

## SUPPORTING STATEMENT

### SUBSTANTIAL EVIDENCE OF EFFECTIVENESS OF NEW ANIMAL DRUGS

#### A. JUSTIFICATION

##### 1. Circumstances Making the Information Collection Necessary

Sections 512(a)(1) and (2) of the Federal Food, Drug, and Cosmetic Act (the act) state that a new animal drug, or an animal feed bearing or containing a new animal drug, is unsafe unless it is the subject of an approved new animal drug application (NADA). Approval of an NADA requires, among other things, a demonstration of the effectiveness of a new animal drug by “substantial evidence” derived from adequate and well controlled studies to establish the drug’s effectiveness.

On October 9, 1996, Congress enacted the Animal Drug Availability Act (ADAA) (Pub. L. 104-250). The purpose of the ADAA is to ease the approval and marketing of new animal drugs and medicated feeds. To facilitate this, section 2(a) of the ADAA amended section 512(d)(3) of the act to revise the definition of “substantial evidence.” Section 2(e) of the ADAA directed FDA to issue proposed regulations to further define the term “substantial evidence” in a manner that encourages the submission of NADA’s and supplemental NADA’s. Section 2(e) also directed FDA to issue regulations to encourage dose range labeling. A final rule

accomplishing this was published in the July 28, 1999 **Federal Register** (64 FR 40746).

We are requesting OMB approval for the following collection of information requirements

**21 CFR 514.4a, Reporting** -- Specifies requirements for submitting adequate and well-controlled studies to provide substantial evidence of effectiveness for a new animal drug..

**2. Purpose and Use of the Information**

The act requires us to issue an order refusing to approve a New Animal Drug Application (NADA), if there is a lack of substantial evidence that a new animal drug will have the effect it is purported or represented to have under the conditions of use prescribed in the proposed labeling. Therefore, substantial evidence must be submitted to the FDA as part of the NADA to establish effectiveness of a drug.

**3. Use of Information Technology and Burden Reduction**

We are continuously seeking ways through advances in information technology to reduce the burden on the government and sponsor. We recently published guidance on the electronic submission of information relating to “substantial evidence”. The guidance deals with submission of information, a request for a meeting with the FDA, and notices advising us of disposition of

test animals. This should increase the efficiency of industry as well as the review process.

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

There are no other regulations or Federal Agencies that require the submission of the same type information. There are no similar data/information that could be substituted for that required by these regulations.

#### **5. Impact on Small Businesses or Other Small Entities**

Our charge to approve only those new animal drugs that have been demonstrated to be effective applies whether small and large businesses sponsor drug studies. To support an NADA, we believe that the law and corresponding regulations 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 the development of evidence of safety and effectiveness to support approval of an NADA.

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

There are no specific regulatory time frames imposed on a sponsor for the

collection or recording of information. After the initial submission of an application, the sponsor can submit any required information whenever the sponsor sees fit.

**7. Special Circumstances relating to the Guidelines of 5 CFR 1320.5**

None of the information collection requirements are inconsistent with 5 CFR 1320.5.

**8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside Agency**

An advanced notice of proposed rulemaking (61 FR 59209, November 21, 1996) “New Animal Drugs for Investigational Use and New Animal Drug Application” solicited comment on our intent to propose revisions to regulations mandated by ADAA. Among them was a request for comment on the further definition of “substantial evidence.” No comments were received relative to paperwork issues. Several major drug firms and individuals were contacted in September, 1997, and asked to provide an estimate of the hour and dollar burden associated with the development of “substantial evidence” to support NADA approvals prior to enactment of the ADAA. In addition, in the **Federal Register** of August 16, 2000, (65 FR 49989), the FDA published a 60 day notice soliciting comment on the proposed extension of this collection of information. No comments were received on the estimated annual reporting burden.

**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 USC 1905 and 21 USC 331(j), as well as Section 301(j) of the Act.

**11. Justification for Sensitive Questions**

There are no questions or references pertaining to sex behavior, attitude, religious beliefs, or any other matters that are commonly considered private or sensitive in nature.

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

From consultation with several of the largest research and development (R&D), firms in 1997 and review of our data bases, we estimate that the 10 largest R&D firms are responsible for 90% of all “substantial evidence” expenditures. Data supplied by these firms, indicates an annual average of 86 studies by each firm with an average of 632.6 hours expended for each study, at an average cost of \$140 per hour. This results in an annual hourly burden of 544,036 hours (10 firms X 86 studies X 632.6 hours). Cost is estimated at \$76,165,040 (544,036 hours X \$140/hour). This figure includes time spent from inception to completion of a study and submission to the FDA. To project this figure to a total burden on industry, we would need to include the additional estimated 10% of studies submitted annually by the remainder of firms conducting studies to demonstrate substantial evidence. However, since we estimate that under the proposed definition of “substantial evidence” the number of adequate and well-controlled studies necessary to demonstrate efficacy will be reduced by approximately 10%, the two

adjustments would essentially offset each other, leaving the total at \$76,165,040.

Respondents, while not all submit studies in any given year, total 190, the number of sponsors of approved applications listed in 21 CFR 510.600.

This burden estimate includes submission of new animal drug applications and supplemental new animal drug applications for single ingredient and combination new animal drugs. It also includes estimates for dose range labeling studies.

Estimated annual reporting burden<sup>1</sup>

21 CFR	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
21 CFR 514.4a	190	4.526	860	632.6	544,036

<sup>1</sup>There are no capital costs or operating and maintenance costs associated with this collection.

**13. Estimate of Other Total Annual Cost Burden To Respondents**

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

**14. Annualized Cost to the Federal Government**

Based on historical data and an estimated workload under the proposed definition of substantial evidence, we estimate that approximately 30.8 FTEs will be expended annually in discussion with sponsors and premarket review of effectiveness data. Number of FTEs per grade and grade

salary were weighted to calculate an average FTE salary of \$67,784. At a rate of \$67,784 per each of the 30.8 FTEs, total government cost would be \$2,087,747 annually (\$67,784 X 30.8).

**15. Explanation for Program Changes or Adjustments**

There are no program changes or adjustments. Burden remains similar to that reported in the final rule for this regulation published on July 28, 1999.

**16. Plans for Tabulation and Publication and Project Time Schedules**

There are no plans for tabulation and publication.

**17. Displaying of OMB Expiration Date**

The agency is not seeking to not display the expiration date for OMB approval of the information collection.

**18. Exception to the Certification Statement - Item 19**

There are no exceptions to the certification statement identified in Item 19. " Certification for Paperwork Reduction Act Submission," of OMB Form 83-I.