

clarifies the procedures and requirements for demonstrating chemical and physical stability of a drug in liquid feed; (5) permits submission of the stability data through a MF for reference by a subsequent applicant; (6) explains what information will be included in the published approval of a drug for use in liquid feed; (7) identifies the conditions under which an approved medicated feed mill license will be required for the manufacture of a liquid medicated feed; and (8) describes the labeling provisions for several drugs approved for use in water but not in liquid feed.

#### *D. Discussion of Proposed § 558.5*

Proposed § 558.5(a) and (b) describe the types of liquid medicated feed covered by the proposed rule.

Proposed § 558.5(c) states that an approved NADA, a supplemental NADA, or an abbreviated NADA is required for new animal drugs intended for use in liquid feed.

An approved, supplemental, or abbreviated NADA for new animal drugs intended for use in liquid feed is required for the same reasons we described when § 558.5 was proposed in 1973. First, some reports had demonstrated the instability of certain drugs (bacitracin, oxytetracycline, and chlortetracycline) in liquid feed (37 FR 27634, December 19, 1972). Second, liquid animal feed differs substantially from dry feeds or dry feed supplements in that small variations in some of the components of liquid feed have a marked effect on the stability of added drugs that may compromise the safety and efficacy of such drugs (38 FR 21178, August 6, 1973). We concluded that the manufacture of liquid feed is inherently more difficult to control than the manufacture of dry feed; and therefore, it should be more closely regulated (38 FR 21178).

Proposed § 558.5(d) clarifies approval requirements for new animal drugs intended for use in liquid feed including the specific stability data necessary for liquid medicated feed to meet the requirements of § 514.1(b)(5)(x). Chemical stability data must be submitted for all drugs intended for use in liquid medicated feed. Because of the potential for the uneven distribution of an animal drug in a liquid feed, the physical stability for liquid medicated feeds must also be demonstrated for an appropriate period of time under field conditions. If not demonstrated, labeling must include instructions for agitation or recirculation before use of the liquid medicated feed.

Proposed § 558.5(e) specifies that the stability data may be submitted either directly as part of the NADA by the sponsor or to an MF that a sponsor may then reference in its NADA with written consent of the MF holder.

Proposed § 558.5(f) explains that the formulas and/or specifications for the liquid medicated feed will be codified in the CFR if requested by the sponsor or MF holder. Otherwise, the approval codified in the CFR will not include the formula and/or specifications, but instead will state that the approval has been granted for a proprietary formula and/or specifications.

Proposed § 558.5(g) states that an approved medicated feed mill license is required for the manufacture of a liquid feed that contains any Category II drug, or a Category I drug that is manufactured with a proprietary formula and/or specifications.

Proposed § 558.5(h) spells out labeling requirements for certain drugs that are intended for use in animal feed and/or drinking water. As previously noted, we are concerned about these drugs because of their demonstrated instability in liquid feed. The purpose of this paragraph is to prevent use of such drugs in liquid medicated feeds.

Proposed § 558.5(i) explains conditions and procedures for obtaining a waiver from labeling provisions outlined in § 558.5(h). We are considering removing this waiver option because since its inception in 1973 it has never been utilized. We are seeking comments on this issue.

Proposed § 558.5(j) includes additional information on the labeling provisions of § 558.5(h).

## **II. Free-Choice Medicated Feed**

### *A. Current Regulation in § 510.455*

The current regulation explains that free-choice medicated feed products such as medicated blocks (agglomerated feed compressed or rendered into a solid mass cohesive enough to hold its form), mineral mixes, and liquid feed tank supplements containing one or more animal drugs, are placed in feeding or grazing areas for consumption and are not intended to be consumed fully at a single feeding or to constitute the entire diet of the animal. This regulation reflects our concerns about the safety and effectiveness of animal drugs when administered free-choice by stating that an approved NADA is required for a drug intended for use in free-choice medicated feed, and that a medicated feed mill license is required for feed mills that manufacture free-choice medicated feeds.

Finally, as with all drugs intended for use in animal feeds, all applicants have to demonstrate that such drugs are stable and safe and effective when offered free-choice (§ 514.1(b)(5)(x) and (b)(8)).

### *B. The Advance Notice of Proposed Rulemaking (ANPR) and AFIA Response*

On November 21, 1996 (61 FR 59209), we issued an ANPR seeking comments concerning various issues for the development of regulations implementing the provisions of the ADAA. In a comment in response to the ANPR, dated December 6, 1996, the AFIA suggested a revised version of § 510.455 that would adopt the terms of feed mill licensing in accordance with the ADAA and allow a feed manufacturer to submit an NADA for the approval of a Type A medicated article for use in the subsequent manufacture of a free-choice medicated feed. In this response, as well as in its other response from April 30, 1993, the AFIA suggested language for § 558.5 that would clarify that liquid medicated feeds intended for use free-choice are also subject to the requirements of § 510.455.

We agree that the terms of feed mill licensing in accordance with the ADAA must be adopted in the provisions for free-choice feed. As we already stated for liquid feeds, where feed manufacturers would like to use Type A medicated articles in the manufacture of free-choice medicated feeds with formulas and/or specifications differing from those in approvals already codified in the CFR, there must be a separate NADA approved for such use containing the safety and consumption/effectiveness data required by § 514.1, and the stability data required by §§ 514.1 and 558.5. In such circumstances, under this proposed rule the drug sponsor could submit an NADA containing the safety and consumption/effectiveness data required by § 514.1, the feed manufacturer (or any other third party) could submit the stability data for the free-choice feed in an MF, and the sponsor could reference the MF in its NADA rather than including its own stability data. Under the proposed rule, on request of the owner of the formula and/or specifications for the free-choice feed, this information will be included in the published approval. Otherwise, we will not publish the formula and/or specifications because it is generally trade secret information entitled to protection under section 301(j) of the act. Where we do not publish the formula and/or specifications, we will include a statement that the free-choice