DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

(4)

November 2, 1989

Dear Sir or Madam:

This is the fourth in a series of policy letters regarding the implementation of the Generic Animal Drug and Patent Term Restoration Act (GADPTRA), which was signed into law on November 16, 1988.

We are introducing three policy statements (refer to attachment) which address our continuing implementation of the new law . The policy statements are entitled as follows:

1) "Actions Concerning ANADAs When a Pioneer Drug Has Been Withdrawn from Sale"

2) "Effect of GADPTRA on Approval of Pre-62 Drugs Under the DESI Program"

3) "Generic Feed Use Combination Drugs (Type A Article, Type B or Type C Medicated Feeds)"

We welcome comments and questions on the policy statements from all interested parties. If any changes are made, the revised policy statements will be placed on public display, and a notice of availability will be published in the Federal Register.

Comments on the draft policy statements may be addressed to:

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Generic Animal Drug and Patent Term Restoration Act (GADPTRA)
Draft Policy Statements

1) Actions Concerning ANADAs When a Pioneer Drug Has Been Withdrawn from Sale

Section 512(c)(2)(G) of the Act provides that the approval of an abbreviated new animal drug application (ANADA) is to be suspended if the ANADA refers to a drug which has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale was not for safety or effectiveness reasons. Section 512(n)(4)(C) provides that a pioneer drug may not be listed if the Secretary determines that the drug has been withdrawn from sale for safety or effectiveness reasons. If the listed drug is withdrawn from sale subsequent to the listing, the drug is to be removed from the list until either its sale resumes, or the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

Thus the Food and Drug Administration (FDA) is required, in several circumstances, to determine whether the discontinued marketing of a drug covered by a new animal drug application (NADA) was for safety or effectiveness reasons. Pending the adoption of its own regulations, the Center for Veterinary Medicine (CVM) intends to follow generally the principles and procedures that are contained in the regulations that FDA has proposed for the implementation of the human drug generic law. See 54 Fed. Reg. 28872 (July 10, 1989), in particular proposed 21 CFR 314.153 and 314.161, and the discussion at 54 Fed. Reg. at 28907-08. Among other things, the proposal provides for the deferral of the safety and effectiveness determinations until the time that the determinations are actually needed as determined by certain "triggering" circumstances (e.g. the submission of an ANADA that references the drug).

CVM has also decided to provide guidance as to one particular situation that is not specifically addressed by the July 10 proposal. This is the circumstance in which (a) a sponsor of a listed NADA voluntarily requests withdrawal of the approval of its NADA, after having discontinued marketing of the drug, and (b) the safety and effectiveness determination has not yet been made. In that case, the request to withdraw approval will not, per se, be a triggering circumstance. That is, the Center will withdraw approval of the drug but will defer the safety or effectiveness determination until such time as a triggering circumstance does occur. (However, if an approved

ANADA references the particular pioneer drug, the safety and effectiveness determination will be made at that time). In the meantime, the pioneer drug will remain a listed drug, although it will be placed on a separately identified list. CVM believes that it is permissible to continue to list the drug, even though its approval is withdrawn, because the act provides that a listed drug is to be delisted only when the approval is withdrawn on the grounds stated in 512(e). A voluntary withdrawal of approval based only on discontinuance of sale is not based on section 512(e).

CVM has, in supplements to the original list published in accordance with section 512(n)(4), removed from the list NADAs whose approvals have been voluntarily withdrawn since the list was first published. Because safety and effectiveness determinations have not been made as to these NADAs, the NADAs will be restored to the list. However, as explained in the previous paragraph, they will be placed in a separate category along with the NADAs whose approvals are voluntarily withdrawn in the future.

Finally, ANADA sponsors should be aware that the list that the Center originally published included all NADAs that had been approved for safety and effectiveness as of the effective date of the GADPTRA, including those whose marketing had been discontinued but whose approval had not been withdrawn. Although the NADAs in the latter category (along with NADAs for drugs whose marketing has been discontinued since the effective date of the GADPTRA) are not separately identified, ANADAs that reference those NADAs will not be approved until CVM determines that the marketing was not discontinued for safety and effectiveness reasons. Accordingly, ANADA sponsors are cautioned of the need to inquire, in cases where there is doubt as to whether marketing of a drug they wish to reference has been discontinued, to determine whether in fact marketing has been stopped. (As time and resources permit, CVM will identify those drugs that are on the list whose marketing has been discontinued.) In addition, as explained in the July 10 human drug proposal, ANADA sponsors will bear the burden of establishing that marketing of a discontinued drug was not stopped for safety or effectiveness reasons.

2) Effect of GADPTRA on Approval of Pre-62 Drugs Under the DESI Program

The Generic Animal Drug and Patent Term Restoration Act (GADPTRA) provides for the generic copying of pioneer animal drugs that have been approved for safety and effectiveness by FDA. The new law, therefore, covers drugs that were approved for safety by FDA prior to 1962, and subsequently approved for effectiveness under the Drug Effectiveness Study Implementation (DESI). FDA has approved generic copies of such drugs, under the DESI program, for a number of years. Requirements and procedures for approval of generic drugs under the DESI program differ in some respects from those for approval of generic drugs under GADPTRA.

Under GADPTRA, FDA is not permitted to approve abbreviated new animal drug applications (ANADAs) for generic animal drugs until January 1, 1991. In passing GADPTRA, Congress did not revoke the authority for FDA to approve generic copies of pre-62 drugs under the DESI program. It is clearly not the intention of the agency to have two separate policies for the approval of generic animal drugs, once generic drugs can be approved under GADPTRA. However, the Center for Veterinary Medicine (CVM) will in the interim continue to process and approve generic drugs under the DESI program subject to the following provisions:

- CVM will not accept a DESI application unless it believes that is likely that the application can be approved prior to January 1, 1991.

- Generic equivalents of pre-62 drugs will not be approved under the DESI program after December 31, 1990, but will be approved under GADPTRA after that date. However, the foregoing statement will not apply to a DESI application that is pending on that date, provided that the sponsor has exercised due diligence in pursuing the approval and continues to do so. In such a case, the application will be approved as a DESI application.

- The Center's current bioequivalence guidelines will be applied to all pending and future DESI applications, unless commitments have already been made for different bioequivalence requirements.

3) Generic Feed Use Combination Drugs (Type A Article, Type B or Type C Medicated Feeds)

Following the approval of an abbreviated new animal drug application (ANADA) for a generic Type A Article, the generic sponsor is entitled to approval for all of the combination products (Type B or Type C Medicated Feeds), for which the pioneer product is approved. Bioequivalency and tissue residue studies are not required for the approval of the generic feed use combinations (Type B or Type C Medicated Feeds). However, after the ANADA has been approved for the generic Type A Article, an ANADA must be submitted for each feed use combination product for which the generic sponsor seeks approval. The ANADA for each feed use combination should provide medicated feed labeling (Blue Bird labeling) which copies the pioneer medicated feed labeling, environmental assessment, and a Freedom of Information (FOI) Summary. The application should also identify the specific subsection of the CFR Section 500 that must be amended to include the generic drug sponsor on the list of approved sponsors for each feed use combination product.