Guidance for Industry - Formal Dispute Resolution:
Scientific and Technical Issues Related to Pharmaceutical CGMP

0910-0563

SUPPORTING STATEMENT

Terms of Clearance: None.

A. Justification

1. Circumstances Making the Collection of Information Necessary

This information collection approval request is for a Food and Drug Administration (FDA) guidance for industry entitled "Formal Dispute Resolution: Scientific and Technical Issues Related to Pharmaceutical CGMP." The guidance was drafted as part of the FDA initiative "Pharmaceutical cGMPs for the 21st Century: A Risk-Based Approach," which was announced in August 2002. The initiative focuses on FDA's current CGMP program and covers the manufacture of veterinary and human drugs, including human biological drug products. The Agency formed the Dispute Resolution Working Group comprising representatives from the Office of Regulatory Affairs (ORA), the Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), and the Center for Veterinary Medicine (CVM). The working group met weekly on issues related to the dispute resolution process and met with stakeholders in December 2002 to seek their input.

The guidance was initiated in response to industry's request for a formal dispute resolution process to resolve differences related to scientific and technical issues that arise between investigators and pharmaceutical manufacturers during FDA inspections of foreign and domestic manufacturers. In addition to encouraging manufacturers to use currently available

dispute resolution processes, the guidance describes a formal two-tiered dispute resolution process that provides a formal mechanism for requesting review and decision on issues that arise during inspections:

- Tier-one of the dispute resolution process provides a mechanism to raise scientific or technical issues to the ORA and center levels.
- Tier-two of the dispute resolution process provides a mechanism to raise scientific or technical issues to the Agency's Dispute Resolution Panel for Scientific and Technical Issues Related to Pharmaceutical CGMP (DR Panel).
- The guidance also covers the following topics:
    - The suitability of certain issues for the formal dispute resolution process, including examples of some issues with a discussion of their appropriateness for the dispute resolution process.
    - Instructions on how to submit requests for formal dispute resolution and a list of the supporting information that should accompany these requests.
    - Public availability of decisions reached during the dispute resolution process to promote consistent application and interpretation of drug quality-related regulations.

When a scientific or technical issue arises during an FDA inspection, the manufacturer should initially attempt to reach agreement on the issue informally with the investigator. Certain scientific or technical issues may be too complex or time-consuming to resolve during the inspection. If resolution of a scientific or technical issue is not accomplished through informal mechanisms prior to the issuance of the Form FDA 483 (Inspectional Observations), the manufacturer can formally request dispute resolution and can use the formal two-tiered dispute resolution process described in the guidance.

Tier-one of the formal dispute resolution process involves scientific or technical issues raised by a manufacturer to the ORA and Center levels. If a manufacturer disagrees with the tier-one decision, tier-two of the formal dispute resolution process would then be available for appealing that decision to the DR Panel.

If a manufacturer disagrees with the scientific or technical basis for an observation listed by an investigator on a Form FDA 483, the manufacturer can file a written request for formal dispute resolution with the appropriate ORA unit as described in the guidance. The request for formal dispute resolution should be made within 10 days of the completion of an inspection, and should include all supporting documentation and arguments for review, as described below. If a manufacturer disagrees with the tier-one decision in the formal dispute resolution process, the manufacturer can file a written request for formal dispute resolution by the DR Panel. The manufacturer should provide the written request for formal dispute resolution and all supporting documentation and arguments, as described below, to the DR Panel within 60 days of issuance of the tier-one decision.

2. Purpose and Use of Information Collection

The guidance is intended to provide information to manufacturers of veterinary and human drugs, including human biological drug products, on how to resolve disputes of scientific and technical issues relating to CGMP. Disputes related to scientific and technical issues may arise during FDA inspections of pharmaceutical manufacturers to determine compliance with CGMP requirements, or during FDA's assessment of corrective actions undertaken as a result of such inspections. The guidance provides procedures that will encourage open and prompt

discussion of disputes and lead to their resolution. The guidance describes procedures for raising such disputes to the ORA and Center levels and for requesting review by the DR Panel.

3. Use of Improved Information Technology and Burden Reductions

The guidance requests that the information be submitted in writing and mailed to the appropriate office listed in the guidance.

4. Efforts to Identify Duplication and Use of Similar Information

The information collection requested under the guidance does not duplicate any other information collection.

5. Involvement of Small Businesses or Other Small Entities

Although new drug development is typically an activity completed by large multinational drug firms, the information collection requested under the guidance applies to small as well as large companies. Under the Regulatory Flexibility Act, FDA regularly analyzes regulatory options that would minimize any significant impact on small entities. FDA also assists small businesses in complying with regulatory requirements.

6. Consequences of Collecting the Information Less Frequently

The frequency of information submission recommended by the guidance is intended to provide assistance to manufacturers on how to resolve disputes of scientific and technical issues relating to CGMP. The guidance provides procedures that will encourage open and prompt

discussion of disputes and lead to their resolution. The guidance describes procedures for raising such disputes to the ORA and Center levels and for requesting review by the DR Panel. These benefits will be lessened without the assistance provided by the guidance.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5(d)(2)

This guidance contains no inconsistency with the guidelines in 5 CFR 1320.5(d)(2).

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 for public comment in the FEDERAL REGISTER of 8/11/2014, 2014 (79 FR 46836). No comments were received.

9. Explanation of Any Payment or Gift to Respondents

FDA has not provided and has no intention of providing any payment or gift to respondents under this guidance.

10. Assurance of Confidentiality Provided to Respondents

Confidentiality of the information submitted under this guidance is protected under 21 CFR 312.130 and 314.430 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 Federal Food, Drug, and Cosmetic Act.

11. Justification for Sensitive Questions

There are no questions of a sensitive nature.

12. Estimates of Annualized Burden Hours and Costs

12a. Annualized Hour Burden Estimate

Tier-one of the formal DR process involves scientific or technical issues raised by a manufacturer to the ORA and center levels. If a manufacturer disagrees with the tier-one decision, tier-two of the formal DR process would then be available for appealing that decision to the DR panel. The written request for formal DR to the appropriate ORA unit should be made within 30 days of the completion of an inspection, and should include all supporting documentation and arguments for review, as described in this document. The written request for formal DR to the DR Panel should be made within 60 days of receipt of the tier-one decision and should include all supporting documentation and arguments, as described in the following paragraphs.

All requests for formal DR should be in writing and include adequate information to explain the nature of the dispute and to allow FDA to act quickly and efficiently. Each request should be sent to the appropriate address listed in the guidance and include the following:

- Cover sheet that clearly identifies the submission as either a request for tier-one DR or a request for tier-two DR;
- Name and address of manufacturer inspected (as listed on FDA Form 483);
- Date of inspection (as listed on FDA Form 483);
- Date the FDA Form 483 issued (from FDA Form 483);

- Facility Establishment Identifier (FEI) Number, if available (from FDA Form 483);
- FDA employee names and titles that conducted inspection (from FDA Form 483);
- Office responsible for the inspection (e.g., district office, as listed on the FDA Form 483);
- Application number if the inspection was a preapproval inspection;
- Comprehensive statement of each issue to be resolved:
    - Identify the observation in dispute:
    - Clearly present the manufacturer's scientific position or rationale concerning the issue under dispute with any supporting data.
    - State the steps that have been taken to resolve the dispute, including any informal DR that may have occurred before the issuance of the FDA Form 483.
    - Identify possible solutions.
    - State expected outcome.
- Name, title, telephone and FAX number, and email address (as available) of manufacturer contact.

The guidance also covers the following topics:

- The suitability of certain issues for the formal DR process, including examples of some issues with a discussion of their appropriateness for the DR process.
- Instructions on how to submit requests for formal DR and a list of the supporting information that should accompany these requests.
- Public availability of decisions reached during the DR process to promote consistent application and interpretation of drug quality-related regulations.

Description of Respondents: Pharmaceutical manufacturers of veterinary and human drug products and human biological drug products.

Burden Estimate: FDA estimates that approximately two manufacturers will submit approximately two requests annually for a tier-one DR and that there will be one appeal of these requests to the DR Panel (request for tier-two DR). FDA estimates that it will take manufacturers approximately 30 hours to prepare and submit each request for a tier-one DR and approximately 8 hours to prepare and submit each request for a tier-two DR. Table 1 of this document provides an estimate of the annual reporting burden for requests for tier-one and tier-two DRs.

Table 1.--Estimated Annual Reporting Burden

Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Requests for Tier-One Dispute Resolution	2	1	2	30	60
Requests for Tier-Two Dispute Resolution	1	1	1	8	8
Total					68

12b. Annualized Cost Burden Estimates

FDA has estimated an average industry wage rate of $85.00 per hour for preparing and submitting the information collection under this guidance. Using the averaged wage rate of

$85.00 per hour, and multiplied times the total hour burden estimated above, the total cost burden to respondents is $5,780 (68 x $85).

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

There are no capital, start-up, operating or maintenance costs associated with this information collection.

14. Estimates of Annualized Cost Burden to the Government

FDA estimates that review by FDA staff of the submissions recommended by the guidance would require approximately 10 hours per request (10 hours x 3 requests = 30 hours). Assuming each reviewer earned approximately $45 per hour, the total Federal cots would be $1,350.00.

15. Explanation for Program Changes or Adjustments

The increased burden is the result of adding the request for Tier-Two Dispute Resolution to the burden chart.

16. Plans for Tabulation and Publication and Project Time Schedule

There are no plans for publications.

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

The Agency is not seeking to display the expiration date for OMB approval of the

information collection.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.