in female animals that produce milk for human consumption, include in this subsection of full prescribing information the milk discard time(s), followed by the withdrawal period(s), followed by any residue warning statements.

(E) If the new animal drug is approved or conditionally approved for use in female animals that produce milk for human consumption and there is a milk discard time(s) but no withdrawal period, include in this subsection of full prescribing information the milk discard time(s), followed by the statement “No withdrawal period is required when used according to labeling.”, followed by any residue warning statements.

(F) If the new animal drug is approved or conditionally approved for use in female animals that produce milk for human consumption and there is no

milk discard time but there is a withdrawal period(s), include in this subsection of full prescribing information the withdrawal period(s), followed by the statement “No milk discard time is required when used according to labeling.”, followed by any residue warning statements.

(G) If the new animal drug is approved or conditionally approved for use in female animals that produce milk for human consumption and there is no milk discard time and no withdrawal period, include in this subsection of full prescribing information the statement “No milk discard time and no withdrawal period is required when used according to labeling.”, followed by any residue warning statements.

(ii) “*User Safety Warnings*”. This subsection of full prescribing information is required for all new animal drugs and must include in the following order:

(A) “Not for use in humans. Keep out of reach of children.”

(B) All additional user safety warnings listed in decreasing order of severity or frequency; and

(C) “To obtain a Safety Data Sheet(s), contact [insert name of manufacturer] at [insert manufacturer’s telephone number] or [insert manufacturer’s website].”

(iii) “*Animal Safety Warnings and Precautions*”. All target animal safety warnings that identify any serious adverse reaction or potential hazard to the target animal(s) associated with the use of the new animal drug and all precautions must be included in this subsection of full prescribing information. These items must be listed in decreasing order of severity or frequency.

(iv) “*Environmental Warnings*”. All environmental warnings applicable to the new animal drug that are included in an approved or conditionally approved application must be provided in this subsection of full prescribing information.

(v) “*Other Warnings*”. Any other required warnings must be included in this subsection of full prescribing information.

(11) “*Adverse Reactions*”. Include in this section of full prescribing information the adverse reactions, as determined by FDA, that occur with use of the Rx new animal drug and with use of drugs in the same pharmacologically active and chemically related class, if applicable. Include information necessary to interpret the adverse reactions (e.g., for field studies include total number of animals exposed, extent and nature of exposure). Within the following categories, as applicable,

present the adverse reactions in decreasing order of severity or frequency.

(i) “*Pre-approval experience*”. Include adverse reactions observed in laboratory or field studies in the target animal(s).

(ii) “*Foreign market experience*”. If the drug product has been commercially marketed outside the United States, include information from foreign adverse drug experience reports known prior to U.S. approval.

(iii) “*Post-approval experience*”. Include the adverse reactions identified from domestic and foreign adverse drug experience reports.

(12) “*Contact Information*”. The following statements must be included in this section of full prescribing information: “Contact [insert name of business] at [insert business telephone number] or [insert business web address]. To report suspected adverse drug experiences, contact [insert name of business] at [insert business telephone number]. For additional information about reporting adverse drug experiences for animal drugs, contact FDA at [insert current FDA telephone number for voluntary reporting of adverse drug experiences] or [insert current FDA web address for voluntary reporting of adverse drug experiences].” Use as the name of the business the manufacturer, packer, or distributor identified in the “Name and place of business” section of full prescribing information according to paragraph (a)(22) of this section. If more than one business is identified in the “Name and place of business” section of full prescribing information, select the most appropriate to identify as the “business” in the “Contact Information” section of full prescribing information to provide additional information about the Rx new animal drug and to contact regarding suspected adverse drug experiences.

(13) “*Information for Animal Owner*”. Any specific information that FDA determines is necessary for the animal owner or person treating the animal to use the Rx new animal drug safely and effectively must be included in this section of full prescribing information. If FDA requires additional labeling (e.g., a client information sheet), a printed copy must be attached to, or accompany, the package insert or secondary container labeling if no package insert is provided.

(14) “*Clinical Pharmacology*”. If required by FDA to facilitate the drug’s safe and effective use, include a summary of the clinical pharmacology of the Rx new animal drug in the target animal(s) in this section of full prescribing information, including the

following three subsections, as applicable:

- (i) “Mechanism of action”;
- (ii) “Pharmacodynamics”; and
- (iii) “Pharmacokinetics”.

(15) “*Microbiology*”. This section of full prescribing information is required for all antimicrobial Rx new animal drugs and must include a description of microbiologic data associated with the studies used to support the effectiveness of the drug against the indicated pathogens. Microbiology data must be restricted to organisms named in the approved or conditionally approved indications. If *in vitro* data for antimicrobial new animal drugs are included in this section of full prescribing information that have not been correlated to clinical effectiveness, the data must be immediately preceded by the statement: “The following *in vitro* data are available, but their clinical significance is unknown.”

(16) “*Target Animal Safety*”. This section of full prescribing information must include a summary of the basis for the conclusion that the new animal drug is safe in the target animal(s) when used as approved or conditionally approved.

(17) “*Effectiveness*”. This section of full prescribing information must include a summary of the basis for the conclusion that the new animal drug is effective in the target animal(s) when used as approved. For a conditionally approved new animal drug, include a summary of the basis for the reasonable expectation of effectiveness.

(18) “*Net Contents*”. This section of full prescribing information must identify the contents of the secondary container. Exclude this section from package inserts.

(19) “*How Supplied*”. This section of full prescribing information must include information on the available drug strengths, concentrations, and container sizes to which the labeling applies. Revise this section of full prescribing information if new strengths, concentrations, or container sizes are added.

(20) “*Storage, Handling, and Disposal*”. This section of full prescribing information must include drug storage information. Also include any required handling and drug disposal information in this section.

(21) “*NADA/ANADA approval statement*”. In accordance with section 502(w)(3) of the Federal Food, Drug, and Cosmetic Act, approved new animal drugs must include the following statement in this section of full prescribing information: “Approved by FDA under NADA # xxx-xxx”. Approved generic new animal drugs must include the following statement in

this section of full prescribing information: “Approved by FDA under ANADA # xxx-xxx”. This statement must appear in this section of full prescribing information and:

(i) Appear on one straight line unless there is insufficient space, in which case the statement may appear on two straight lines;

(ii) Not be incorporated into a seal, stamp, logo or other graphic;

(iii) Be of consistent type size, color, and contrast and be of no greater prominence than the rest of the labeling text; and

(iv) Not obscure or otherwise render less conspicuous any word, statement, or other information required by FDA.

(22) *Name and place of business.* This section of full prescribing information must include the name and place of business of the manufacturer, packer, or distributor.

(23) *“Lot Number and Expiration Date”.* This section is required when full prescribing information is provided on the secondary container labeling. This section must include the identifying lot or control number of the Rx new animal drug within the secondary container. This section must also include the expiration date of the Rx new animal drug within the secondary container, in accordance with § 201.17. Alternatively, this section must refer to the location on the secondary container labeling or secondary container where the lot or control number and expiration date are printed. In accordance with § 201.17, an expiration date may be excluded from the secondary container labeling or secondary container if the expiration date provided on the label or immediate container is easily legible through the secondary container.

(24) *“Revision Date”.* This section of full prescribing information must include the date of the most recent revision of the component of labeling that provides full prescribing information, listing the month followed by the year.

(b) *Prescription new animal drug label (Rx label).* All approved or conditionally approved Rx new animal drugs must provide a label (Rx label). The following information, as applicable, must appear in the order listed on the Rx label. If there is insufficient space on the immediate container for a label to provide for all of the following information, then an Rx small label is required instead. The requirements for an Rx small label are provided in paragraph (c) of this section. Section headings and other text presented in quotations in this paragraph must appear verbatim on the Rx label.

Sections are not numbered on the Rx label. For Rx labels with a front panel and one side or back panel, the information identified in paragraph (b)(1) of this section must be provided on the front panel in the order listed, and the information identified in paragraph (b)(2) of this section must be provided on the side or back panel in the order listed. If the Rx label consists of a single panel, the information identified in paragraph (b)(1) must be provided on the Rx label in the order listed followed by the information identified in paragraph (b)(2) in the order listed. For Rx labels with a front panel and multiple side and/or back panels, the information identified in paragraph (b)(1) must be provided on the Rx label in the order listed followed by the information identified in paragraph (b)(2) in the order listed, starting on the front panel, continuing on the panel immediately to the right of the front panel, and continuing to fill the panels to the right until all of the information is presented. In all instances, the information specified in paragraphs (b)(2)(iii) and (iv) must appear on the same panel.

(1) *Front panel.* The following information must appear on the front panel of the Rx label in the order listed.

(i) *Drug product identification.* This section of the Rx label must include:

(A) The proprietary name of the finished drug product;

(B) The established name of the drug product;

(C) The route(s) of administration, if not included as part of the established name of the drug product;

(D) The dosage form of the finished drug product, if not included as part of the established name of the drug product;

(E) The established name and strength or concentration of each active ingredient;

(F) If applicable, a statement that the product is sterile;

(G) The pharmacological class of the new animal drug, if required to facilitate the drug’s safe and effective use; and

(H) For controlled substances, the required controlled substance symbol, in accordance with part 1302 of this title designating the schedule for the drug substance.

(ii) *Prescription statement.* This section of the Rx label must include the following statement, in accordance with section 503(f)(4) of the Federal Food, Drug, and Cosmetic Act: “Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.”

(iii) *Conditional approval statement.* For conditionally approved new animal

drugs, the requirements of paragraph (a)(3) of this section apply.

(iv) *Boxed warnings.* For Rx new animal drugs that have boxed warnings, the requirements of paragraph (a)(4) of this section apply.

(v) *“Indications for Use”.* The requirements of paragraph (a)(7) of this section apply. However, if there is insufficient space on the Rx label for the complete “Indications for Use” section as specified in paragraph (a)(7), then include the statement required in paragraph (a)(7)(i) or, if there is insufficient space on the Rx label for the statement in paragraph (a)(7)(i), then include the statement, “For [abbreviated indication(s)] in [target animal(s)]”. In either situation where there is insufficient space on the Rx label for the complete “Indications for Use” section as specified in paragraph (a)(7), the required statement must be followed by, “See package insert for complete ‘Indications for Use’” if full prescribing information is provided on a package insert, or “See package labeling for complete ‘Indications for Use’” if full prescribing information is provided on the secondary container labeling.

(vi) *Extralabel use prohibition statement.* For approved new animal drugs prohibited from extralabel use as listed under § 530.41 of this chapter, the requirements of paragraph (a)(5) of this section apply.

(vii) *“Withdrawal Periods and Residue Warnings” or “Withdrawal Periods”.* For new animal drugs approved or conditionally approved for use in food-producing animals, the requirements of paragraph (a)(10)(i) of this section apply. If there is insufficient space on the front panel of Rx labels consisting of only a front panel and one side or back panel for the information required in paragraph (a)(10)(i), this section must be provided on the side or back panel of the Rx label immediately following the full prescribing information statement specified in paragraph (b)(2)(i) of this section.

(viii) *“Net Contents”.* This section of the Rx label must identify the contents of the immediate container, in accordance with § 201.5.

(ix) *NADA/ANADA approval statement.* For approved new animal drugs or approved generic new animal drugs, the requirements of paragraph (a)(21) of this section apply.

(2) *Side or back panel.* The following information must appear on the side or back panel of the Rx label in the order listed.

(i) *Full prescribing information statement.* This section of the Rx label must include one of two statements. If full prescribing information is provided

on the package insert, the following statement must be used: "Before using this drug, read package insert for full prescribing information." If full prescribing information is provided on the secondary container labeling, the following statement must be used: "Before using this drug, read package labeling for full prescribing information."

(ii) "*Dosage and Administration*".

The requirements of paragraph (a)(8) of this section apply. If there is insufficient space on the Rx label for the complete requirements as specified in paragraph (a)(8) or if it is necessary for additional information provided in full prescribing information that is not provided on the Rx label to be read before administering the drug, FDA may allow this section to be excluded from the Rx label.

(iii) "*Active Ingredient*" or "*Active Ingredients*". This section of the Rx label must provide the established name and strength or concentration of each active ingredient. If the Rx new animal drug contains one active ingredient, this section of the Rx label must be entitled "Active Ingredient". If the Rx new animal drug contains more than one active ingredient, this section of the Rx label must be entitled "Active Ingredients."

(iv) "*Inactive Ingredients*". The requirements of paragraph (a)(6)(viii) of this section apply.

(v) "*Storage, Handling, and Disposal*". The requirements of paragraph (a)(20) of this section apply.

(vi) "*Name and place of business*". This section of the Rx label must include the name and place of business of the manufacturer, packer, or distributor, in accordance with section 502(b) of the Federal Food, Drug, and Cosmetic Act.

(vii) "*Lot Number and Expiration Date*" or "*Lot Number*". This section of the Rx label must include the identifying lot or control number of the Rx new animal drug within the immediate container. This section of the Rx label must also include the expiration date of the Rx new animal drug within the immediate container, in accordance with § 201.17. Alternatively, this section must refer to the location on the Rx label or immediate container where the lot or control number and expiration date are printed. In accordance with § 201.17, if the immediate container provides a single dose of the Rx new animal drug and is packaged individually in a secondary container that provides an expiration date on the secondary container labeling or secondary container, an expiration date is not required on the Rx label or immediate container. If an expiration date is not provided on the Rx label or

immediate container per this provision, then this section of the Rx label must be entitled "Lot Number."

(viii) "*Revision Date*". This section of the Rx label must include the date of the most recent revision of the Rx label, listing the month followed by the year.

(c) "*Prescription new animal drug small label (Rx small label)*". The following information, as applicable, must appear in the order listed on the Rx small label. 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 paragraph (b) of this section, taking into consideration readability and legibility of the information. Section headings and other text presented in quotations in this paragraph must appear verbatim on the Rx small label. Sections are not numbered on the Rx small label.

(1) "*Proprietary name*". This section of the Rx small label must provide the proprietary name of the finished drug product.

(2) "*Established name*". This section of the Rx small label must provide the established name of the drug product.

(3) "*Active ingredient(s)*". This section of the Rx small label must provide the established name and strength or concentration of each active ingredient.

(4) "*Controlled substance symbol*". For controlled substances, this section of the Rx small label must include the required controlled substance symbol, in accordance with part 1302 of this title designating the schedule for the drug substance.

(5) "*Prescription statement*". This section of the Rx small label must include the following: "Rx Animal Use".

(6) "*Target animals*". This section of the Rx small label must include the statement: "For [target animal(s)] only".

(7) "*Full prescribing information statement*". This section of the Rx small label must include one of two statements. If full prescribing information is provided on the package insert, the following statement must be used: "Read package insert for full prescribing information." If full prescribing information is provided on the secondary container labeling, the following statement must be used: "Read package labeling for full prescribing information."

(8) "*Net Contents*". This section of the Rx small label must identify the contents of the immediate container, in accordance with § 201.51.

(9) "*Name and place of business*". This section of the Rx small label must include the name and place of business of the manufacturer, packer, or

distributor, in accordance with section 502(b) of the Federal Food, Drug, and Cosmetic Act.

(10) "*Lot, Exp. and Storage*" or "*Lot and Storage*". This section of the Rx small label must include the identifying lot or control number of the Rx new animal drug within the immediate container. This section of the Rx small label must also include the expiration date of the Rx new animal drug within the immediate container, in accordance with § 201.17. Drug storage information for the Rx new animal drug must also be included in this section of the Rx small label. In accordance with § 201.17, if the immediate container provides a single dose of the Rx new animal drug and is packaged individually in a secondary container that provides an expiration date on the secondary container labeling or secondary container, an expiration date is not required on the Rx small label or immediate container. If an expiration date is not provided on the Rx small label or immediate container per this provision, then this section of the Rx small label must be entitled "Lot and Storage."

(11) "*Revision Date*". This section of the Rx small label must include the date of the most recent revision of the Rx small label, listing the month followed by the year.

(d) "*Labeling for secondary containers for Rx new animal drugs that include a package insert (Rx secondary container labeling)*". If a secondary container is provided for an approved or conditionally approved Rx new animal drug and the Rx new animal drug includes a package insert, the following information, as applicable, must appear in the order listed on the secondary container labeling (Rx secondary container labeling). In accordance with section 201(k) of the Federal Food, Drug, and Cosmetic Act, the Rx secondary container labeling may exclude any of the information described in this subsection that is required by paragraphs (b) or (c) of this section to appear on the label if such information is easily legible through the Rx secondary container. Section headings, subsection headings, and other text presented in quotations in this paragraph must appear verbatim on the Rx secondary container labeling. Sections and subsections are not numbered on the Rx secondary container labeling. For Rx secondary container labeling with a front panel and one side or back panel, the information identified in paragraph (d)(1) of this section must be provided on the front panel in the order listed, and the information identified in

paragraph (d)(2) of this section must be provided on the side or back panel in the order listed. For Rx secondary container labeling with a front panel and multiple side and/or back panels, the information identified in paragraph (d)(1) must be provided on the Rx secondary container labeling in the order listed followed by the information identified in paragraph (d)(2) in the order listed, starting on the front panel, continuing on the panel immediately to the right of the front panel, and continuing to fill the panels to the right until all of the information is presented. In all instances, the information specified in paragraphs (d)(2)(v) and (vi) of this section must appear on the same panel.

(1) *Front panel.* The following information must appear on the front panel of the Rx secondary container labeling in the order listed.

(i) *Drug product identification.* This section of the Rx secondary container labeling must include:

(A) The proprietary name of the finished drug product;

(B) The established name of the drug product;

(C) The route(s) of administration, if not included as part of the established name of the drug product;

(D) The dosage form of the finished drug product, if not included as part of the established name of the drug product;

(E) The established name and strength or concentration of each active ingredient;

(F) If applicable, a statement that the product is sterile;

(G) The pharmacological class of the new animal drug, if required to facilitate the drug's safe and effective use; and

(H) For controlled substances, the required controlled substance symbol, in accordance with part 1302 of this title designating the schedule for the drug substance.

(ii) *Prescription statement.* The requirements of paragraph (a)(2) of this section apply.

(iii) *Conditional approval statement.* The requirements of paragraph (a)(3) of this section apply.

(iv) *Boxed warnings.* The requirements of paragraph (a)(4) of this section apply.

(v) *Indications for Use.* The requirements of paragraph (a)(7) of this section apply.

(vi) *Extralabel use prohibition statement.* For approved new animal drugs prohibited from extralabel use as listed under § 530.41 of this chapter, the requirements of paragraph (a)(5) of this section apply.

(vii) *Net Contents.* This section of the Rx secondary container labeling

must identify the contents of the secondary container.

(viii) *NADA/ANADA approval statement.* For approved new animal drugs or approved generic new animal drugs, the requirements of paragraph (a)(21) of this section apply.

(2) *Side or back panel.* The following information must appear on the side or back panel of the Rx secondary container labeling in the order listed.

(i) *Full prescribing information statement.* This section of the Rx secondary container labeling must include the following statement: "Before using this drug, read package insert for full prescribing information."

(ii) *"Dosage and Administration".* The requirements of paragraph (a)(8) of this section apply.

(iii) *"Contraindications".* The requirements of paragraph (a)(9) of this section apply.

(iv) *"Warnings and Precautions".* The requirements of paragraph (a)(10) of this section apply.

(v) *"Active Ingredient" or "Active Ingredients".* The requirements of paragraph (b)(2)(iii) of this section apply.

(vi) *"Inactive Ingredients".* The requirements of paragraph (a)(6)(viii) of this section apply.

(vii) *"Storage, Handling, and Disposal".* The requirements of paragraph (a)(20) of this section apply.

(viii) *Name and place of business.* The requirements of paragraph (a)(22) of this section apply.

(ix) *"Lot Number and Expiration Date".* This section of the Rx secondary container labeling must include the identifying lot or control number of the Rx new animal drug within the secondary container. This section of the Rx secondary container labeling must also include the expiration date of the Rx new animal drug within the secondary container, in accordance with § 201.17. Alternatively, this section must refer to the location on the Rx secondary container labeling or secondary container where the lot or control number and expiration date are printed. In accordance with § 201.17, an expiration date may be excluded from the Rx secondary container labeling or secondary container if the expiration date provided on the Rx label, Rx small label, or immediate container is easily legible through the secondary container.

(x) *"Revision Date".* This section of the Rx secondary container labeling must include the date of the most recent version of the Rx secondary container labeling, listing the month followed by the year.

(e) *Shipping labeling for Rx new animal drugs (Rx shipping labeling).* If

shipping labeling is provided for an approved or conditionally approved Rx new animal drug (Rx shipping labeling), the following information, as applicable, must appear in the order listed on the Rx shipping labeling. Section headings and other text presented in quotations in this paragraph must appear verbatim on the Rx shipping labeling. Sections are not numbered on the Rx shipping labeling.

(1) *Proprietary name.* This section of the Rx shipping labeling must provide the proprietary name of the finished drug product, unless the Rx new animal drug is a controlled substance.

(2) *Established name.* This section of the Rx shipping labeling must provide the established name of the drug product, unless the Rx new animal drug is a controlled substance.

(3) *Active ingredient(s).* This section of the Rx shipping labeling must provide the established name and strength or concentration of each active ingredient, unless the Rx new animal drug is a controlled substance.

(4) *Conditional approval statement.* The requirements of paragraph (a)(3) of this section apply, unless the Rx new animal drug is a controlled substance.

(5) *"Net Contents".* This section of the Rx shipping labeling must identify the contents of the shipping carton.

(6) *"Storage and Handling".* This section of the Rx shipping labeling must include drug storage information. If required by FDA to facilitate the drug's safe and effective use, also include handling information.

(7) *NADA/ANADA approval statement.* For approved new animal drugs or approved generic new animal drugs, the requirements of paragraph (a)(21) of this section apply, unless the Rx new animal drug is a controlled substance.

(8) *Name and place of business.* The requirements of paragraph (a)(22) of this section apply.

(9) *"Lot Number and Expiration Date".* This section of the Rx shipping labeling must include the identifying lot or control number(s) and the expiration date(s) of the Rx new animal drug within the shipping carton.

(10) *"Revision Date".* This section of the Rx shipping labeling must include the date of the most recent revision of the Rx shipping labeling, listing the month followed by the year.

(f) *Other approved labeling for Rx new animal drugs (Rx other approved labeling).* If other approved labeling is provided for an approved or conditionally approved Rx new animal drug (Rx other approved labeling), such as labeling on display cartons and multi-unit cartons (excluding shipping

cartons), the following information, as applicable, must appear in the order listed on the Rx other approved labeling. Section headings and other text presented in quotations in this paragraph must appear verbatim on the Rx other approved labeling. Sections are not numbered on the Rx other approved labeling.

(1) *Proprietary name*. This section of the Rx other approved labeling must provide the proprietary name of the finished drug product.

(2) *Established Name*. This section of the Rx other approved labeling must provide the established name of the drug product.

(3) *Active ingredient(s)*. This section of the Rx other approved labeling must provide the established name and strength or concentration of each active ingredient.

(4) *Controlled substance symbol*. For controlled substances, this section of the Rx other approved labeling must include the required controlled substance symbol, in accordance with part 1302 of this title designating the schedule for the drug substance.

(5) *Prescription statement*. The requirements of paragraph (a)(2) of this section apply.

(6) *Conditional approval statement*. The requirements of paragraph (a)(3) of this section apply.

(7) *Boxed warnings*. The requirements of paragraph (a)(4) of this section apply.

(8) *Extralabel use prohibition statement*. For approved new animal drugs prohibited from extralabel use as listed under § 530.41 of this chapter, the requirements of paragraph (a)(5) of this section apply.

(9) *“Net Contents”*. This section of the Rx other approved labeling must identify the contents of the container to which the Rx other approved labeling applies.

(10) *“Storage, Handling, and Disposal”*. The requirements of paragraph (a)(20) of this section apply.

(11) *NADA/ANADA approval statement*. For approved new animal drugs or approved generic new animal drugs, the requirements of paragraph (a)(21) of this section apply.

(12) *Name and place of business*. The requirements of paragraph (a)(22) of this section apply.

(13) *“Lot Number and Expiration Date”*. This section of the Rx other approved labeling must include the identifying lot or control number of the Rx new animal drug within the container to which the Rx other approved labeling applies. This section of the Rx other approved labeling must also include the expiration date of the Rx new animal drug within the

container to which the Rx other approved labeling applies. In accordance with § 201.17, an expiration date may be excluded from the Rx other approved labeling if the expiration date provided on containers within or their labeling is easily legible through the container to which the Rx other approved labeling applies.

(14) *“Revision Date”*. This section of the Rx other approved labeling must include the date of the most recent revision of the Rx other approved labeling, listing the month followed by the year.

**§ 201.407 Content and format for over-the-counter (OTC) new animal drug labeling.**

This section describes specific content and format requirements for the labeling of approved or conditionally approved OTC new animal drugs other than those for use in animal feeds that are subject to part 558 of this chapter. See § 201.409 for content and format requirements for the labeling of approved or conditionally approved new animal drugs for use in animal feeds that are subject to part 558 of this chapter. Omit labeling sections or subsections that do not apply to the OTC new animal drug. The final content of each applicable component and section of labeling is determined by FDA. In addition to the content and format requirements in this section, the labeling of approved or conditionally approved OTC new animal drugs must comply with other applicable requirements in this subpart.

(a) *Labeling providing full product information*. All approved or conditionally approved OTC new animal drugs must provide full product information as described in this paragraph. The package insert must include full product information. If no package insert is provided, the secondary container labeling must include full product information as described in this paragraph. If neither a package insert nor a secondary container is provided, the label must include full product information as described in this paragraph. The following information, as applicable, must appear in the order listed on the labeling component providing full product information. If full product information is provided on the secondary container labeling, in accordance with section 201(k) of the Federal Food, Drug, and Cosmetic Act, the secondary container labeling may exclude any of the information described in this subsection that is required by paragraphs (b) or (c) of this section to appear on the label if such information is easily legible through the

secondary container. Section headings, subsection headings, and other text presented in quotations in this paragraph must appear verbatim on the labeling providing full product information. Sections and subsections are not numbered on full product information.

(1) *Drug product identification*. This section of full product information must include:

(i) The proprietary name of the finished drug product;

(ii) The established name of the drug product;

(iii) The route(s) of administration, if not included as part of the established name of the drug product;

(iv) The dosage form of the finished drug product, if not included as part of the established name of the drug product;

(v) The established name and strength or concentration of each active ingredient, except that the strength or concentration may be excluded from full product information provided on a package insert that applies to multiple strengths or concentrations; and

(vi) The pharmacological class of the new animal drug, if required to facilitate the drug's safe and effective use.

(2) *Conditional approval statement*. The requirements of § 201.405(a)(3) apply.

(3) *“Uses”*. Include the following information in this section of full product information in order:

(i) The approved or conditionally approved indication(s) and target animal(s) in the following format: “For [indication(s)] in [target animal(s)]”;

(ii) A statement indicating that the new animal drug is approved or conditionally approved for use only under specific conditions, if applicable;

(iii) A statement describing the relative effectiveness of doses within the approved range of doses, if required by FDA to facilitate the drug's safe and effective use; and

(iv) A statement(s) indicating animals for which the new animal drug is not approved or conditionally approved, if FDA determines such a statement(s) is required for safety and/or effectiveness reasons.

(4) *Extralabel use statement*. This section of full product information must include the following extralabel use statement: “It is a violation of Federal law to use this drug product other than as directed in the labeling or as directed by your veterinarian.”

(5) *Extralabel use prohibition statement*. For approved new animal drugs prohibited from extralabel use as listed under § 530.41 of this chapter, the requirements of § 201.405(a)(5) apply.

(6) “*Description*”. This section of full product information must include:

- (i) The proprietary name of the finished drug product;
- (ii) The established name of the drug product;
- (iii) The route(s) of administration, if not included as part of the established name of the drug product;
- (iv) The dosage form of the finished drug product, if not included as part of the established name of the drug product;
- (v) A description of the identifying characteristics of the dosage form, such as color, shape, coating, scoring, and imprinting;
- (vi) The established name and strength or concentration of each active ingredient, including all available strengths or concentrations to which full product information applies;
- (vii) If applicable, a statement that the product is sterile; and
- (viii) When inactive ingredients are provided on full product information, the requirements of § 201.405(a)(6)(viii) apply.

(7) “*Warnings*”. This section of full product information is required for all approved or conditionally approved new animal drugs. Include in the following order all applicable subsections, headings, and information:

- (i) “*Withdrawal Periods and Residue Warnings*” or “*Withdrawal Periods*”. The requirements of § 201.405(a)(10)(i) apply.
- (ii) “*User Safety Warnings*”. The requirements of § 201.405(a)(10)(ii) apply.
- (iii) “*Animal Safety Warnings*”. All contraindications, target animal safety warnings that identify any serious adverse reaction or potential hazard to the target animal(s) associated with the use of the new animal drug, adverse reactions, and post-approval adverse drug experiences must be included in this subsection of full product information. These items must be listed in decreasing order of severity or frequency.

(iv) “*Environmental Warnings*”. The requirements of § 201.405(a)(10)(iv) apply.

(v) “*Other Warnings*”. The requirements of § 201.405(a)(10)(v) apply.

(8) “*Additional Recommendations*”. This section of full product information must include all precautions.

(9) “*Other Effects You May Notice*”. This section of full product information must include all statements required by FDA that identify any effects of the OTC new animal drug on the target animal(s) that are not considered contraindications, target animal safety

warnings, adverse reactions, or post-approval adverse drug experiences.

(10) “*Directions*”. This section of full product information must include for each indication and target animal:

- (i) The route(s) of administration, and specific site(s) of administration, if applicable;
- (ii) The dose (or dose range);
- (iii) The intervals between doses, if applicable;
- (iv) The duration of treatment;
- (v) The maximum volume per injection site, if required to facilitate the drug’s safe and effective use; and
- (vi) Other information regarding administration, if required by FDA to facilitate the drug’s safe and effective use.

(11) “*Net Contents*”. This section of full product information, when presented on the label or the secondary container labeling, must identify the contents of the immediate container, in accordance with § 201.62, or the secondary container, respectively. Exclude this section from package inserts.

(12) “*How Supplied*”. The requirements of § 201.405(a)(19) apply.

(13) “*Storage, Handling, and Disposal*”. The requirements of § 201.405(a)(20) apply.

(14) “*Questions/Comments?*”. The following statements must be included in this section of full product information: “Contact [insert name of business] at [insert business telephone number] or [insert business web address]. To report side effects, contact [insert name of business] at [insert business telephone number]. For additional information about reporting side effects for animal drugs, contact FDA at [insert current FDA telephone number for voluntary reporting of adverse drug experiences] or [insert current FDA web address for voluntary reporting of adverse drug experiences].” Use as the name of the business the manufacturer, packer, or distributor identified in the “Name and place of business” section of full product information according to paragraph (a)(16) of this section. If more than one business is identified in the “Name and place of business” section of full product information, select the most appropriate to identify as the “business” in the “Questions/Comments?” section of full product information to provide additional information about the OTC new animal drug and to contact regarding suspected adverse drug experiences.

(15) *NADA/ANADA approval statement*. For approved new animal drugs or approved generic new animal

drugs, the requirements of § 201.405(a)(21) apply.

(16) *Name and place of business*. The requirements of § 201.405(a)(22) apply.

(17) “*Lot Number and Expiration Date*”. This section is required when full product information is provided on the secondary container labeling or the label. This section must include the identifying lot or control number of the OTC new animal drug within the secondary container or immediate container. This section must also include the expiration date of the OTC new animal drug within the secondary container or immediate container, in accordance with § 201.17. Alternatively, this section must refer to the location on the secondary container labeling, secondary container, label, or immediate container where the lot or control number and expiration date are printed. If full product information is provided on the secondary container labeling, in accordance with § 201.17, an expiration date may be excluded from the secondary container labeling or secondary container if the expiration date provided on the label or immediate container is easily legible through the secondary container.

(18) “*Revision Date*”. This section of full product information must include the date of the most recent revision of the component of labeling that provides full product information, listing the month followed by the year.

(b) *OTC new animal drug label not providing full product information (OTC label)*. All approved or conditionally approved OTC new animal drugs must provide a label. If a package insert or secondary container labeling with full product information is provided for an approved or conditionally approved OTC new animal drug and the label does not provide full product information in accordance with paragraph (a) of this section, the following information, as applicable, must appear in the order listed on the label for approved or conditionally approved OTC new animal drugs (OTC label). If there is insufficient space on the immediate container for a label to provide for all of the following information, then an OTC small label is required instead. The requirements for an OTC small label are provided in paragraph (c) of this section. Section headings and other text presented in quotations in this paragraph must appear verbatim on the OTC label. Sections are not numbered on the OTC label. For OTC labels with a front panel and one side or back panel, the information identified in paragraph (b)(1) of this section must be provided on the front panel in the order listed,

and the information identified in paragraph (b)(2) of this section must be provided on the side or back panel in the order listed. If the OTC label consists of a single panel, the information identified in paragraph (b)(1) of this section must be provided on the OTC label in the order listed followed by the information identified in paragraph (b)(2) in the order listed. For OTC labels with a front panel and multiple side and/or back panels, the information identified in paragraph (b)(1) must be provided on the OTC label in the order listed followed by the information identified in paragraph (b)(2) in the order listed, starting on the front panel, continuing on the panel immediately to the right of the front panel, and continuing to fill the panels to the right until all of the information is presented. In all instances, the information specified in paragraphs (b)(2)(iii) and (iv) of this section must appear on the same panel.

(1) *Front panel.* The following information must appear on the front panel of the OTC label in the order listed.

(i) *Drug product identification.* This section of the OTC label must include:

(A) The proprietary name of the finished drug product;

(B) The established name of the drug product;

(C) The route(s) of administration, if not included as part of the established name of the drug product;

(D) The dosage form of the finished drug product, if not included as part of the established name of the drug product;

(E) The established name and strength or concentration of each active ingredient;

(F) If applicable, a statement that the product is sterile; and

(G) The pharmacological class of the new animal drug, if required to facilitate the drug's safe and effective use.

(ii) *Conditional approval statement.* For conditionally approved new animal drugs, the requirements of § 201.405(a)(3) apply.

(iii) *"Uses"*. The requirements of paragraph (a)(3) of this section apply. However, if there is insufficient space on the OTC label for the complete "Uses" section as specified in paragraph (a)(3), then include the statement required in paragraph (a)(3)(i) or, if there is insufficient space on the OTC label for the statement in paragraph (a)(3)(i), then include the statement, "For [abbreviated indication(s)] in [target animal(s)]". In either situation where there is insufficient space on the OTC label for the complete "Uses" section as specified in paragraph (a)(3),

the required statement must be followed by, "See package insert for complete 'Uses'" if full product information is provided on a package insert, or "See package labeling for complete 'Uses'" if full product information is provided on the secondary container labeling.

(iv) *Extralabel use statement.* The requirements of paragraph (a)(4) of this section apply.

(v) *Extralabel use prohibition statement.* For approved new animal drugs prohibited from extralabel use as listed under § 530.41 of this chapter, the requirements of § 201.405(a)(5) apply.

(vi) *"Withdrawal Periods and Residue Warnings" or "Withdrawal Periods"*.

For new animal drugs approved or conditionally approved for use in food-producing animals, the requirements of § 201.405(a)(10)(i) apply. If there is insufficient space on the front panel of OTC labels consisting of only a front panel and one side or back panel for the information required in

§ 201.405(a)(10)(i), this section must be provided on the side or back panel of the OTC label immediately following the complete product information statement specified in paragraph (b)(2)(i) of this section.

(vii) *"Net Contents"*. This section of the OTC label must identify the contents of the immediate container, in accordance with § 201.62.

(viii) *NADA/ANADA approval statement.* For approved new animal drugs or approved generic new animal drugs, the requirements of § 201.405(a)(21) apply.

(2) *Side or back panel.* The following information must appear on the side or back panel of the OTC label in the order listed.

(i) *Complete product information statement.* This section of the OTC label must include one of two statements. If full product information is provided on the package insert, the following statement must be used: "Before using this drug, read package insert for complete product information." If full product information is provided on the secondary container labeling, the following statement must be used: "Before using this drug, read package labeling for complete product information."

(ii) *"Directions"*. The requirements of paragraph (a)(10) of this section apply. If there is insufficient space on the OTC label for complete requirements as specified in paragraph (a)(10) of this section or if it is necessary for additional information provided in full product information that is not provided on the OTC label to be read before administering the drug, FDA may allow

this section to be excluded from the OTC label.

(iii) *"Active Ingredient" or "Active Ingredients"*. This section of the OTC label must provide the established name and strength or concentration of each active ingredient. If the OTC new animal drug contains one active ingredient, this section of the OTC label must be entitled "Active Ingredient". If the OTC new animal drug contains more than one active ingredient, this section of the OTC label must be entitled "Active Ingredients."

(iv) *"Inactive Ingredients"*. When inactive ingredients are provided on the OTC label, the requirements of § 201.405(a)(6)(viii) apply.

(v) *"Storage, Handling, and Disposal"*. The requirements of § 201.405(a)(20) apply.

(vi) *Name and place of business.* This section of the OTC label must include the name and place of business of the manufacturer, packer, or distributor, in accordance with section 502(b) of the Federal Food, Drug, and Cosmetic Act.

(vii) *"Lot Number and Expiration Date" or "Lot Number"*. This section of the OTC label must include the identifying lot or control number of the OTC new animal drug within the immediate container. This section of the OTC label must also include the expiration date of the OTC new animal drug within the immediate container, in accordance with § 201.17. Alternatively, this section must refer to the location on the OTC label or immediate container where the lot or control number and expiration date are printed. In accordance with § 201.17, if the immediate container provides a single dose of the OTC new animal drug and is packaged individually in a secondary container that provides an expiration date on the secondary container labeling or secondary container, an expiration date is not required on the OTC label or immediate container. If an expiration date is not provided on the OTC label or immediate container per this provision, then this section of the OTC label must be titled "Lot Number."

(viii) *"Revision Date"*. This section of the OTC label must include the date of the most recent revision of the OTC label, listing the month followed by the year.

(c) *OTC new animal drug small label (OTC small label).* The following information must appear in the order listed on the OTC small label. 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 paragraph (b) of this section, taking into consideration readability and legibility

of the information. Section headings and other text presented in quotations in this paragraph must appear verbatim on the OTC small label. Sections are not numbered on the OTC small label.

(1) *Proprietary name*. This section of the OTC small label must provide the proprietary name of the finished drug product.

(2) *Established name*. This section of the OTC small label must provide the established name of the drug product.

(3) *Active ingredient(s)*. This section of the OTC small label must provide the established name and strength or concentration of each active ingredient.

(4) *Target animals*. This section of the OTC small label must include the statement: "For [target animal(s)] only."

(5) *Complete product information statement*. This section of the OTC small label must include one of two statements. If full product information is provided on the package insert, the following statement must be used: "Read package insert for complete product information." If full product information is provided on the secondary container labeling, the following statement must be used: "Read package labeling for complete product information."

(6) *"Net Contents"*. This section of the OTC small label must identify the contents of the immediate container, in accordance with § 201.62.

(7) *Name and place of business*. This section of the OTC small label must include the name and place of business of the manufacturer, packer, or distributor, in accordance with section 502(b) of the Federal Food, Drug, and Cosmetic Act.

(8) *"Lot, Exp. and Storage" or "Lot and Storage"*. This section of the OTC small label must include the identifying lot or control number of the OTC new animal drug within the immediate container. This section of the OTC small label must also include the expiration date of the OTC new animal drugs within the immediate container, in accordance with § 201.17. Drug storage information for the OTC new animal drug must also be included in this section of the OTC small label. In accordance with § 201.17, if the immediate container provides a single dose of the OTC new animal drug and is packaged individually in a secondary container that provides an expiration date on the secondary container labeling or secondary container, an expiration date is not required on the OTC small label or immediate container. If an expiration date is not provided on the OTC small label or immediate container per this provision, then this section of

the OTC small label must be entitled "Lot and Storage."

(9) *"Revision Date"*. This section of the OTC small label must include the date of the most recent revision of the OTC small label, listing the month followed by the year.

(d) *Labeling for secondary containers for OTC new animal drugs that include a package insert (OTC secondary container labeling)*. If a secondary container is provided for an approved or conditionally approved OTC new animal drug and the OTC new animal drug includes a package insert, the following information, as applicable, must appear in the order listed on the secondary container labeling (OTC secondary container labeling). In accordance with section 201(k) of the Federal Food, Drug, and Cosmetic Act, the OTC secondary container labeling may exclude any of the information described in this subsection that is required by paragraphs (b) or (c) of this section to appear on the label if such information is easily legible through the OTC secondary container. Section headings, subsection headings, and other text presented in quotations in this paragraph must appear verbatim on the OTC secondary container labeling. Sections and subsections are not numbered on the OTC secondary container labeling. For OTC secondary container labeling with a front panel and one side or back panel, the information identified in paragraph (d)(1) of this section must be provided on the front panel in the order listed, and the information identified in paragraph (d)(2) of this section must be provided on the side or back panel in the order listed. For OTC secondary container labeling with a front panel and multiple side and/or back panels, the information identified in paragraph (d)(1) of this section must be provided on the OTC secondary container labeling in the order listed followed by the information identified in paragraph (d)(2) of this section in the order listed, starting on the front panel, continuing on the panel immediately to the right of the front panel, and continuing to fill the panels to the right until all of the information is presented. In all instances, the information specified in paragraphs (d)(2)(iv) and (v) of this section must appear on the same panel.

(1) *Front panel*. The following information must appear on the front panel of the OTC secondary container labeling in the order listed.

(i) *Drug product identification*. This section of the OTC secondary container labeling must include:

(A) The proprietary name of the finished drug product;

(B) The established name of the drug product;

(C) The route(s) of administration, if not included as part of the established name of the drug product;

(D) The dosage form of the finished drug product, if not included as part of the established name of the drug product;

(E) The established name and strength or concentration of each active ingredient;

(F) If applicable, a statement that the product is sterile; and

(G) The pharmacological class of the new animal drug, if required to facilitate the drug's safe and effective use.

(ii) *Conditional approval statement*. The requirements of § 201.405(a)(3) apply.

(iii) *"Uses"*. The requirements of paragraph (a)(3) of this section apply.

(iv) *Extralabel use statement*. The requirements of paragraph (a)(4) of this section apply.

(v) *Extralabel use prohibition statement*. For approved new animal drugs prohibited from extralabel use as listed under § 530.41 of this chapter, the requirements of § 201.405(a)(5) apply.

(vi) *"Net Contents"*. This section of the OTC secondary container labeling must identify the contents of the secondary container.

(vii) *NADA/ANADA approval statement*. For approved new animal drugs or approved generic new animal drugs, the requirements of § 201.405(a)(21) apply.

(2) *Side or back panel*. The following information must appear on the side or back panel of the OTC secondary container labeling in the order listed.

(i) *Complete product information statement*. This section of the OTC secondary container labeling must include the following statement: "Before using this drug, read package insert for complete product information."

(ii) *"Directions"*. The requirements of paragraph (a)(10) of this section apply.

(iii) *"Warnings"*. The requirements of paragraph (a)(7) of this section apply.

(iv) *"Active Ingredient" or "Active Ingredients"*. The requirements of paragraph (b)(2)(iii) of this section apply.

(v) *"Inactive Ingredients"*. When inactive ingredients are provided on the OTC secondary container labeling, the requirements of § 201.405(a)(6)(viii) apply.

(vi) *"Storage, Handling, and Disposal"*. The requirements of § 201.405(a)(20) apply.

(vii) *Name and place of business*. The requirements of § 201.405(a)(22) apply.

(viii) *"Lot Number and Expiration Date"*. This section of the OTC

secondary container labeling must include the identifying lot or control number of the OTC new animal drug within the secondary container. This section of the OTC secondary container labeling must also include the expiration date of the OTC new animal drug within the secondary container, in accordance with § 201.17. Alternatively, this section must refer to the location on the OTC secondary container labeling or secondary container where the lot or control number and expiration date are printed. In accordance with § 201.17, an expiration date may be excluded from the OTC secondary container labeling or secondary container if the expiration date provided on the OTC label, OTC small label, or immediate container is easily legible through the secondary container.

(ix) “*Revision Date*”. This section of the OTC secondary container labeling must include the date of the most recent revision of the OTC secondary container labeling, listing the month followed by the year.

(e) *Shipping labeling for OTC new animal drugs (OTC shipping labeling)*. If shipping labeling is provided for an approved or conditionally approved OTC new animal drug (OTC shipping labeling), the following information, as applicable, must appear in the order listed on the OTC shipping labeling. Section headings and other text presented in quotations in this paragraph must appear verbatim on the OTC shipping labeling. Sections are not numbered on the OTC shipping labeling.

(1) *Proprietary name*. This section of the OTC shipping labeling must provide the proprietary name of the finished drug product.

(2) *Established name*. This section of the OTC shipping labeling must provide the established name of the drug product.

(3) *Active ingredient(s)*. This section of the OTC shipping labeling must provide the established name and strength or concentration of each active ingredient.

(4) *Conditional approval statement*. The requirements of § 201.405(a)(3) apply.

(5) “*Net Contents*”. This section of the OTC shipping labeling must identify the contents of the shipping carton.

(6) “*Storage and Handling*”. This section of the OTC shipping labeling must include drug storage information. If required by FDA to facilitate the drug’s safe and effective use, also include handling information.

(7) *NADA/ANADA approval statement*. For approved new animal drugs or approved generic new animal

drugs, the requirements of § 201.405(a)(21) apply.

(8) *Name and place of business*. The requirements of § 201.405(a)(22) apply.

(9) “*Lot Number and Expiration Date*”. This section of the OTC shipping labeling must include the identifying lot or control number(s) and the expiration date(s) of the OTC new animal drug within the shipping carton.

(10) “*Revision Date*”. This section of the OTC shipping labeling must include the date of the most recent revision of OTC shipping labeling, listing the month followed by the year.

(f) *Other approved labeling for OTC new animal drugs (OTC other approved labeling)*. If other approved labeling is provided for an approved or conditionally approved OTC new animal drug (OTC other approved labeling), such as labeling on display cartons and multi-unit cartons (excluding shipping cartons), the following information, as applicable, must appear in the order listed on the OTC other approved labeling. Section headings and other text presented in quotations in this paragraph must appear verbatim on the OTC other approved labeling. Sections are not numbered on the OTC other approved labeling.

(1) *Proprietary name*. This section of the OTC other approved labeling must provide the proprietary name of the finished drug product.

(2) *Established name*. This section of the OTC other approved labeling must provide the established name of the drug product.

(3) *Active ingredient(s)*. This section of the OTC other approved labeling must provide the established name and strength or concentration of each active ingredient.

(4) *Conditional approval statement*. The requirements of § 201.405(a)(3) apply.

(5) *Extralabel use statement*. The requirements of paragraph (a)(4) of this section apply.

(6) *Extralabel use prohibition statement*. For approved new animal drugs prohibited from extralabel use as listed under § 530.41 of this chapter, the requirements of § 201.405(a)(5) apply.

(7) “*Net Contents*”. This section of the OTC other approved labeling must identify the contents of the container to which the OTC other approved labeling applies.

(8) “*Storage, Handling, and Disposal*”. The requirements of § 201.405(a)(20) apply.

(9) *NADA/ANADA approval statement*. For approved new animal drugs or approved generic new animal

drugs, the requirements of § 201.405(a)(21) apply.

(10) *Name and place of business*. The requirements of § 201.405(a)(22) apply.

(11) “*Lot Number and Expiration Date*”. This section of the OTC other approved labeling must include the identifying lot or control number of the OTC new animal drug within the container to which the OTC other approved labeling applies. This section of the OTC other approved labeling must also include the expiration date of the OTC new animal drug within the container to which the OTC other approved labeling applies. In accordance with § 201.17, an expiration date may be excluded from the OTC other approved labeling if the expiration date on containers within or their labeling is easily legible through the container to which the OTC other approved labeling applies.

(12) “*Revision Date*”. This section of the OTC other approved labeling must include the date of the most recent revision of the OTC other approved labeling, listing the month followed by the year.

#### **§ 201.409 Content and format of labeling for new animal drugs for use in animal feeds.**

This section describes specific content and format requirements for the labeling of approved or conditionally approved new animal drugs for use in animal feeds and that are subject to part 558 of this chapter, including VFD drugs. Omit labeling sections or subsections that do not apply to the new animal drug for use in animal feeds. The final content of each applicable component and section of labeling is determined by FDA. In addition to the content and format requirements in this section, the labeling of approved or conditionally approved new animal drugs for use in animal feeds and that are subject to part 558 of this chapter must comply with other applicable requirements in this subpart.

(a) *Type A medicated article label*. All approved or conditionally approved Type A medicated articles must provide a Type A medicated article label as described in this paragraph. The following information, as applicable, must appear in the order listed on the Type A medicated article label. Section headings, subsection headings, and other text presented in quotations in this paragraph must appear verbatim on the Type A medicated article label. Sections and subsections are not numbered on the Type A medicated article label.

(1) *Type A medicated article identification*. This section of the Type

A medicated article label must include in order:

- (i) The proprietary name of the Type A medicated article;
- (ii) The established name of the Type A medicated article; and
- (iii) The phrase “Type A medicated article” or “Type A liquid medicated article,” as applicable, if not included as part of the established name of the Type A medicated article.

(2) *VFD cautionary statement*. For VFD drugs, this section of the Type A medicated article label must prominently and conspicuously display the cautionary statement, in accordance with § 558.6(a)(6) of this chapter.

(3) *Manufacturing statement*. This section of the Type A medicated article label must include the statement: “For further manufacturing only.”

(4) *Conditional approval statement*. The requirements of § 201.405(a)(3) apply.

(5) *Indications for Use*. The requirements of § 201.407(a)(3) apply.

(6) *Extralabel use statement*. This section of the Type A medicated article label must include the following extralabel use statement: “It is a violation of Federal law to use other than as directed in the labeling.”

(7) *Active Ingredient* or *Active Ingredients*. This section of the Type A medicated article label must provide the established name and concentration of each active ingredient in the Type A medicated article. If the Type A medicated article contains one active ingredient, this section of the Type A medicated article label must be entitled “Active Ingredient.” If the Type A medicated article contains more than one active ingredient, this section of the Type A medicated article label must be entitled “Active Ingredients.”

(8) *Inactive Ingredients*. When inactive ingredients are provided on the Type A medicated article label, the requirements of § 201.405(a)(6)(viii) apply.

(9) *Directions*. This section of the Type A medicated article label must include the following three subsections in order:

- (i) *Approved Concentration(s) of [Active Ingredient or Active Moiety] in Type C Medicated Feeds*. This subsection of the Type A medicated article label must provide the approved concentration(s) of each active ingredient in Type C medicated feeds to be manufactured from the Type A medicated article for each approved or conditionally approved indications for use. If an active ingredient is a salt or other noncovalent derivative and its concentration(s) in paragraph (a)(7) of this section is expressed based on the

active moiety, the approved concentration(s) in the Type C medicated feeds must be expressed based on the active moiety, and the title of this subsection must include the name of the active moiety instead of the active ingredient.

(ii) *Mixing Directions*. This subsection of the Type A medicated article label must provide the approved mixing directions for the manufacture of approved medicated feeds from this Type A medicated article for each approved or conditionally approved indications for use, including an intermediate mixing step (*i.e.*, preblend step) if required.

(iii) *Feeding Directions*. This subsection of the Type A medicated article label must provide the approved feeding directions for each approved or conditionally approved indications for use for Type C medicated feeds manufactured from this Type A medicated article.

(10) *Warnings*. This section of the Type A medicated article label is required for all Type A medicated articles. Include in the following order all applicable subsections, headings, and information:

(i) *Withdrawal Periods and Residue Warnings* or *Withdrawal Periods*. The requirements of § 201.405(a)(10)(i) apply.

(ii) *User Safety Warnings*. The requirements of § 201.405(a)(10)(ii) apply.

(iii) *Animal Safety Warnings*. The requirements of § 201.407(a)(7)(iii) apply.

(iv) *Environmental Warnings*. The requirements of § 201.405(a)(10)(iv) apply.

(v) *Other Warnings*. The requirements of § 201.405(a)(10)(v) apply.

(11) *Additional Recommendations*. The requirements of § 201.407(a)(8) apply.

(12) *Other Effects You May Notice*. The requirements of § 201.407(a)(9) apply.

(13) *Net Weight*. This section of the Type A medicated article label must list the net weight of the Type A medicated article in the immediate container.

(14) *Storage, Handling, and Disposal*. The requirements of § 201.405(a)(20) apply.

(15) *Questions/Comments?*. The following statements must be included in this section of the Type A medicated article label: “Contact [insert name of business] at [insert business telephone number] or [insert business web address]. To report side effects, contact [insert name of business] at [insert business telephone number]. For

additional information about reporting side effects for animal drugs, contact FDA at [insert current FDA telephone number for voluntary reporting of adverse drug experiences] or [insert current FDA web address for voluntary reporting of adverse drug experiences].” Use as the name of the business the manufacturer, packer, or distributor identified in the “Name and place of business” section of the Type A medicated article label according to paragraph (a)(17) of this section. If more than one business is identified in the “Name and place of business” section of the Type A medicated article label, select the most appropriate to identify as the “business” in the “Questions/Comments?” section of the Type A medicated article label to provide additional information about the Type A medicated article and to contact regarding suspected adverse drug experiences.

(16) *NADA/ANADA approval statement*. For approved new animal drugs or approved generic new animal drugs, the requirements of § 201.405(a)(21) apply.

(17) *Name and place of business*. The requirements of § 201.405(a)(22) apply.

(18) *Lot Number and Expiration Date*. This section of the Type A medicated article label must include the identifying lot or control number of the Type A medicated article within the immediate container. In accordance with § 226.58(d) of this chapter, this section of the Type A medicated article label must also include the expiration date of the Type A medicated article within the immediate container.

Alternatively, this section must refer to the location on the Type A medicated article label or immediate container where the lot or control number and expiration date are printed.

(19) *Revision Date*. This section of the Type A medicated article label must include the date of the most recent revision of the Type A medicated article label, listing the month followed by the year.

(b) *Representative Type B medicated feed labeling*. The following information, as applicable, must appear in the order listed on the representative Type B medicated feed labeling. Section headings, subsection headings, and other text presented in quotations in this paragraph must appear verbatim on the representative Type B medicated feed labeling. Sections and subsections are not numbered on the representative Type B medicated feed labeling.

(1) *Description of the Type B medicated feed*. This section of the representative Type B medicated feed labeling serves as a placeholder for the

proprietary name to be added by the feed manufacturer to the label of the final Type B medicated feed manufactured in accordance with the approved representative Type B labeling. The description of the Type B medicated feed must:

(i) Distinguish the Type B medicated feed from any other Type B medicated feeds approved or conditionally approved within the same application; and

(ii) Not include the proprietary name of a Type A medicated article.

(2) *Established name of the Type B medicated feed.* The established name of the Type B medicated feed must include in the following order:

(i) The active moiety or active ingredient of each new animal drug, as determined by FDA; and

(ii) One of the following statements, as applicable: “Type B medicated feed” or “Type B liquid medicated feed”.

(3) *VFD cautionary statement.* The requirements of paragraph (a)(2) of this section apply.

(4) *Undiluted statement.* This section of the representative Type B medicated feed labeling must include the statement: “Do Not Feed Undiluted.”

(5) *Conditional approval statement.* The requirements of § 201.405(a)(3) apply.

(6) *“Indications for Use”.* The requirements of § 201.407(a)(3) apply. Include only the approved or conditionally approved indications for use for the specific Type B medicated feed to which the representative Type B medicated feed labeling applies.

(7) *Extralabel use statement.* The requirements of paragraph (a)(6) of this section apply.

(8) *“Active Ingredient” or “Active Ingredients”.* This section of the representative Type B medicated feed labeling must include the following information for the specific Type B medicated feed to which the representative Type B medicated feed labeling applies. If the Type B medicated feed contains one active ingredient, this section of the representative Type B medicated feed labeling must be entitled “Active Ingredient.” If the Type B medicated feed contains more than one active ingredient, this section of the representative Type B medicated feed labeling must be entitled “Active Ingredients.”

(i) The established name of each active ingredient; and

(ii) The concentration or range of concentrations of each active ingredient as approved by FDA. If included as a range, the active ingredient concentrations must reference a footnote

at the bottom of this page of the representative Type B labeling indicating that each final printed Type B medicated feed label must only include a single concentration of each active ingredient.

(9) *“Guaranteed Analysis”.* This section of the representative Type B medicated feed labeling must provide for the nutritional content guarantees of the Type B medicated feed appropriate for the target animal(s) in addition to any other required specifications.

(10) *“Ingredients”.* This section of the representative Type B medicated feed labeling must include the following:

(i) A statement that feed ingredients must be listed on each final printed Type B medicated feed label by their common or usual names in descending order of predominance by weight, in accordance with § 501.4(a) of this chapter, including their collective names where permitted, in accordance with § 501.4(b)(13) of this chapter; and

(ii) A statement that spices, flavorings, colorings, and chemical preservatives, if used, must be declared on each final printed Type B medicated feed label, in accordance with § 501.22 of this chapter.

(11) *“Mixing Directions”.* This section of the representative Type B medicated feed labeling must provide the approved mixing directions for the manufacture of a Type C medicated feed(s) or another Type B medicated feed(s), as applicable, from the Type B medicated feed for which the representative Type B medicated feed labeling applies.

(12) *“Warnings”.* The requirements of paragraph (a)(10) of this section apply. Include only the warnings for the specific Type B medicated feed to which the representative Type B medicated feed labeling applies.

(13) *“Additional Recommendations”.* The requirements of § 201.407(a)(8) apply. Include only the precautions for the specific Type B medicated feed to which the representative Type B medicated feed labeling applies.

(14) *“Other Effects You May Notice”.* The requirements of § 201.407(a)(9) apply. Include only statements of other effects for the specific Type B medicated feed to which the representative Type B medicated feed labeling applies.

(15) *Name and place of business.* This section of the representative Type B medicated feed labeling must provide for the name and place of business of the manufacturer, packer, or distributor of the final Type B medicated feed, in accordance with § 501.5 of this chapter.

(16) *“Net Weight”.* This section of the representative Type B medicated feed labeling must provide for the statement on the final printed Type B medicated

feed label of the net weight of the Type B medicated feed in the immediate container.

(17) *“Storage, Handling, and Disposal”.* The requirements of § 201.405(a)(20) apply.

(18) *“Questions/Comments”.* The following statements must be included in this section of the representative Type B medicated feed labeling: “Contact [name of business] at [business telephone number] or [business web address]. For additional information about reporting problems with medicated feeds, contact FDA at [insert current FDA telephone number for voluntary reporting of adverse drug experiences] or [insert current FDA web address for voluntary reporting of adverse drug experiences].” The information in the bracketed areas of the first statement are placeholders for the business of the manufacturer, packer, or distributor of the final Type B medicated feed to insert their name and contact information. The information in the bracketed areas of the second statement must be inserted by the sponsor of the new animal drug application.

(19) *“Lot, Batch, or Control Number”.* This section of the representative Type B medicated feed labeling must provide for an identifying lot, batch, or control number on the final printed Type B medicated feed label.

(20) *“Expiration Date”.* If an expiration date is required, in accordance with § 514.1(b)(5)(x) of this chapter, then this section of the representative Type B medicated feed labeling must provide for the expiration date to be printed on the final printed Type B medicated feed label. The approved expiration period must also be included in this section of the representative Type B medicated feed labeling.

(21) *“Revision Date”.* This section of the representative Type B medicated feed labeling must include the date of the most recent revision of the representative Type B medicated feed labeling, listing the month followed by the year.

(c) *Representative Type C medicated feed labeling.* The following information, as applicable, must appear in the order listed on the representative Type C medicated feed labeling. Section headings, subsection headings, and other text presented in quotations in this paragraph must appear verbatim on the representative Type C medicated feed labeling. Sections and subsections are not numbered on the representative Type C medicated feed labeling.

(1) *Description of the Type C medicated feed.* This section of the

representative Type C medicated feed labeling serves as a placeholder for the proprietary name to be added by the feed manufacturer to the label of the final Type C medicated feed manufactured in accordance with the approved representative Type C medicated feed labeling. The description of the Type C medicated feeds must:

(i) Distinguish the Type C medicated feed from any other Type C medicated feeds approved or conditionally approved within the same application; and

(ii) Not include the proprietary name of a Type A medicated article.

(2) *Established name of the Type C medicated feed*. The established name of the Type C medicated feed must include in the following order:

(i) The active moiety or active ingredient of each new animal drug, as determined by FDA; and

(ii) One of the following statements, as applicable: “Type C medicated feed,” “Type C liquid medicated feed,” “Type C top-dress medicated feed,” “Type C free-choice medicated feed,” or “Type C liquid free-choice medicated feed”.

(3) *VFD cautionary statement*. The requirements of paragraph (a)(2) of this section apply.

(4) *Conditional approval statement*. The requirements of § 201.405(a)(3) apply.

(5) *“Indications for Use”*. The requirements of § 201.407(a)(3) apply. Include only the approved or conditionally approved indications for use for the specific Type C medicated feed to which the representative Type C medicated feed labeling applies.

(6) *Extralabel use statement*. The requirements of paragraph (a)(6) of this section apply.

(7) *“Active Ingredient” or “Active Ingredients”*. This section of the representative Type C medicated feed labeling must include the following information for the specific Type C medicated feed to which the representative Type C medicated feed labeling applies. If the Type C medicated feed contains one active ingredient, this section of the representative Type C medicated feed labeling must be entitled “Active Ingredient.” If the Type C medicated feed contains more than one active ingredient, this section of the representative Type C medicated feed labeling must be entitled “Active Ingredients.”

(i) The established name of each active ingredient; and

(ii) The concentration or range of concentrations of each active ingredient as approved by FDA. If included as a

range, the active ingredient concentrations must reference a footnote at the bottom of this page of the representative Type C medicated feed labeling indicating that each final printed Type C medicated feed label must only include a single concentration of each active ingredient.

(8) *“Guaranteed Analysis”*. The requirements of paragraph (b)(9) of this section apply.

(9) *“Ingredients”*. This section of the representative Type C medicated feed labeling must include the following:

(i) For Type C medicated feeds that are not Type C free-choice medicated feeds:

(A) A statement that feed ingredients must be listed on each final printed Type C medicated feed label by their common or usual names in descending order of predominance by weight, in accordance with § 501.4(a) of this chapter, including their collective names where permitted, in accordance with § 501.4(b)(13) of this chapter; and

(B) A statement that spices, flavorings, colorings, and chemical preservatives, if used, must be declared on each final printed Type C medicated feed label, in accordance with § 501.22 of this chapter.

(ii) For Type C free-choice medicated feeds, a list of the feed ingredients and their inclusion rates, including the drug concentrations exactly as they appear in the approved non-proprietary formula published for the specific new animal drug in part 558 of this chapter.

(10) *“Feeding Directions”*. The requirements of paragraph (a)(9)(iii) of this section apply. This section of the representative Type C medicated feed labeling must include the approved feeding directions for the specific Type C medicated feed for which the representative Type C medicated feed labeling applies.

(11) *“Warnings”*. The requirements of paragraph (a)(10) of this section apply. Include only the warnings for the specific Type C medicated feed to which the representative Type C medicated feed labeling applies.

(12) *“Additional Recommendations”*. The requirements of § 201.407(a)(8) apply. Include only the precautions for the specific Type C medicated feed to which the representative Type C medicated feed labeling applies.

(13) *“Other Effects You May Notice”*. The requirements of § 201.407(a)(9) apply. Include only statements of other effects for the specific Type C medicated feed to which the representative Type C medicated feed labeling applies.

(14) *Name and place of business*. This section of the representative Type C medicated feed labeling must provide

for the name and place of business of the manufacturer, packer, or distributor of the final Type C medicated feed, in accordance with § 501.5 of this chapter.

(15) *“Net Weight”*. This section of the representative Type C medicated feed labeling must provide for the statement of net weight on the final printed Type C medicated feed label of the Type C medicated feed in the immediate container.

(16) *“Storage, Handling, and Disposal”*. The requirements of § 201.405(a)(20) apply.

(17) *“Questions/Comments?”*. The following statements must be included in this section of the representative Type C medicated feed labeling: “Contact [name of business] at [business telephone number] or [business web address]. For additional information about reporting side effects or other problems with medicated feeds, contact FDA at [insert current FDA telephone number for voluntary reporting of adverse drug experiences] or [insert current FDA web address for voluntary reporting of adverse drug experiences].” The information in the bracketed areas of the first statement are placeholders for the business of the manufacturer, packer, or distributor of the final Type C medicated feed to insert their name and contact information. The information in the bracketed areas of the second statement must be inserted by the sponsor of the new animal drug application.

(18) *“Lot, Batch, or Control Number”*. This section of the representative Type C medicated feed labeling must provide for an identifying lot, batch, or control number on the final printed Type C medicated feed label.

(19) *“Expiration Date”*. If an expiration date is required, in accordance with § 514.1(b)(5)(x) of this chapter, then this section of the representative Type C medicated feed labeling must provide for the expiration date to be printed on the final printed Type C medicated feed label. The approved expiration period must also be included in this section of the representative Type C medicated feed labeling.

(20) *“Revision Date”*. This section of representative Type C medicated feed labeling must include the date of the most recent revision of the representative Type C medicated feed labeling, listing the month followed by the year.

(d) *Proprietary Type B medicated feed label*. The following information, as applicable, must appear in the order listed on the proprietary Type B medicated feed label. Section headings, subsection headings, and other text

presented in quotations in this paragraph must appear verbatim on the proprietary Type B medicated feed label. Sections and subsections are not numbered on the proprietary Type B medicated feed label.

(1) *Proprietary Type B medicated feed identification*. This section of the proprietary Type B medicated feed label must include in order:

(i) Proprietary name of the Type B medicated feed; and

(ii) Established name of the Type B medicated feed. The established name of the Type B medicated feed must include in the following order:

(A) The active moiety or active ingredient of each new animal drug, as determined by FDA; and

(B) One of the following statements, as applicable: “Type B medicated feed” or “Type B liquid medicated feed”.

(2) *VFD cautionary statement*. The requirements of paragraph (a)(2) of this section apply.

(3) *Undiluted statement*. This section of the proprietary Type B medicated feed label must include the statement: “Do Not Feed Undiluted”.

(4) *Conditional approval statement*. The requirements of § 201.405(a)(3) apply.

(5) *“Indications for Use”*. The requirements of § 201.407(a)(3) apply.

(6) *Extralabel use statement*. The requirements of paragraph (a)(6) of this section apply.

(7) *“Active Ingredient” or “Active Ingredients”*. This section of the proprietary Type B medicated feed label must include the established name and concentration of each active ingredient in the proprietary Type B medicated feed. If the proprietary Type B medicated feed contains one active ingredient, this section of the proprietary Type B medicated feed label must be entitled “Active Ingredient.” If the proprietary Type B medicated feed contains more than one active ingredient, this section of the proprietary Type B medicated feed label must be entitled “Active Ingredients.”

(8) *“Guaranteed Analysis”*. This section of the proprietary Type B medicated feed label must provide the nutritional content guarantees of the proprietary Type B medicated feed appropriate for the target animal(s) in addition to any other required specifications.

(9) *“Ingredients”*. This section of the proprietary Type B medicated feed label must include:

(i) A listing of the feed ingredients in the proprietary Type B medicated feed by their common or usual names in descending order of predominance by weight, in accordance with § 501.4(a) of

this chapter, including their collective names where permitted, in accordance with § 501.4(b)(13) of this chapter; and

(ii) A declaration of spices, flavorings, colorings, and chemical preservatives, if used, in accordance with § 501.22 of this chapter.

(10) *“Mixing Directions”*. This section of the proprietary Type B medicated feed label must provide the approved mixing directions for the manufacture of a Type C medicated feed(s) or another Type B medicated feed(s), as applicable, from the proprietary Type B medicated feed.

(11) *“Warnings”*. The requirements of paragraph (a)(10) of this section apply.

(12) *“Additional Recommendations”*. The requirements of § 201.407(a)(8) apply.

(13) *“Other Effects You May Notice”*. The requirements of § 201.407(a)(9) apply.

(14) *“Net Weight”*. This section of the proprietary Type B medicated feed label must list the net weight of the Type B medicated feed in the immediate container.

(15) *“Storage, Handling, and Disposal”*. The requirements of § 201.405(a)(20) apply.

(16) *“Questions/Comments?”*. The following statements must be included in this section of the proprietary Type B medicated feed label: “Contact [insert name of business] at [insert business telephone number] or [insert business web address]. For additional information about reporting problems with medicated feeds, contact FDA at [insert current FDA telephone number for voluntary reporting of adverse drug experiences] or [insert current FDA web address for voluntary reporting of adverse drug experiences].” Use as the name of the business the manufacturer, packer, or distributor identified in the “Name and place of business” section of the proprietary Type B medicated feed label according to paragraph (d)(18) of this section. If more than one business is identified in the “Name and place of business” section of the proprietary Type B medicated feed label, select the most appropriate to identify as the “business” in the “Questions/Comments?” section of the proprietary Type B medicated feed label to provide additional information about the Type B medicated feed and to contact regarding problems with this medicated feed.

(17) *NADA/ANADA approval statement*. For approved new animal drugs or approved generic new animal drugs, the requirements of § 201.405(a)(21) apply.

(18) *Name and place of business*. The requirements of § 201.405(a)(22) apply.

(19) *“Lot, Batch, or Control Number”*. This section of the proprietary Type B medicated feed label must include the identifying lot, batch, or control number of the Type B medicated feed.

Alternatively, this section must refer to the location on the proprietary Type B medicated feed label or immediate container where the lot, batch, or control number is printed.

(20) *“Expiration Date”*. If an expiration date is required, in accordance with § 514.1(b)(5)(x) of this chapter, this section must be included on the proprietary Type B medicated feed label and must provide the expiration date of the proprietary Type B medicated feed. Alternatively, this section must refer to the location on the proprietary Type B medicated feed label or immediate container where the expiration date is printed.

(21) *“Revision Date”*. This section of the proprietary Type B medicated feed label must include the date of the most recent revision of the proprietary Type B medicated feed label, listing the month followed by the year.

(e) *Proprietary Type C medicated feed label*. The following information, as applicable, must appear in the order listed on the proprietary Type C medicated feed label. Section headings, subsection headings, and other text presented in quotations in this paragraph must appear verbatim on the proprietary Type C medicated feed label. Sections and subsections are not numbered on the proprietary Type C medicated feed label.

(1) *Proprietary Type C medicated feed identification*. This section of the proprietary Type C medicated feed label must include in order:

(i) Proprietary name of the Type C medicated feed; and

(ii) Established name of the Type C medicated feed. The established name of the Type C medicated feed must include in the following order:

(A) The active moiety or active ingredient of each new animal drug, as determined by FDA; and

(B) One of the following statements, as applicable: “Type C medicated feed,” “Type C liquid medicated feed,” “Type C top-dress medicated feed,” “Type C free-choice medicated feed,” or “Type C liquid free-choice medicated feed.”

(2) *VFD cautionary statement*. The requirements of paragraph (a)(2) of this section apply.

(3) *Conditional approval statement*. The requirements of § 201.405(a)(3) apply.

(4) *“Indications for Use”*. The requirements of § 201.407(a)(3) apply.

(5) *Extralabel use statement*. The requirements of paragraph (a)(6) of this section apply.

(6) “*Active Ingredient*” or “*Active Ingredients*”. This section of the proprietary Type C medicated feed label must include the established name and concentration of each active ingredient in the proprietary Type C medicated feed. If the proprietary Type C medicated feed contains one active ingredient, this section of the proprietary Type C medicated feed label must be entitled “Active Ingredient.” If the proprietary Type C medicated feed contains more than one active ingredient, this section of the proprietary Type C medicated feed label must be entitled “Active Ingredients.”

(7) “*Guaranteed Analysis*”. The requirements of paragraph (d)(8) of this section apply.

(8) “*Ingredients*”. The requirements of paragraph (d)(9) of this section apply.

(9) “*Feeding Directions*”. This section of the proprietary Type C medicated feed label must include the approved feeding directions for the proprietary Type C medicated feed.

(10) “*Warnings*”. The requirements of paragraph (a)(10) of this section apply.

(11) “*Additional Recommendations*”. The requirements of § 201.407(a)(8) apply.

(12) “*Other Effects You May Notice*”. The requirements of § 201.407(a)(9) apply.

(13) “*Net Weight*”. This section of the proprietary Type C medicated feed label must list the net weight of the Type C medicated feed in the immediate container.

(14) “*Storage, Handling, and Disposal*”. The requirements of § 201.405(a)(20) apply.

(15) “*Questions/Comments*”. The following statements must be included in this section of the proprietary Type C medicated feed label: “Contact [insert name of business] at [insert business telephone number] or [insert business web address]. For additional information about reporting side effects or other problems with medicated feeds, contact FDA at [insert current FDA telephone number for voluntary reporting of adverse drug experiences] or [insert current FDA web address for voluntary reporting of adverse drug experiences].” Use as the name of the business the manufacturer, packer, or distributor identified in the “Name and place of business” section of the proprietary Type C medicated feed label according to paragraph (e)(17) of this section. If more than one business is identified in the “Name and place of business” section of the proprietary Type C medicated feed label, select the

most appropriate to identify as the “business” in the “Questions/Comments?” section of the proprietary Type C medicated feed label to provide additional information about the Type C medicated feed and to contact regarding suspected adverse drug experiences.

(16) *NADA/ANADA approval statement*. For approved new animal drugs or approved generic new animal drugs, the requirements of § 201.405(a)(21) apply.

(17) *Name and place of business*. The requirements of § 201.405(a)(22) apply.

(18) “*Lot, Batch, or Control Number*”. This section of the proprietary Type C medicated feed label must include the identifying lot, batch, or control number of the Type C medicated feed. Alternatively, this section must refer to the location on the proprietary Type C medicated feed label or immediate container where the lot, batch, or control number is printed.

(19) “*Expiration Date*”. If an expiration date is required, in accordance with § 514.1(b)(5)(x) of this chapter, this section must be included on the proprietary Type C medicated feed label and must provide the expiration date of the proprietary Type C medicated feed label. Alternatively, this section must refer to the location on the proprietary Type C medicated feed label or immediate container where the expiration date is printed.

(20) “*Revision Date*”. This section of the proprietary Type C medicated feed label must include the date of the most recent revision of the proprietary Type C medicated feed label, listing the month followed by the year.

(f) *Other approved labeling for Type A medicated articles*. If other approved labeling associated with approved or conditionally approved Type A medicated articles is provided (other approved labeling for Type A medicated articles), such as shipping labeling, the following information, as applicable, must appear in the order listed on the other approved labeling for Type A medicated articles. Section headings and other text presented in quotations in this paragraph must appear verbatim on the other approved labeling for Type A medicated articles. Sections are not numbered on other approved labeling for Type A medicated articles.

(1) *Type A medicated article identification*. This section of the other approved labeling for Type A medicated articles must include in order:

- (i) Proprietary name of the Type A medicated article; and
- (ii) Established name of the Type A medicated article.

(2) *VFD cautionary statement*. The requirements of paragraph (a)(2) of this section apply.

(3) “*Active Ingredient*” or “*Active Ingredients*”. This section of the other approved labeling for Type A medicated articles must provide the established name and concentration of each active ingredient in the Type A medicated article. If the Type A medicated article contains one active ingredient, this section of the other approved labeling for Type A medicated articles must be entitled “Active Ingredient.” If the Type A medicated article contains more than one active ingredient, this section of the other approved labeling for Type A medicated articles must be entitled “Active Ingredients.”

(4) *Conditional approval statement*. The requirements of § 201.405(a)(3) apply.

(5) “*Net Contents*”. This section of the other approved labeling for Type A medicated articles must identify the contents of the container to which the other approved labeling for Type A medicated articles applies.

(6) “*Storage and Handling*”. This section of the other approved labeling for Type A medicated articles must include storage information for the Type A medicated article. If required by FDA to facilitate the drug’s safe and effective use, also include handling information.

(7) *NADA/ANADA approval statement*. For approved new animal drugs or approved generic new animal drugs, the requirements of § 201.405(a)(21) apply.

(8) *Name and place of business*. The requirements of § 201.405(a)(22) apply.

(9) “*Lot Number and Expiration Date*”. This section of the other approved labeling for Type A medicated articles must include the identifying lot or control number(s) and the expiration date(s) of the Type A medicated article within the container.

(10) “*Revision Date*”. This section of the other approved labeling for Type A medicated articles must include the date of the most recent revision of the other approved labeling for Type A medicated articles, listing the month followed by the year.

#### § 201.411 Exemptions from labeling requirements for approved or conditionally approved new animal drugs.

(a) In response to a request from the sponsor that includes the information in paragraph (b) of this section, FDA may exempt, based on the circumstances presented, one or more specific requirements set forth in this subpart. A separate request must be submitted for each approved or conditionally approved new animal drug for which an

exemption is sought. Sponsors must submit such requests to the application or the investigational new animal drug file (INAD) for the new animal drug. Requests will be granted or denied by the Director of FDA's Center for Veterinary Medicine or the Director's designee.

(b) Exemption requests must:

(1) Describe why the particular requirement for which the exemption is requested is not appropriate for the new animal drug;

(2) Describe why granting the exemption would not adversely impact the safety or effectiveness of the use of the new animal drug; and

(3) Include copies of all draft labeling proposed to be used for the new animal drug.

#### **§ 201.413 Labeling requirements for certain approved or conditionally approved new animal drugs.**

In addition to labeling requirements elsewhere in this subpart, the labeling requirements in this section apply to the following approved or conditionally approved new animal drugs:

(a) *Approved or conditionally approved corticosteroid-containing new animal drugs for oral, injectable, and/or ophthalmic use.* Approved or conditionally approved corticosteroid-containing new animal drugs for oral, injectable, and/or ophthalmic use are subject to the labeling requirements for Rx new animal drugs in this subpart. In view of adverse reproductive effects associated with use of certain corticosteroid drugs in animals, approved or conditionally approved corticosteroid new animal drugs intended for oral and/or injectable use must also include the following statements in the "Animal Safety Warnings and Precautions" subsection of labeling: "Clinical and experimental data have demonstrated that corticosteroids administered orally or by injection to animals may induce the first stage of parturition if used during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis. Additionally, corticosteroids administered during pregnancy can be teratogenic." These statements must also be included in the "Animal Safety Warnings and Precautions" subsection of labeling for approved or conditionally approved corticosteroid new animal drugs intended for ophthalmic use, if required by FDA to facilitate the drug's safe and effective use.

(b) *Anthelmintic new animal drugs—*

(1) *OTC anthelmintic new animal drugs.* To ensure that OTC anthelmintic new

animal drugs provide adequate directions for their effective use, all approved or conditionally approved OTC anthelmintic new animal drugs, including OTC anthelmintic new animal drugs for use in animal feeds, must include the following statement in the "Additional Recommendations" section of labeling: "Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism."

(2) *Anthelmintic new animal drugs for use in sheep, goats, cattle, horses, swine, and/or poultry.* All approved or conditionally approved anthelmintic new animal drugs for use in sheep, goats, cattle, horses, swine, and/or poultry must include statements on their labeling providing information to end users to minimize antiparasitic resistance development, including information on appropriate dosing, anthelmintic drug selection, effectiveness monitoring, the integration of anthelmintic drug use with other parasite management practices, and other information as needed. The statements must be included in the "Other Warnings" subsection of labeling, and if applicable, additional statements may be required in the "Dosage and Administration" section of labeling for Rx anthelmintic new animal drugs, the "Directions" section of labeling for OTC anthelmintic new animal drugs, or the "Feeding Directions" section or subsection of labeling for anthelmintic new animal drugs for use in animal feeds.

(c) *New animal drugs for use in horses.* All new animal drugs approved or conditionally approved for use in horses must include in the "Other Warnings" subsection of labeling a statement advising against the use of the drug in horses intended for human consumption.

#### **PART 500—GENERAL**

■ 6. The authority citation for part 500 continues to read as follows:

**Authority:** 21 U.S.C. 321, 331, 342, 343, 348, 351, 352, 353, 360b, 371, 379e.

#### **§§ 500.25 and 500.55 [Removed]**

■ 7. Remove §§ 500.25 and 500.55.

#### **PART 501—ANIMAL FOOD LABELING**

■ 8. The authority citation for part 501 continues to read as follows:

**Authority:** 15 U.S.C. 1453, 1454, 1455; 21 U.S.C. 321, 331, 342, 343, 348, 371.

■ 9. Add § 501.19 to subpart A to read as follows:

#### **§ 501.19 Animal food; labeling of animal food containing new animal drugs.**

The requirements for the labeling of animal food containing an approved or conditionally approved new animal drug are found in § 201.409 of this chapter. Requirements of this part apply only as specified in § 201.409.

#### **PART 510—NEW ANIMAL DRUGS**

■ 10. The authority citation for part 510 continues to read as follows:

**Authority:** 21 U.S.C. 321, 331, 351, 352, 353, 360b, 371, 379e.

#### **§§ 510.105, 510.106, and 510.410 [Removed]**

■ 11. Remove §§ 510.105, 510.106, and 510.410.

#### **PART 514—NEW ANIMAL DRUG APPLICATIONS**

■ 12. The authority citation for part 514 continues to read as follows:

**Authority:** 21 U.S.C. 321, 331, 351, 352, 354, 356a, 360b, 360ccc, 371, 379e, 381.

■ 13. In § 514.1, revise paragraph (b)(3) to read as follows:

#### **§ 514.1 Applications.**

\* \* \* \* \*

(b) \* \* \*

(3) *Labeling.* Three copies of each piece of all labeling to be used for the article (total of 9).

(i) All labeling should be identified to show its position on, or the manner in which it is to accompany the market package.

(ii) The content and format of all proposed labeling must comply with subpart H of part 201 of this chapter.

(iii) Labeling for nonprescription new animal drugs should include adequate directions for use by the layperson under all conditions of use for which the new animal drug is intended, recommended, or suggested in any of the labeling or advertising sponsored by the applicant.

(iv) Labeling for prescription new animal drugs should bear adequate information for use under which veterinarians can use the new animal drug safely and for the purposes for which it is intended, including those purposes for which it is to be advertised or represented, in accord with § 201.105 of this chapter.

(v) All labeling for prescription or nonprescription new animal drugs must be submitted with any necessary use restrictions prominently and conspicuously displayed.

(vi) Labeling for new animal drugs intended for use in the manufacture of medicated feeds must include:

(A) Specimens of labeling to be used for such new animal drug with adequate directions for the manufacture and use of finished feeds for all conditions for which the new animal drug is intended, recommended, or suggested in any of the labeling, including advertising, sponsored by the applicant. Ingredient labeling may utilize collective names as provided in § 501.110 of this chapter.

(B) Representative labeling proposed to be used for Type B and Type C medicated feeds containing the new animal drug.

(vii) Draft labeling may be submitted for preliminary consideration of an application. Final printed labeling will ordinarily be required prior to approval of an application. Proposed advertising

for prescription new animal drugs may be submitted for comment or approval.

\* \* \* \* \*

**PART 516—NEW ANIMAL DRUGS FOR MINOR USE AND MINOR SPECIES**

■ 14. The authority citation for part 516 continues to read as follows:

**Authority:** 21 U.S.C. 360ccc-1, 360ccc-2, 371.

■ 15. In § 516.155, redesignate paragraph (c) as paragraph (d) and add a new paragraph (c) to read as follows:

**§ 516.155 Labeling of indexed drugs.**

\* \* \* \* \*

(c) To ensure that OTC anthelmintic new animal drugs provide adequate directions for their effective use, the

labeling of all OTC indexed anthelmintic drugs, including those used in animal feeds, must include the following statement: “Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.” The labeling revisions required for compliance with this section may be placed into effect without prior granting of a request for a modification, as provided for in § 516.161(b)(1).

\* \* \* \* \*

Dated: March 1, 2024.

**Robert M. Califf,**

*Commissioner of Food and Drugs.*

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