Supporting Statement for
Presubmission Conferences, New Animal Drug Applications (NADA) and Supporting Regulations, and Guidance 152 and Form FDA 356V
OMB #0910-0032

* Consolidating OMB #s 0910-0032, 0910-0555, 0910-0356, 0910-0522, and 0910-0600

A. JUSTIFICATION

1. Need and Legal Basis

Under section 512(b)(3) of the Federal Food, Drug and Cosmetic Act (the act), any person intending to file a New Animal Drug Application (NADA)or supplemental NADA or a request for an investigational exemption under section 512(j) of the act is entitled to one or more conferences with FDA to reach an agreement acceptable to FDA establishing a submission or investigational requirement. FDA and industry have found that these meetings increased the efficiency of the drug development and drug review processes.

Under section 512(b)(1) of the the act, any person may file an NADA seeking approval to legally market a new animal drug. Section 512(b)(1) sets forth the information required to be submitted in an NADA. FDA allows applicants to submit a complete NADA or to submit information in support of an NADA for phased review followed by submission of an administrative NADA when FDA finds all the applicable technical sections are complete.

In addition to an extension request, this submission is a consolidation of information collection activities, also approved under 21 CFR Part 500, that are associated with approval of new animal drugs. (see attachment I) To comply with this consolidation FDA revised the existing Form FDA 356 V for which OMB approval is also being requested. Further, the Animal Drug User Fee Act of 2003 (ADUFA) (P.L. 108 – 130), (21 U.S.C. 379J-11), amended the Federal Food and Drug Cosmetic Act (FD&C Act) and authorizes FDA to collect fees for certain establishments, products and sponsors. As a result of enactment of ADUFA legislation, and with better metrics with which to estimate paperwork burden, CVM recognized a significant decrease (program change(s)) in the burden estimates for each collections of information being consolidated, (see attachment I)

21 CFR 514.1 interprets section 512(b)(1) of the act and further describes the information that must be submitted as part of the NADA and the manner and form in which the NADA must be assembled and submitted. The application must include safety and effectiveness data, proposed labeling, product manufacturing information, and where necessary, complete information on food safety (including microbial food safety) and any methods used to determine residues of drug chemicals in edible tissue from food producing animals. Guidance 152 outlines a risk assessment approach for evaluating the microbial food safety of antimicrobial new animal drugs. FDA requests that an applicant accompany NADAs, supplemental NADAs, and requests for phased review of data to support NADAs, with the Form FDA 356V to ensure efficient and accurate processing of information to support new animal drug approval.

The Animal Drug Availability Act of 1996 required FDA to further define “substantial evidence” of effectiveness, and FDA further defined the term at 21 CFR 514.4.

21 CFR 514.8 describes the information that must be submitted as part of a supplemental application to support proposed changes to an approved NADA. An applicant may reference existing information from the NADA in the supplemental NADA, but must submit some subset of information required in §514.1 to support the proposed changes.

21 CFR 514.1 and 514.6 - Reporting

Specifies content and format of the New Animal Drug Application and amendment of a pending application.

21 CFR 514.8(c)(1) – reporting

Specifies the information that must be provided to FDA to support a supplemental application, which describes each change in each condition established in an approved application.

21 CFR 514.1(b)(8) and 514.8(c)(1) and guidance #152 – Reporting

Specifies information NADAs and supplements for antimicrobial animal drugs. Guidance #152 provides sponsors with a recommended approach to assessing antimicrobial concerns as part of the overall pre-approval safety evaluation.

21 CFR 514.4

Specifies definition of substantial evidence of effectiveness. (No burden hours associated with this definition).

21 CFR 514.5(b),(d) and (f) – Reporting

Specifies paperwork needed to request a presubmission conference, provide the advanced materials, and comment on the memorandum of conference.

21 CFR 514.8(b)

Specifies required information for supplements requesting approval of changes to manufacturing for an approved new animal drug.

21 CFR 514.8(c)(2) and (c)(3) – Reporting

Specifies paperwork an applicant submits to support supplemental applications seeking changes to approved labeling.

21 CFR 514.11 – Reporting

Specifies requirements for freedom of information summaries of information and data for an NADA. FDA generally takes responsibility for preparing the FOI Summary.

21 CFR 558.5(i) – Reporting

Specifies requirements for obtaining a waiver (filing a petition) from labeling requirements for certain drugs intended for use in animal feed or drinking water.

FDA is also requesting approval of the revised FDA Form 356V- New Animal Drug Application

2. Information Users

Required information to support a NADA or supplement NADA is accompanied by an FDA Form 356V – New Animal Drug Application. The information submitted is reviewed by professional personnel in the Center for Veterinary Medicine, in the FDA, including veterinarians, chemists, microbiologists, toxicologists, physiologists, pharmacologists, nutritionists, statisticians, consumer safety officers, and paid FDA consultants, as necessary, to determine if a new animal drug can be approved. In order to get approval of a new animal drug, the applicant must, among other things, demonstrate that the new animal drug is safe and effective for its intended uses.

3. Improved Information Technology

FDA accepts the submission of some data to support NADAs and supplements electronically.

4. Duplication of Similar Information

The information as provided in an application for approval of a new animal drug is unique to the particular product covered by the application. There are no other regulations that require the submission of this same information. The information is generally not available from any recognized scientific sources, unless the information has been made public by the NADA applicant.

5. Small Businesses

Because of the critical nature of the products, their uses and the impact on the consumer or user, any submission of an application for approval of a new animal drug from a small business concern is treated with the same rigorous scientific and technical review as that submitted by a large pharmaceutical firm. However, FDA does assist small businesses to meet the part 514 requirements through the Office of Small Manufacturers Association through the scientific and administrative staff within the Center.

6. Less Frequent Collection

There are no specific regulatory time frames imposed on an applicant for the collection or recording of information. After the initial submission of an application, the applicant can submit any required information as he/she sees fit or as may be imposed by the regulations under 21 CFR 514, 558, 211, 225, or 226.

7. Special Circumstances

There are no reports required to be submitted which are inconsistent with 5 CFR 1320.5.

8. Federal Register Notice/Outside Consultation

In accordance with 5 CFR 1320.8(d), on July 9, 2007, in Volume 72, No. 130, page 37240, a 60-day notice for public comment was published in the ***Federal Register*****.** One comment was received but it did not relate to the paperwork implications of the proposed information collection.

9. Payment/Gift to Respondent

There are no payments or gifts to respondents.

10. Confidentiality

Only FDA employees and contractors have access to the administrative files on a need to know basis during working hours. 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 or consistent with relevant disclosure laws. Confidentiality of the information submitted under these reporting requirements is protected under 21 CFR 514.11. The unauthorized use or disclosure of trade secrets required in applications is specifically prohibited under section 310(j) of the act.

11. Sensitive Questions

This information collection does not contain questions of a sensitive nature.

12. Burden Estimate (Total Hours and Wages)

Table 1 – NADAs - Estimated Annual Reporting Burden[1]

21 CFR Section/FDA FORM #	No. of Respondents	Annual Frequency per Responsent	Total Annual Responses	Hours per Response	Total Hours
514.5(b), (d), (f)	134	.7	93	50	4650
514.1 & 514.6	134	.1	19	212	4028
514.4	134	0	0	0	0
514.8(b)	134	3.2	425	35	14875
514.8(c)(1)	134	0.1	14	71	994
514.8(c)(2) & (3)	134	.4	53	20	1060
514.11	134	.1	19	1	19
558.5(i)	134	.01	1.0	5	5
514.1(b)(8) and 514.8(c)(1)[2]	134	.1	10	90	900
FDA FORM 356V	134	5.8	778	5	3890
TOTAL HOURS					30421

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

[2] New Animal Drug Applications and supplements regarding antimicrobial animal drugs that use a recommended approach to assessing antimicrobial concerns as part of the overall pre-approval safety evaluation.

Number of Respondents. Based on the number of sponsors subject to animal drug user fees, FDA estimates that there are 134 respondents. We use this estimate consistently throughout the table and calculate the "annual frequency per respondent" by dividing the total annual responses by number of respondents. Following is a description of how we estimated the total annual responses and calculated total paperwork burden hours by type of submission.

Presubmission Conferences (21 CFR 514.5). Over the past 5 fiscal years, from October 1, 2001 through September 30, 2006, FDA estimates it has conducted an average of 93 presubmission conferences per year. FDA estimates that preparing the paperwork to request the meeting, providing the advance materials, and commenting on the memorandum of conference will take approximately 50 hours. Thus, the total burden hours for presubmission conferences is estimated to be 4650 hours.

NADA (21 CFR 514.1 & 514.6). Over the past 5 fiscal years, FDA has received an average of 19 NADAs per year. FDA estimates that preparing the paperwork required for an NADA under 21 CFR 514.1, whether all of the information is submitted with the NADA or the applicant submits information for phased review followed by an Administrative NADA that references that information, will take approximately 212 hours. Thus, the total burden hours for the submission of an NADA with any amendments is estimated to be 4028 hours.

Substantial Evidence (21 CFR 514.4). Because 21 CFR 514.4 only defines substantial evidence, it should not be viewed as creating an additional collection burden. The collection of information to demonstrate substantial evidence occurs as part of an NADA under 21 CFR 514.1. There is no additional paperwork burden under 21 CFR 514.4.

Supplements fall into one of three categories:

- Manufacturing supplements described at 21 CFR 514.8(b);
- (b)(1) supplements (i.e., supplements seeking changes, other than in manufacturing or labeling, in an established condition of an approval beyond the variations already provided for in the approved application) described at 21 CFR 514.8(c)(1); and,
- labeling supplements described at 21 CFR 514.8(c)(2) & (3).

An applicant may rely on information and data already filed to support those aspects of the NADA for which there are no changes. Thus, an applicant submitting a supplement should only have to prepare supporting information for those aspects of the application for which there are changes and the paperwork burden will be a percentage of the burden of preparing an NADA.

Manufacturing Supplements (21 CFR 514.8(b)). Over the past 5 fiscal years, FDA has received an average of 425 manufacturing supplements annually. FDA estimates that it takes on average 35 hours (1/6 of the time it takes to prepare the paperwork to support a full NADA) to prepare the paperwork to support approval of manufacturing changes. This results in total of 14875 burden hours.

Supplements Seeking Approval of Changes in Intended Uses or Conditions of Use (21 CFR 514.8(c)(1)). Over the past 3 fiscal years, October 1, 2003 through September 2006, FDA has received an average of 14 supplements annually seeking approval for changes in intended uses or conditions of use. FDA used a three year average for this calculation because data for the previous two years for this category of supplements was not tracked as an independent number. FDA estimates that it takes an average of 71 hours (approximately 1/3 of the time it takes to prepare the paperwork to support a full NADA) to prepare the paperwork to support approval for such changes. This results in a total of 994 burden hours.

Labeling Supplements (21 CFR 514.8(c)(2) & (3)). Over the past 5 fiscal years, FDA has received an average of 53 labeling supplements annually. FDA estimates that it takes an average of 20 hours (approximately 1% of the time it takes to prepare the paperwork to support a full NADA) to prepare the paperwork to support approval of a labeling change. This results in a total of 1060 burden hours.

Freedom of Information Summary (21 CFR 514.11). Regulations, 21 CFR 514.11, require the preparation of a summary of the safety and effectiveness data and information submitted with or incorporated by reference in an approved NADA and that the summary be publicly released when the approval is published in the Federal Register. This summary, generally referred to as the Freedom of Information (FOI) Summary, may be prepared by FDA or FDA may require the applicant to prepare the summary. 21 CFR 514.11(e)(ii). In the past, FDA has required the applicant to prepare the FOI Summary. Currently, FDA generally takes responsibility for preparing the FOI Summary. Thus, the paperwork burden on applicants to prepare an FOI Summary has

significantly decreased. Based on the estimate of 19 NADAs received annually and an estimate that applicants now spend little or no time preparing the FOI summary, the estimated burden hours are 19 hours.

Requirements for Liquid Medicated Feeds (21 CFR 558.5(i)). Generally, specific labeling is required to make sure that certain drugs, approved for use in animal feed or drinking water but not in liquid medicated feed, are not diverted to use in liquid feeds. 21 CFR 558.5(i) permits an applicant to seek a waiver from this requirement (21 CFR 558.5(h)) if there is evidence that it is unlikely a new animal drug would be used in the manufacture of a liquid medicated feed. If FDA receives one NADA per year seeking approval of the use of a liquid medicated feed and on average it takes 5 hours to prepare the request for waiver, the estimated paperwork burden is 5 hours.

Risk Assessment of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern. (21 CFR 514.1(b)(8) and 514.8(c)(1)). FDA estimates that it receives 10 risk assessments evaluating the microbial food safety of antimicrobial new animal drugs per year. FDA estimates that it takes on average 90 hours to put together the references and other materials in the format recommended by guidance # 152 and to summarize the hazards and associated risk(s). Thus, the total burden hours for preparing such risk assessments for submission to FDA is estimated to be 900 hours.

Form FDA 356V. FDA requests that an applicant fill out and send in with NADAs and supplemental NADAs, and requests for phased review of data to support NADAs, a Form FDA 356V to ensure efficient and accurate processing of information to support new animal drug approval. Over the past 5 fiscal years, FDA has received an average of 511 NADAs and supplements and 267 submissions of data to support NADAs. FDA estimates that it takes an average of 5 hours to read the instructions and fill out Form FDA 356V and organize the information that it will accompany. This results in a total of 3890 burden hours.

The total annual estimated burden imposed by this collection of information is 30,421 hours annually. The hourly wage of a compliance officer employed by an animal drug sponsor is estimated to be approximately $38 per hour.[1] $38 times 30,421 equals $1,155,998.

13. Capital Costs (Maintenance of Capital Costs)

There are no capital costs or operating and maintenance costs associated with this collection.

14, Cost to Federal Government

For calendar year 2007, we expended approximately 186,000 person hours in review, support and supervisory support of the review of submissions. We estimate about 1650 hours of work is performed per FTE. So, about 112.7 FTEs are used for application review work. We estimate a compensation cost of $84,691 per FTE (Washington Metro Area pay scale), which is the salary of a GS13/3, the average grade among the personnel involved in the review. Multiplying this figure by 112.7 FTEs = $9,544,675 as the cost for one year of review work. The agency anticipates that

[1] 2006 National Industry-Specific Occupational Employment and Wage Estimates, US Department of Labor, Bureau of Labor Statistics (www.bls.gov/oes/current/naics4_325400.htm) $29.27 hourly wage plus 30% adjusted for benefits.

the review of a petition will require the services of a GS – 14 review scientist for 5 hours at an hourly wage of $44.96 per hour. The cost of the one time review would be $224.80.

15. Program or Burden Changes

Enactment of ADUFA has resulted in less respondents, 190 to 134. Implementation of better metrics has provided the Center with tools that more clearly when applied, reflect an better accurate estimate of the burden. The existing Form FDA 356 V overestimated burden hours by counting more than reading the instructions and filling out the form. The newly revised form FDA 356 V more closely follows the administrative process. As a result of the ADUFA legislation and the sequence of events for the additional requlatory initiatives by CVM , there has been a program change (decrease) for this consolidated collection of information of 955,487 hours ! (see attachment 1)

16. Publication and Tabulation Dates

Information is not to be published for statistical use.

17. Display of OMB Approval Date

FDA is not seeking approval of an exemption from displaying the expiration date for OMB approval

18. Exceptions to "Certification for Paperwork Reduction Act Submissions"

There are no exceptions to Item 19 of OMB Form 83-I.