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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

AUG 2 1989

Dear Sir or Madam:

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

As part of our continuing implementation of the new law, we are introducing five draft policy statements (refer to attachment) which are entitled as follows:

1) "Exclusivity for Human Food Safety Data Submitted in a Supplemental Application."

2) "Withdrawal Period for Generic Drugs."

3) "Substitution of an Active Ingredient in a Combination Drug or in a Feed Use Combination."

4) "Labeling Requirements for Generic Drugs."

5) "Can A Generic Animal Drug Sponsor Obtain Exclusivity for an Innovation Approved Under a Supplement to an ANADA and Can the Pioneer Drug Sponsor Copy the Generic Innovation Without Submitting Additional Data?"

The policy statements are issued as draft statements. Comments and questions regarding the statements are invited from all interested parties. If any changes are made, the revised draft 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:
Dr. Richard B. Talbot
Office of New Animal Drug Evaluation
Center for Veterinary Medicine
5600 Fishers Lane
Rockville, MD 20857
(301) 443-4313

Additional policy statements will be forthcoming as we continue the development of our policies regarding the new law.

Sincerely yours,

Gerald B. Guest

Gerald B. Guest, DVM
Director, Center for
Veterinary Medicine

Attachment

AUG 2 1989

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

1) Exclusivity for Human Food Safety Data Submitted in a Supplemental Application

GADPTRA (the new law) provides that a sponsor of an approved NADA obtains exclusivity for a change approved in a supplement if that sponsor submitted human food safety studies other than bioequivalence or residue studies in support of the change. However, the Center for Veterinary Medicine (CVM) believes that this provision does not apply in the case of human food safety studies submitted to obtain a different tolerance,* because a tolerance for a drug substance necessarily applies to all products containing that same drug substance. In such cases, a newly established tolerance will apply immediately to generic drug products as well as the pioneer drug product. If a new withdrawal time is established in connection with the establishment of a new tolerance, the sponsor will not obtain exclusivity for that new withdrawal time.

* CVM uses the term "tolerance" to include "safe concentration." Thus, where CVM establishes only a safe concentration and not a tolerance, the new safe concentration will apply immediately to generic drug products as well as the pioneer drug product.

2) Withdrawal Period for Generic Drugs

A generic sponsor will ordinarily be granted the same withdrawal period as the pioneer sponsor if bioequivalence, using blood level data, is demonstrated. However, even if bioequivalence is demonstrated using blood level data, a generic sponsor may still attempt to get a shorter withdrawal period than that granted to the pioneer sponsor. The shorter withdrawal period shall be granted if appropriate tissue depletion data, using methods of statistical analysis and interpretation described in the guidelines entitled "General Principles for Evaluating the Safety of Compounds used in Food-Producing Animals" justify a shorter withdrawal period.

If bioequivalence is demonstrated using pharmacological or clinical endpoint studies, then the generic sponsor must ordinarily collect tissue residue depletion data to establish the appropriate withdrawal period. The withdrawal period established in this manner need not be the same as the withdrawal period for the pioneer drug.

This policy will apply to all generic applications, whether or not the data and information that supports the pioneer approval meets current standards. As long as the pioneer drug is eligible for listing under the new law, the pioneer drug is considered to be safe and effective regardless of the adequacy of the underlying data in the NADA.

3) Substitution of an Active Ingredient in a Combination Drug or in a Feed Use Combination

The new law allows a generic sponsor to request substitution, under certain circumstances, of an active ingredient in a combination drug (or in a feed-mixed combination) with another active ingredient. The generic sponsor must submit to CVM a suitability petition requesting permission to file an ANADA with the proposed change from the pioneer drug. If CVM approves the petition, the generic sponsor must — in lieu of submitting bioequivalence information — show that the substituted active ingredient is of the same pharmacological or therapeutic class as the active ingredient for which it is substituted, and that the generic drug can be expected to have the same therapeutic effect as the pioneer.

CVM is required to disapprove the suitability petition if it finds that the generic sponsor must conduct investigations to show the effectiveness, safety to the animal, or safety for human consumption of the proposed combination. ("Investigations" do not include bioequivalence or residue depletion studies.) Although each petition will be examined on its individual merits, CVM has concluded that such investigations must ordinarily be conducted unless there are clearly no concerns that the proposed substitution will adversely affect the combination's effectiveness, target animal safety, and human food safety.

4) Labeling Requirements for Generic Drugs

The new law requires the labeling of a generic drug product to be the same as the pioneer's labeling, except for changes resulting from an approved suitability petition, differences in withdrawal periods, or differences in the manufacturers distributing or producing the products. In addition, labeling differences may be required because of patent or exclusivity provisions that apply to the pioneer product.

CVM will require that the labeling of a generic drug product be the same as the labeling of the pioneer drug product, except for the differences listed above. This means, for example, that the generic drug must be labeled for all the species and claims for which the pioneer is labeled (minus species and claims covered by patent or exclusivity protection).

5) Can a Generic Animal Drug Sponsor Obtain Exclusivity for an Innovation Approved Under a Supplement To an ANADA and Can the Pioneer Drug Sponsor Copy the Generic Innovation Without Submitting Additional Data?

CVM has considered whether the exclusivity provisions in the new law can be applied to innovations in the generic animal drug product approved under a supplement to an ANADA, and whether the pioneer drug sponsor can copy the generic innovation without submitting additional data.

The issue of exclusivity for a generic drug product may arise if the generic sponsor wishes to obtain approval under a supplement for a different dosage form, strength, route of administration or active ingredient, for which a suitability petition can not be approved because studies are necessary for approval of the innovations. Similarly, the generic sponsor may file a supplement to an ANADA to obtain approval for claims or species which differ from those of the pioneer product.

The position can be taken that the new law does not provide for the generic product to obtain exclusivity for an innovation, and the pioneer can not copy a generic innovation without the pioneer submitting its own data. Under Section 512(c)(2)(F), exclusivity specifically applies only to applications filed under Section 512(b)(1) [i.e. NADAs as distinguished from ANADAs filed under Section 512(b)(2) of the new law]. With respect to copying, it could be argued that a pioneer sponsor can not copy a generic innovation on the grounds that a generic drug is not a "listed" drug under Section 512(n)(4) because it has not been approved for safety and effectiveness. Under that section, only drugs that have been so approved may be listed, and only listed drugs may be copied.

However, CVM has tentatively decided to adopt interpretations of the new law which would provide exclusivity for innovation by the generic sponsor, and which would permit the pioneer sponsor to copy a generic innovation without submission of additional data. CVM believes that these interpretations would meet important goals of the generic legislation: to avoid duplicative research, to provide incentive for generic sponsors to innovate, and to make the conditions of use of the pioneer and generic drugs the same to the maximum extent possible. Because the generic sponsor would submit safety and effectiveness data to support the proposed innovation, the supplemental application would be considered to have been filed under section 512(b)(1), thus making it eligible for exclusivity. Morever, the generic drug would be considered to be "approved for safety and effectiveness," both on the basis of its having been shown to be bioequivalent to a drug that has been approved as safe and effective, and because of the safety and effectiveness data submitted to support the innovation. Thus, the generic drug would be a "listed" drug, eligible for copying.

Because the generic law does not definitively resolve these issues, CVM will consider comments from interested parties before deciding whether to adopt finally its tentative position on the issues.