OMB CONTROL #0910-0575
SUPPORTING STATEMENT

Waivers of *In Vivo* Demonstration of Bioequivalence of Animal Drugs in Soluble Powder Oral Dosage Form Products and Type A Medicated Articles

A. Justification

Abstract

1. Circumstances Making this Information Collection Necessary

The Center for Veterinary Medicine has written this guidance to address a perceived need for agency guidance in its work with the animal health industry. This guidance describes the procedures that the agency recommends for the review of requests for waiver of *in vivo* demonstration of bioequivalence for generic soluble powder oral dosage form products and Type A medicated articles.

The Generic Animal Drug and Patent Term Registration Act (GADPTRA) of 1988 (Pub. L. 100-670) permitted the generic drug manufacturers to copy those pioneer drug products that were no longer subject to patent or other marketing exclusivity protection. The approval for marketing these generic products is based, in part, upon a demonstration of bioequivalence between the generic product and the pioneer product. This guidance clarifies circumstances under which FDA believes the demonstration of bioequivalence required by the statute does not need to be established on the basis of *in vivo* studies for soluble powder oral dosage form products and Type A medicated articles. The data submitted in support of the waiver request are necessary to validate the waiver decision.

This information collection is not related to the American Recovery and Reinvestment Act of 1990.

2. Purpose and Use for the Information Collection

The respondents for this collection of information are pharmaceutical companies manufacturing animal drugs. The requirement to establish bioequivalence through *in vivo* studies may be waived for soluble powder oral dosage form products or Type A medicated articles in either of two ways. A biowaiver may be granted if it can be shown that the generic product contains the same active and inactive ingredient(s) and is produced using the same manufacturing processes as the approved comparator product or article. Alternatively, a biowaiver may be granted without direct comparison to the pioneer product's formulation and manufacturing process if it can be shown that the active pharmaceutical ingredients(s) (API) is the same as the pioneer product, is soluble, and that there are no ingredients in the formulation likely to cause adverse pharmacologic effects. For the purpose of evaluating soluble powder oral dosage form products and Type A medicated articles, solubility can be demonstrated in one of two ways: "USP definition" approach and "Dosage adjusted" approach.

The purpose of collecting information is to prove that *in vivo* studies are not necessary to establish the bioequivalence of the generic product. This is desirable because the pharmaceutical companies would save the funds otherwise expended on *in vivo* studies by providing the data requested.

3. Use of Improved Information Technology and Burden Reduction

As a part of the reauthorization of the Animal Drug User Fee Act (ADUFA) in 2008, CVM committed to developing an electronic submission tool for industry submissions within 24 months of appropriated ADUFA funds for FY 2009. The tool was made available by CVM's Office of New Animal Drug Evaluation (ONADE), for voluntary use by sponsors and manufacturers in the animal health industry, on March 11, 2011. The animal health industry may now use the eSubmitter, a secure online submission tool, for all submissions related to the new animal drug approval process. FDA eSubmitter is available at http://www.fda.gov/ForIndustry/FDAeSubmitter/default.htm.

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 by 21 CFR 514.1(b)(7) and (8) does not duplicate any other information collection.

5. Impact on Small Businesses or Other Small Entities

Some of the comments to the draft guidance indicated that this bioequivalence waiver process would reduce the regulatory burden on the animal drug industry. A large number of these drug companies are classified as small businesses.

6. Consequences of Collecting the Information Less Frequently

This information is collected only once in the generic animal drug approval process. If this data is not provided, the animal drug industry, which is largely composed of small businesses, would need to conduct costly *in vivo* animal drug testing to prove bioequivalence of the generic animal drug.

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

The information collection is consistent with 5 CFR 1320.5 and 5 CFR 1320.6.

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

In accordance with 5 CFR 1320.8(d), FDA published a 60-day notice in the Federal Register of October 24, 2011 (76 FR 65734) (vol.76, no. 205). FDA received one comment, which, however, did not address the questions posed in 60-day notice regarding the collection of information. The comment supported the bioequivalence program but suggested a revision to the determination of bioequivalence, which relates to the substance of the scientific recommendations in the guidance document. Under FDA's Good Guidance Practices regulations, 21 CFR 10.115(f)(4), the public may suggest at anytime that FDA revise a guidance document and under 21 CFR 10.115(g)(5), FDA will revise guidance documents in response to comments when appropriate.

9. Explanation of any Payment or Gift 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 databases on a need to know basis. During duty and non-duty hours building security is provided through a contract with a private protection agency.

FDA regulations (21 CFR 20.61) prohibit the agency from disclosing trade secrets and confidential commercial information. All information will be kept confidential in accordance with 18 USC 1905 and 21 USC 331(j). None of these provisions bar the release of the confidential information if disclosure is ordered by a court of law.

11. Justification for Sensitive Questions

This information collection does not contain questions pertaining to any matter commonly considered private or of a sensitive nature.

12. Burden Hours and Cost Associated with this Burden

The number of respondents and number of responses per response are based on the number of requests for waiver of *in vivo* demonstration of bioequivalence for generic soluble powder oral dosage form products the Agency has received in the past three years. The estimate of the average burden per response is based on Agency communication with industry.

Table 1. Estimated Annual Reporting Burden for Water Soluble Powders[1]

	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response (hr.)	Total Hours
Same formulation/ manufacturing process approach	1	2	2	5	10
Same API/ solubility approach	5	2	10	10	100
Total Burden Hours					110

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

The number of respondents and number of responses per response are based on the number of requests for waiver of *in vivo* demonstration of bioequivalence for generic Type A medicated articles the Agency has received in the past three years. The estimate of the average burden per response is based on Agency communication with industry.

Table 2. Estimated Annual Reporting Burden for Type A Medicated Articles[1]

	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Same formulation/ manufacturing process approach	2	2	4	5	20
Same API/ solubility approach	10	2	20	20	400
Total Burden Hours					420

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

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Respondent

			Costs
Animal drug industry compliance officer	530	$39[1]	$20,670

Table 3: Estimation of Annualized Hour Costs Burden

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

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

14. Annual Cost Estimate to FDA

The hourly review burden is about 4 hours per submission (18 submissions) or 72 hours overall. Adding overhead in the Document Control Unit for logging, delivering, tracking, etc. brings the total to about 5 hours per submission or 90 hours overall. Ninety hours is about .04 full time employee (FTE) and an average employee grade GS-13 FTE costs CVM about $100,000 per year (with benefits), so the annual cost in dollars to FDA is on the order of $4000 to process the projected 18 submissions.

15. Changes from Previous Approval

The hourly burden has not changed.

16. Publishing the Results of this Information Collection

The results of this information collection are not to be published.

17. Reason for Not Displaying the OMB approval date.

FDA will display the OMB approval date.

18. Exceptions to Section 19, "Certification for Paperwork Reduction Act Submissions"

There are no exceptions.

[1] Bureau of Labor Statistics, Occupational Employment and Wages, May 2010, 13-1041 Compliance Officers, @$30 + (30x.3) = -$39, includes 30% estimated benefits.