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

OMB Control No. 0910-0575

SUPPORTING STATEMENT

A. Justification

1. Circumstances Making the Collection of Information Necessary

The Center for Veterinary Medicine has written this guidance to describe 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 generic animal drug manufacturers to copy those pioneer animal 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 of 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 show 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. While only a small percentage of respondents avail themselves of this capability, CVM expects the number to grow.

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 animal drug companies are classified as small businesses.

6. Consequences of Collecting the Information Less Frequently

This information is collected only once during 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 show bioequivalence of the generic animal drug.

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

There are no special circumstances for this collection of information.

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

   In accordance with 5 CFR 1320.8(d), FDA published a 60-day notice in the Federal Register of January 12, 2015 (80 FR 1506). One comment was received; however, it did not respond to any of the four information collection topics solicited and is, and therefore was not addressed by the agency.

9. Explanation of any Payment or Gift to Respondents

   There are no payments or gifts to respondents.

10. Assurance of Confidentiality Provided to Respondents

    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. Estimates of Annualized Burden Hours and Costs

    12 a. Annualized Hour Burden Estimate

    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 informal agency communication with industry.

    FDA estimates the burden of this information collection as follows:

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

CVM Guidance for Industry #171	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Avg. Burden per Response	Total Hours
Same formulation/ manufacturing process approach	1	1	1	5	5
Same API/ solubility approach	5	5	5	10	50
Total Burden Hours					55

[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]

CVM Guidance for Industry #171	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Avg. Burden per Response	Total Hours
Same formulation/ manufacturing process approach	2	2	2	5	10
Same API/ solubility approach	10	10	10	20	200
Total Burden Hours					210

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

12b. Annualized Cost Burden Estimate

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
Compliance Officer	265	$38	$10,070

As indicated in Tables 1 and 2 above, FDA estimates the total burden hours for requests for waiver of *in vivo* demonstration of bioequivalence for generic soluble powder oral dosage form products and Type A medicated articles to be 265 hours. FDA estimates the total hour burden costs to respondents choosing to submit a request for waiver of *in vivo* demonstration of bioequivalence to be $10,070. We calculated this estimate by multiplying the total burden of 265 hours times the hourly wage of a compliance officer ($38), the private employee equivalent to which we believe best represents the approximate cost of preparing and submitting the request for waiver of *in vivo* demonstration of bioequivalence.

13. Estimate of Other Total Annual Costs to Respondents and/or Recordkeepers/Capital Costs

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

14. Annualized Cost to the Federal Government

    The estimated time for reviewing each submission is about 4 hours per submission (18 submissions) or a total of 72 hours. Adding overhead in the Document Control Unit (logging, delivering, tracking, etc.) brings the total to about 5 hours per submission or a total of 90 hours for review of requests for waiver of *in vivo* demonstration of bioequivalence. Therefore, the cost to the Federal Government is estimated to be $4,500 (90 hours times $50/hour – the average GS-13 wage rate).

15. Explanation of Program Changes or Adjustments

    The burden estimate has been revised to reflect the decrease in number of respondents who have requested waivers, resulting in a decrease of 265 annual hours, and 18 annual responses.

16. Plans for Tabulation and Publication and Project Time Schedule

    Not applicable.

17. Reason(s) Display of OMB Expiration Date is Inappropriate

    Not applicable.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

    There are no exceptions to the certification.