

SUPPORTING STATEMENT

EXTRA-LABEL DRUG USE IN ANIMALS

A. JUSTIFICATION

1. Circumstances Making the Information Collection Necessary.

The Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA), (Pub. L. 103 - 396), amended the Food, Drug and Cosmetic Act ( the Act), to permit licensed veterinarians to prescribe extralabel use in animals of approved human and animal drugs. Regulations implementing provisions of AMDUCA are codified under 21 CFR Part 530. Section 21 CFR 530.22(b) permits FDA to establish a safe level for extralabel use of an approved new drug or new animal drug when we find there is a reasonable probability that an extralabel use may present a risk to the public health. When establishing a safe level, we may require the development of an acceptable analytical method for the quantification of drug residues. The sponsor may be willing to provide the methodology for residue detection in some cases, while in others, FDA, the sponsor, USDA, States or a consortium of interested parties may negotiate a cooperative arrangement to develop methodology. Conceivably a third party, who might submit such data could include a distributor or group of distributors who wish to make the drug available.

We request OMB approval for information collection required by the following citation:

21 CFR 530.22(b) - Reporting - Reporting requirement for development and submission of acceptable analytical methodology for drug residue quantification above any safe level established.

2. Purpose and Use of the Information

The analytical method developed would be used by FDA and other State and Federal agencies to assure the safety of the food supply when drugs are used in an extralabel manner.

3. Use of Information Technology and Burden Reduction.

The regulation does not specifically prescribe the use of automated, electronic, mechanical or other technological techniques. Firms are free to use whatever forms of information technology may best assist them in development and submission of acceptable analytical methodology for drug residue quantification above any safe level established.

#### 4. Efforts to Identify Duplication and Use of Similar Information

This collection requires development and submission of an acceptable analytical methodology for drug residue quantification when such methodology is not available. By definition, no similar data/information exists.

#### 5. Impact on Small Business or Other Small Entities

The proposed collection of information carries the same burden for small or large firms. The law and corresponding regulations governing methodology development must be applied consistently and equally to all enterprises. While we cannot establish different standards with respect to statutory requirements, we do provide special help to small businesses. A small business coordinator has been established on the Commissioner's staff to ensure that small businesses have an adequate opportunity to express their concerns and to keep our management apprised of how its regulatory decisions may impact the small business community. Furthermore, we encourage sponsors, whether small or large businesses, to meet with The Center for Veterinary Medicine to discuss development and submission of the required residue methodology.

#### 6. Consequences of Collecting the Information Less Frequently.

If the information is not reported, we may not be able to determine the risk to public health of an extralabel use of a drug. If we find that an extralabel animal drug use presents a risk to public health, and no analytical method has been developed and submitted, the agency may prohibit such extralabel use.

#### 7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

All of the reporting requirements are consistent with 5 CFR 1320.5

#### 8. Efforts to Obtain Comments on the Information Collection Before Submission to

## OMB.

In the Federal Register of March 1, 1999, (64 F.R. 10002), the agency requested comments on the proposed collection of information. In response, FDA received one comment, which included several parts with questions. The comments and questions are listed below with the agency's responses:

The comment asked: "How will FDA determine a safe level?" As stated in the preamble to the final rule, the agency may establish a finite safe level based on all relevant scientific information, (61 F.R. 57731, 57741).

The comment asked: "What will they use?" As stated in the rule, the agency may establish a safe level based on the lowest level that can be measured by a practical analytical method; or establish a safe level based on other appropriate scientific technical or regulatory criteria.

The comment asked: "If data [is] not in the approved information or in [the] general domain, then how will they collect it and who will pay for it?" As stated in the preamble to the final rule, (61 F.R. 57731), the sponsor may be willing to provide the methodology for residue detection in some cases, while in others, FDA, the sponsor, USDA, States, or a consortium of interested parties may negotiate a cooperative arrangement to develop methodology. Conceivably, a third party who might submit such data could include a distributor or group of distributors who wish to make the drug available for extralabel use.

The comment asked: "Will they force [a] company to collect the data to establish a safe level?" FDA has no authority under AMDUCA or its implementing regulations to require a sponsor or any other person to collect data to establish a safe level for extralabel use if the sponsor or other person is not willing to do so. If the agency determines that an extralabel use in animals of a particular human drug or animal drug presents a risk to the public health, or if no required acceptable analytical method has been developed, the agency would be permitted to prohibit extralabel use of the drug.

The comment asked: "How much data will they demand to be collected?" The nature and extent of data necessary to establish a safe level or to develop an analytical method will be determined on a case-by-case basis

The comment asked: "Will this rule apply to old approved drugs or just new approvals?" This rule applies to the extralabel use in animals of currently approved new animal and human drugs and new approvals of human and new animal drugs.

The comment asked: "Who pays to have the analytical method developed?" As stated above, the sponsor may be willing to provide the methodology for assay of residue in some cases, while in others, FDA, the sponsor, USDA, States, or a consortium of interested parties may negotiate a cooperative arrangement to development the methodology. Conceivably, a third party who might submit such data could include a distributor or group of distributors who wish to make a drug available for extra label use.

The comment asked: “To what extent will it have to be validated and how many tissues will it have to be validated for?” As stated in the preamble to the final rule, methods validation is anticipated to be necessary. The number of tissues for which method validation might be required would be determined on a case-by-case basis.

The comment asked: “ If [there are] multiple approvals of [the] same active [ingredient], will they force all manufacturers to do the same work because of a different salt? If not, how will they decide who does the work?” As was stated in the preamble to the final rule, the sponsor may be willing to provide the methodology for residue detection in some case, while in others, FDA, the sponsor, States, USDA, or a consortium of interested parties could negotiate a cooperative arrangement to develop the methodology. The third party could conceivably include a group of drug sponsors who might cooperatively submit data on behalf of all drugs with a particular active drug ingredient.

The comment asked: “What will they do to generic approvals? Force the originator to pay?” FDA does not contemplate requiring a sponsor or any other person to collect data to establish a safe level for extralabel use if the sponsor or other person is not willing to do so. If the agency determines that an extralabel use in animals of a particular human drug or animal drug presents a risk to the public health, or if no required acceptable analytical method has been developed, the agency would be permitted to prohibit extralabel use of the drug.

The comment asked: "If it is FDA's plan to demand this data for all existing drug[s] that might be used in food animals, please announce your intentions." FDA has no plan to require the submission of data for extralabel use for all existing drugs that might be used in food-producing animals. None of these comments had an impact on the proposed burden estimate.

## 9. Explanation of Any Payment or Gift to Respondent

There are no payments or gifts to respondents.

## 10. Assurance of Confidentiality Provided to Respondent

Information will be kept confidential in accordance with 18 U.S.C. 1905 and 21 U.S.C. 331(j), as well as section 301 (j) of the Act

## 11. Justification for Sensitive Questions

This information does not contain questions pertaining to sex behavior, attitude, religious beliefs, or any other matter commonly considered private or of a sensitive nature.

## 12. Estimates of Hour Burden Including Annualized Hourly Costs

This information collection requires reporting of an analytical method for residue detection of an extralabel use in animals of an approved animal or human drug. In the three years since the regulation requiring this information collection was finalized, we have not found circumstance to require the establishment of a safe level and subsequent development of analytical methodology. However, as we stated when the regulation was proposed on May 17, 1996, we believe that there will be instances when analytical methodology will be required. Thus, we will continue to estimate burden based on the possibility of requiring development and submission of methodology for up to two drugs per year. Estimated burden remains as in the 1996 proposal and is as follows:

Estimated Annual Reporting Burden					
21 CFR	No. of Respondents	No. Of Responses per Respondent	Total Annual Responses	Hours per Response	Total Hours
530.22(b)	2	1	2	4,160	8,320
TOTAL HOURS					8,320

## 13. Estimate of Other Total Cost Burden to Respondents and Recordkeepers

Total annual cost burden is included in the preceding paragraph. There are no additional costs to respondents.

## 14. Annualized Cost to the Federal Government

For the same reasons expressed in paragraph 12 above, estimates will be the same as those in the proposal of May 17, 1996, as follows:

The estimate incorporates the review of the method and does not include costs involved should FDA participate in method development. Burden from any FDA participation would be captured in paragraph 12.

Estimated total number of hours per year per method.....160  
Estimated number of analytical methods developed each year.....2  
Estimated number of hours for record review.....320  
Estimated total cost for review of methodology.....\$9,600\*

\* (320 hours x \$30/hour for review by mid-grade GS-13)

15. Explanation of Program Changes or Adjustments

There are no changes or adjustments to previous burden estimates.

16. Plans for Tabulation and Publication and Project Time Schedule.

Information is not to be published for statistical use.