OMB Control Number 0910-0284
SUPPORTING STATEMENT

RECORDS AND REPORTS CONCERNING EXPERIENCE WITH APPROVED NEW ANIMAL DRUGS

A. JUSTIFICATION

1. Circumstances Making the Information Collection Necessary

Implementation of Section 512(l) of the Federal Food, Drug and Cosmetic Act and 21 CFR 514.80 requires applicants of approved new animal drug applications and abbreviated new animal drug applications to submit product/manufacturing defects, initial and follow-up reports for adverse drug experiences and lack of effectiveness of new animal drugs, increased frequency 15-day alert reports, periodic drug experience reports (annually or semi-annually in a specific format), and other reports (special drug experience reports, advertisement and promotional material submissions, and distributor statements.

This continuous monitoring of approved NADA`s affords the primary means by which FDA obtains information regarding potential problems in safety and effectiveness of marketed animal drugs and potential manufacturing problems. Current data on file with FDA is not adequate because animal drug effects can change over time, and less apparent effects may take years to manifest themselves.

Adverse reaction reports are required to be submitted by the drug manufacturer on FDA Forms 1932 or 1932a (voluntary reporting form), following complaints from animal owners or veterinarians. Also, product defects and lack of effectiveness complaints are submitted to FDA by the drug manufacturer following their own detection of a problem or complaints from product users or their veterinarians using FDA forms 1932 and 1932a. Form FDA 2301 is used to submit the required transmittal of periodic reports and promotional material for new animal drugs.

The specific citations within 21 CFR Part 514 regarding information collection requirements for which we request OMB approval are:

21 CFR 514.80 (e) Recordkeeping.

Cites requirements that an applicant and nonapplicant establish and maintain records and files containing full records of information pertinent to the safety or effectiveness of a new animal drug that have not been previously submitted as part of the application.

21 CFR 514.80(b)(1) Reporting.

Specifies information to be submitted product defect/manufacturing defect that may result in serious adverse drug events are to be reported within 3 working days of first becoming aware

that a defect may exist. Product defect/manufacturing defects is the deviation of a distributed product from the standards specified in the approved application. Specifies information to be submitted concerning significant chemical, physical or other change, or deterioration of the product; product contamination; a mix-up in a drug or its labeling; defective packaging; damage from disaster; or failure of a drug to meet established specifications.

21 CFR 514.80(b)(2)(i) Reporting.

Specifies requirements for submitting initial reports of serious adverse drug events and unexpected adverse drug events that include but are not limited to adverse events occurring in animals, failure of a new animal drug to produce its expected pharmacological properties or clinical effect (lack of effectiveness), and an adverse event occurring in humans from exposure to a new animal drug are to be reported within 15 working days of first receiving the information.

21 CFR 514.80(b)(2)(ii) Reporting.

Specifies requirements for submitting follow-up reports to the initial report of serious adverse drug events and unexpected adverse drug events.

21 CFR 514.80(b)(2)(iii) Reporting.

Specifies requirements for periodically reviewing the incidence of reports of adverse drug experiences to determine an increase in frequency of serious (expected and unexpected) adverse drug events. Specifies the information and format to be submitted.

21 CFR 514.80(b)(3) Reporting.

Specifies requirements by nonapplicants to forward reports of adverse drug events to the applicant within 3 working days of first receiving the information. Nonapplicants may also elect to submit reports directly to FDA within 15 working days of first receiving the information.

21 CFR 514.80(b)(4) Reporting

Specifies requirements for submitting 6 month periodic drug experience reports for first two years following approval and then yearly thereafter. Specifies for yearly drug experience reports that applicants my petition FDA to change the date of reporting and(or) the frequency of reporting. Specifies requirements for submitting distribution data for each new animal drug product for quantities distributed domestically and quantities exported; applicant and distributor current package labeling; Nonclinical laboratory studies and clinical data not previously submitted; and adverse drug experiences not previously submitted in the periodic drug experience reports.

21 CFR 514.80(b)(5)(i) Reporting

Specifies requirements for submitting special drug experience reports at different times or more frequently from those stated in 21 CFR 514.80.

21 CFR 514.80(b)(5)(ii) Reporting

Specifies requirements for submitting advertisements and promotional labeling.

21 CFR 514.80(b)(5)(iii) Reporting

Specifies requirements for submitting distributor statements.

FDA is also requesting approval of the following forms:

Form FDA - 1932, Veterinary Adverse Drug Reaction, Lack of Effectiveness or Product Defect Report

Form FDA 1932a, Veterinary Adverse Reaction, Lack of Effectiveness

or Product Defect Report (Voluntary).

Form FDA-2301, Transmittal of Periodic Reports and Promotional Material for New Animal Drugs

2. Purpose and Use of the Information

The information obtained for 21 CFR 514.80(b)(1) on product and manufacturing defects may originate from an owner of an animal, a veterinarian, a nonapplicant, or the applicant. The applicant is then required to report the episode to the Food and Drug Administration on the Form FDA 1932. Monitoring for product and manufacturing defects is an essential part of the FDA's regulatory mission. These product and manufacturing defect reports are used by CVM as a primary means of obtaining information regarding potential product and manufacturing problems with specific lots of marketed animal drug products. Reports from veterinarians and others are essential because there is no other effective way of obtaining this needed information. The reports are reviewed to identify any potential violation of the FD&C Act. If a violation of the FD&C Act appears to exist, the report is followed up with an assignment memorandum to the appropriate FDA field office requesting a limited inspection of the firm to gather more facts and needed evidence in support of a product recall or regulatory action such as seizure or injunction. Alternatively, when the drug is the subject of a new animal drug application (NADA) the sponsor may be asked to investigate the cause and effect of the product defect and supplement their NADA to provide for appropriate changes in the manufacturing control section of the NADA.

The information obtained for 21 CFR 514.80(b)(2) may originate from an owner of an animal, who registers a complaint with the applicant, who is then required to report the episode to the Food and Drug Administration on the Form FDA 1932. Alternatively, the information obtained for 21 CFR 514.80(b)(3) may originate from an owner of an animal, who registers a complaint with the nonapplicant, who registers a complaint with the applicant, who is then required to report the episode to the Food and Drug Administration on the FDA Form 1932. Further, the safety and effectiveness of monitoring activities involving drug products also relies on voluntary reports of suspected drug effects, or drug ineffectiveness complaints from practicing veterinarians or animal owners. These reports are usually submitted directly to FDA, Center for Veterinary Medicine, on Form FDA 1932a, a short, convenient, easily completed form. The product that is the subject of the complaint may be either an over-the-counter product (available to anyone), or it may be a prescription product (available only to or by order of a veterinarian). In either case, the name of the owner of the animal(s) is germane to the identification of the episode in order that a specific reaction not be counted twice. The safety and effectiveness of monitoring activities involving drug products also relies on voluntary reports of suspected drug effects, or drug ineffectiveness complaints from practicing veterinarians. The reports are reviewed by an FDA Veterinary Medical Officer to determine the probability that the drug caused the adverse effect, or that the drug was ineffective. After the individual report is reviewed, it is added to Division of Surveillance's Adverse Drug Experience (ADE) computer database file containing other previously reported ADE data for that drug. Applicants are being required to periodically review their incidences of adverse drug experiences to determine to

determine if any changes in the specific product or labeling are needed. Careful evaluation sometimes leads to label or package insert changes, dosage changes, additional warnings or contraindications, product reformulation, or on rare occasions withdrawal of the approved new animal drug application.

The information obtained for 21 CFR 514.80(b)(4) may originate from a nonapplicant, who reports the information to the applicant, who is then required to reports to the Food and Drug Administration accompanied with Form FDA 2301. The applicant is required to submit reports every 6 months for the first two years following approval of an ANADA or NADA and yearly thereafter. The applicant must submit distribution data; labeling for both applicant and distributor; description of manufacturing and control changes; non-clinical laboratory studies and clinical data not previously reported, and adverse drug experiences not previously reported under 21 CFR 514.80(b)(1) and (b)(2). The applicant must report to the FDA of all reports of information from any source pertinent to the safety and effectiveness of the new animal drug for the purpose of determining whether there are ground for withdrawing or suspending approval. The information undergoes a full and comprehensive review by FDA scientists to evaluate the impact and significance of reported manufacturing and control changes, and non-clinical laboratory studies and clinical data on the safety and effectiveness of the product. Labeling is reviewed for accuracy of claims, directions for use and general compliance with the Act and regulations. Adverse drug experiences undergo the aforementioned review (21 CFR 514.80(b)(1) and (b)(2)). The distribution data is reviewed to determine eminency of product shortages, and availability for bioterrorism issues. Upon determination of a product shortage, a review of the distribution data for other products will indicate alternate therapeutic products to be used.

The information obtained for 21 CFR 514.80(b)(5)(ii) may originate from a nonapplicant, who reports the information to the applicant, who is then required to reports to the Food and Drug Administration accompanied by a completed Form FDA 2301. The applicant must submit mailing pieces and other labeling for prescription and over-the-counter new animal drugs at the time of initial dissemination. For prescription animal drugs, the applicant must submit advertisements at the time of initial publication or broadcast. The information is reviewed by Center Scientist for accuracy of claims, fair balance of safety and effectiveness information, and general compliance with the Act and regulations.

The information obtained for 21 CFR 514.80(b)(5)(iii) originates from a nonapplicant, who reports the information with the applicant, who is then required to reports to the Food and Drug Administration accompanied by a completed Form FDA 2301. The applicant must submit the current product labeling for both the applicant and distributor. Additionally, a signed statement from the distributor must be completed. The labeling for the applicant and distributor must be identical except for a different and suitable proprietary name, and the name and address of the distributor. The name and address of the distributor must be preceded by an appropriate qualifying phrase such as “manufactured for” or “distributed by” or as specified in other regulations. The labeling is for accuracy as mentioned above and for general compliance with the Act and regulations. The distributor states the following in distributor statement: 1) the category of their operation (e.g., wholesale or retail), 2) that they will distribute the new animal drug only under the approved labeling, 3) that they will

advertise the product only for use under the conditions stated in the approved labeling, 4) that they will adhere to the records and reports requirements of 21 CFR 514.80, and 5) that they are regularly and lawfully engaged in the distribution or dispensing of prescription products if the product is a prescription new animal drug.

If the collection of information were not conducted, there would be no continuous monitoring of the safety and effectiveness of marketed animal drugs. Data already on file with CVM is not adequate because new animal drugs are continually being approved, drug effects can change over time, and less apparent effects sometimes take a number of years to detect.

3. Use of Information Technology and Burden Reduction

Many of the applicants have automated systems for reports of adverse drug experiences to new animal drugs. The CVM has provided under 21 CFR 514.80(b) that applicants may computer generate Form FDA 1932 or Form FDA 2301. CVM is working domestically with the animal pharmaceutical industry and internationally under VICH to develop methods and standards for electronic submissions.

4. Efforts to Identify Duplication and Use of Similar Information

This information is not collected by any other Agency in the Government. The information collection required as a result of 21 CFR 514.80 does not duplicate any other information collection.

5. Impact on Small Business or Other Small Entities

Although new animal drug development is typically an activity completed by large drug firms, the information collection required under 21 CFR 514.80 applies to small as well as large companies. However, under the Regulatory Flexibility Act, CVM analyzes regulatory options that would minimize any significant impact on small entities. CVM will assists small businesses in complying with regulatory requirements. FDA will provide help to small firms through the Office of Small Manufacturers Assistance, if requested. This regulation is not expected to have a significant economic impact on these small entities since the final rule is intended to simplify and clarify current recordkeeping and reporting requirements.

6. Consequences of Collecting the Information Less Frequently

Part 514.80 establishes a reporting frequency that is dictated by the need to focus on potential problems concerning the safety and effectiveness of new animal drugs. Less frequent data collection would hinder early detection of such threats to the public health. New, unusual, and serious adverse experiences can suddenly begin to appear due to many reasons and under many circumstances. Also, when a new drug is approved, adverse reactions can appear at any time due to the large distribution of the drug as compared to its

use during the preapproval clinical trials.

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

The reporting requirements under 21 CFR 514.80(b)(1), (b)(2)(i)-(ii), (b)(3), and (e) are inconsistent with 5 CFR 1320.5. This section requires justification for requesting respondents to report more often than quarterly. Pursuant to 21 CFR 514.80(b)(1), the applicant is required to submit product and manufacturing defects that may result in serious adverse drug events are to be reported within 3 working days of first becoming aware that a defect may exist. Pursuant to 21 CFR 514.80(b)(2)(i)-(ii), the applicant is required to submit initial and follow-up reports within 15 working days. Pursuant to 21 CFR 514.80(b)(3), the nonapplicant required to report adverse drug experiences to the applicant within 3 working days of first receiving the information or if reported to FDA within 15 working days. This short time for reporting is necessary so that FDA is informed as soon as possible of any serious problems with a drug product, so that the agency can take appropriate action.

The maintenance period for keeping records is also inconsistent with 5 CFR 1320.6. Pursuant to 21 CFR 514.80(e), the applicant and nonapplicant must maintain records and reports of all information for a period of 5 years after the date of submission. This extended period is due to the potential of litigation, adverse drug experiences, long expiration dates, and needed for studies of delayed effects such as carcinogenicity.

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

In the **Federal Register** of May 19, 2006 [71 FR 29157], FDA published a 60 day notice requesting public comment on the information collection provisions. In response to this notice, FDA received seven comments, four of which required a response by CVM that are addressed as follows: One comment stated that FDAs estimate for the burden of the proposed collection of information seems unrealistic and inaccurate. The commenter proposed 16 hours of response time for Drug Experience Reports(DER), and 49 hours for recordkeeping for each DER. FDA agrees that 16 hours is a reasonable response time required to make a DER report. In view of increased reporting requirements under 21 CFR 514.80 (b) (4), CVM has increased the "Hours per Response" under this citation in “Table I – Estimated Annual Reporting Burden,” from 11 to 16 hours thereby increasing the total burden hours to 19,616. The commenter also proposed 49 hours response time per record for each DER. However, based on CVM` s experience and previous surveys of industry, the 49 hours of response per record for each DER is excessive. In view of increased requirements, under 21 CFR 514.80 (e)3 CVM has increased the "Hours per Record" under this citation in “Table II - Estimated Annual Recordkeeping Burden,” from 10.35 to 14 hours, thereby increasing the total burden hours to 33,320.

Another comment suggested that the burden collections may be potentially reduced by: (1) reducing submission requirements with established safety and (2) by automating the information collection system. FDA agrees with the commenter regarding both suggestions. Under 21 CFR 514.80 (b) (4), it states for yearly periodic DER reports, an applicant may

petition FDA to change the anniversary date and / or change the frequency of reporting. Regarding the comment suggesting automation of the information collection system, future burden estimates for collections of information will be considered when automated reporting requirements are implemented by FDA.

Another comment wanted to know the purpose for submitting a periodic report for a known event for a product with an established record. As previously stated, under 21 CFR 514.80 (b)(4), an applicant may petition FDA to change the anniversary date and / or change the frequency of reporting.

9. Explanation of Any Payment or Gifts to Respondents

There are no payments or gifts to respondents.

10. Assurance of Confidentiality Provided to Respondent

During working hours, only FDA employees have access to the computer files and database on a need to know basis. During duty and non-duty hours building security is provided through a contract with a private protection agency. None of these provisions bar the release of the confidential information if subpoenaed by a court of law. Confidentiality of the information submitted under these reporting requirements is protected under 21 CFR 514.11 and under 21 CFR part 20. The unauthorized use or disclosure of trade secrets required in applications is specifically prohibited under Section 310(j) of the Act. Further, under the terms of the Freedom of Information Act, the veterinarian's name, address, and phone number, and the owner's name, etc., reported on Form FDA 1932 cannot be made available to a public request.

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

Table - 1 ESTIMATED ANNUAL REPORTING BURDEN 1

21 CFR Section	FDA Form No.	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
514.80(b)(1)	1932	190	0.50	95	1	95
514.80(b)(2)(i)	1932	190	64.65	12,283	1	12,283
514.80(b)(2)(ii)	1932	190	31.62	6,007	1	6,007
514.80(b)(3)	1932	340	2.94	1,000	1	1,000
Voluntary reporting FDA Form for Public	1932a	250	1	250	1	250

21 CFR Section	FDA Form No.	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
514.80(b)(4)	2301	190	6.45	1,226	16	19,616
514.80(b)(5)(i)	2301	190	0.13	25	2	50
514.80(b)(5)(ii)	2301	190	4.06	772	2	1544
514.80(b)(5)(iii)	2301	530	0.11	56	2	112
Total Hours						40,957

[1]There are no capital costs or operating and maintenance costs associated with this collection of information.

TABLE 2 - ESTIMATED ANNUAL RECORDKEEPING BURDEN1, 2

21 CFR Section	No. of Recordkeepers	Annual Frequency per Recordkeeping	Total Annual Records	Hours per Record	Total Hours
514.80(e)[2]	530	36.58	19,385	0.5	9,693
514.80(e)[3]	530	4.49	2,380	14	33,320
Total					43,013

[1]There are no capital costs or operating and maintenance costs associated with this collection of information.

[2]Burden estimates were separated between Form FDA 1932 and Form FDA 2301 to reflect the difference in estimates for "Hours per Respondent" required.

[3]Recordkeeping estimates for 514.80(b)(1), 514.80(b)(2)(i), 514.80(b)(2)(ii), and 514.80(b)(3); Form FDA 1932.

[4]Recordkeeping estimates for 514.80(b)(2)(iii), 514.80(b)(4), 514.80(c), and 514.80(b)(5); Form FDA 2301.

Forms FDA 1932 and FDA 2301 for this collection of information are currently approved under OMB Control No. 0910-0284 (expiration date 12/31/06)and will be included in the implementation of this regulation. The reporting and recordkeeping burden estimates in for this document are based on the submission of reports to the Division of Surveillance, Center for Veterinary Medicine and comments to the May 19, 2006 sixty day notice in the **Federal Register** (71 FR 29157). The total annual response numbers are also based on the submission of reports to the Division of Surveillance, Center for Veterinary Medicine. The annual frequency of response was calculated as the total annual responses divided by the number of respondents.

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

CVM used a wage rate of $35.00 per hour, and multiplied times the total hour burden estimated above (69,493 hours), the total cost burden to respondents is $2,432,255 (69,493 hours X $35/hour).

14. Annualized Cost to the Federal Government

The CVM currently has 11 FTEs allocated for post marketing surveillance activities. If each FTE equals approximately $115,000, the total FTE burden to the Federal Government would be $1,265,000. The CVM currently contracts document processing, which costs $100,000 for the post marketing surveillance activities. The total cost burden to the Federal Government would be $1,365,000.

15. Explanation of Program Changes or Adjustments

The reporting and recordkeeping burdens for 514.80 have increased. The increase in the burden for submission of adverse drug reactions on Form FDA-1932, results from a greater awareness of the need for veterinarians and consumers to submit this information to the drug manufacturer; as well as new approvals. While there is an increase in the burden, the corresponding added information generated by the additional submissions greatly enhances the FDA's ability to assess safety and effectiveness of marketed drugs. Further, the increase in burden is due to the increasing number of applications and better burden estimates..

FDA added provisions in final § 514.80(b)(4) that allow applicants to petition FDA to change the date of submission of yearly periodic drug experience reports or the frequency of reporting to intervals greater than annually. This is intended to increase flexibility and to reduce the reporting burden for specific NADAs and ANADAs. Further, in view of increased reporting and recordkeeping requirements under this provision and as a result of comments received in response to the May 19, 2006 Federal register notice (71 FR 29157), there was also an increase (adjustment) in the burden estimate for this particular citation.

16. Plans for Tabulation and Publication and Project Time Schedule

Information is not to be published for statistical use