

a system of medicated feed mill licensing that replaces the provisions for the MFA. Therefore, the requirements specified in the current regulation for liquid medicated feeds, including those in part 558 that provide for the use of specific animal drugs in liquid medicated feeds, must be amended to be consistent with the ADAA provisions for feed mill licensing.

On December 6, 1996, in response to the passage of the ADAA, AFIA filed another amendment to its citizen petition from April 30, 1993. The amended petition revised AFIA's suggested regulation for liquid medicated feeds so that the terms of the regulation are consistent with the provisions for feed mill licensing. Both petitions, the amended and the original, suggested revised language for § 558.5 that would clarify the procedures and requirements for demonstrating chemical and positional (physical) stability for liquid Type B medicated feeds. The suggested language on chemical and positional (physical) stability specifies that the submitted data should describe the relevant ranges of conditions under which the drug would be chemically stable and the conditions under which the drug would be positionally (physically) stable if labeling requiring agitation is not proposed.

The suggested language also stated that the stability data might be submitted by either the sponsor of the new animal drug in an NADA or abbreviated NADA (ANADA) or by a feed manufacturer in a master file (MF), which could be referenced in the NADA or the ANADA. The suggested language also provided that FDA would notify the feed manufacturer by letter that the liquid feed addressed in the MF could be manufactured.

As we have preliminarily stated in correspondence with AFIA, we agree with its request for modification of § 558.5 and inclusion of appropriate directions on chemical and positional (physical) stability. We agree that the clarification of these requirements will enhance the approval process for liquid feeds. We also agree to permit submission of stability data through an MF that can be referenced by a subsequent applicant. This is consistent with the current free-choice medicated feed rule in § 510.455 (21 CFR 510.455).

Where feed manufacturers would like to use Type A medicated articles in the manufacture of liquid medicated feeds with formulas or specifications differing from those in approvals codified in the CFR, there must be a separate NADA approved under part 514 (21 CFR part 514) for such use containing the safety

and 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 effectiveness data required by § 514.1, the feed manufacturer (or any other third party) could submit the stability data for the liquid feed in an MF, and the sponsor could reference the MF in its NADA rather than including its own stability data. On request of the owner of the formula (i.e. ingredient list, product composition) and/or specifications (i.e. other product specific parameters, such as pH data, viscosity, etc.), the formula and/or specifications for the liquid medicated feed will be included in the published approval. We otherwise will not publish the formula and/or specifications because they generally are trade secret information entitled to protection under section 301(j) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 331(j)). Where we do not publish the formula and/or specifications, we will include a statement that the liquid medicated feed has been approved under procedures outlined in proposed § 558.5(f)(2). Because the formula and/or specifications are generally protected information, we expect that such liquid medicated feeds will be manufactured only by the NADA holder, the MF holder, or someone authorized by them. We intend to provide the NADA holder and the MF holder with a certified letter citing the approved formula and/or specifications of the liquid feed where that information is not published. The letter will demonstrate to FDA inspectors that the liquid medicated feed is manufactured using an approved formula and/or specifications.

Since the term "positional stability," as suggested in the citizen petition, is not appropriate in relation to the state of matter, which is either chemical or physical, we are using the term "physical stability" instead of "positional stability." Also, our chemists will determine during the NADA approval process what specifications are required for approval a particular liquid medicated feed.

Finally, we agree with AFIA's request to eliminate the requirement for an approved medicated feed mill license for the manufacture of some liquid medicated feeds that contain a Category I drug. Under this proposed rule an approved feed mill license is required for the manufacture of a liquid medicated feed that contains either any Category II drug or a Category I drug that is manufactured with a formula and/or

specifications that are not published (i.e., proprietary).

Where the formula and/or specifications are published, FDA has an assurance that all medicated feed mills have access to the information necessary to manufacture the approved liquid medicated feed. Where the formula and/or specifications are proprietary, medicated feed mills might attempt to manufacture the liquid medicated feed knowing only that the drug is approved for use in liquid feed, but not knowing the formula and/or specifications. Manufacture of a liquid medicated feed without such crucial information could endanger animal health and public health due to unsafe drug residues. Section 510(h) of the act (21 U.S.C. 360(h)) requires that FDA inspect licensed medicated feed mills at least once every 2 years. During such inspections, we can ensure that medicated feed mills manufacturing liquid medicated feeds with proprietary formulas and/or specifications have the approved formula and/or specifications. For this reason, we tentatively conclude that it is necessary for FDA to maintain greater regulatory oversight over facilities manufacturing liquid medicated feeds with proprietary formulas and/or specifications, and we are proposing that they must have an approved medicated feed mill license. The proposed rule also requires that facilities manufacturing liquid medicated feeds containing Category II drugs have an approved feed mill license because of the potential for unsafe residues associated with Category II drugs (§ 558.3(b)(1)(ii)).

We are proposing to exempt from the feed mill license requirement facilities manufacturing liquid feeds containing a Category I drug with a published formula and/or specifications. Given the reduced risk of unsafe residues from a Category I drug and the assurance that medicated feed mills have the information necessary to manufacture the liquid medicated feed where the formula and/or specifications are published, we believe this exemption is consistent with public health, as required by section 512(m)(6) of the act (21 U.S.C. 360b(m)(6)).

C. Description of the Proposed § 558.5

The proposed rule: (1) Replaces the references to "medicated feed application" in the current rule with the term "medicated feed mill license"; (2) defines the types of liquid medicated feed covered by this regulation; (3) clarifies the types of approvals required for liquid medicated feed; (4) explains that an approval is required for a drug intended for use in a liquid feed and