

Supporting Statement

Salmonella Discovery System Pilot Study

Docket Number 01N-0590

OMB Control Number 0910-0493

A. Justification

1. Circumstances of Information Collection

FDA's Center for Drug Evaluation and Research, Office of Pharmaceutical Science, Informatics and Computational Safety Analysis Staff, intends to conduct a *Salmonella* Discovery System Pilot Study (the pilot study). The primary goal of the pilot study is to construct and execute a mutually beneficial process by which FDA and pharmaceutical companies can share information based on their proprietary toxicology study data and thereby expand their own knowledge databases. This process will be designed and conducted using procedures that do not compromise the identity and chemical structures of the individual collaborator's proprietary chemicals.

The three major objectives of the pilot study are to:

- Build a joint and comprehensive FDA/pharmaceutical industry database for compounds tested in the *Salmonella t.* reverse mutagenicity assay;
- Use these data to construct a new enhanced *Salmonella t.* mutagenicity assay database module for the *MultiCASE* quantitative structure activity relationship software program; and
- Employ the recently developed *MultiCASE* expert system (*MCASE-ES*) to predict the mutagenic response, mutagenic potency, and mechanism of mutagenesis of test chemicals in *Salmonella t.*

The pilot study will be a joint venture designed to maximize the benefits and minimize the risks to all collaborators. FDA intends to send letters to companies that have purchased either *MultiCASE* or *CASETOXII* software programs to invite them to become a collaborator in the project.

FDA intends to request that each collaborator submit the following data electronically: (1) Test compound chemical structures; and (2) assay data, identifying the type of *Salmonella* mutagenicity assay used in the studies, the source and concentration of any exogenous activation system used, and the average number of revertants/plate for the negative control, positive control, and each of the test compound treatment groups. Although there is no minimum requirement for the number of test compounds to be submitted to FDA, the agency would expect to receive at least 200 compounds from each collaborator. Each company will be able to identify its own compounds in the resulting discovery system, and the more data submitted, the greater the coverage will be for each company's molecular universe.

FDA intends to act as the broker for the pilot study and will be responsible for the confidentiality and integrity of each collaborator's proprietary data. The number of compounds in the database module will depend upon the number of collaborators and the size of the data sets they contribute to the pilot study. After the enhanced *Salmonella* discovery system has been constructed and tested, FDA intends to custom prepare individual discovery systems for each collaborator.

The *Salmonella* discovery system provided by FDA will be compatible with each company's current *MultiCASE* software program and will supplement current *Salmonella* modules purchased from MultiCASE, Inc.

Participation in this pilot study will be voluntary. FDA estimates that approximately 12 companies will participate, and that it will take each company approximately 8 hours to compile the information from electronic archives and submit the requested data and information.

## 2. Purpose and Use of Information

This information collection solicits information to enable FDA to construct and utilize a database from which FDA and pharmaceutical companies can share information based on their proprietary toxicology study data to predict the mutagenic response, mutagenic potency, and mechanism of mutagenesis of test chemicals in *Salmonella typhimurium*.

The anticipated benefits to collaborators include:

- Receipt of a new expanded *Salmonella in silico* discovery tool at no cost;
- Access to proprietary molecular fragment data derived from *Salmonella t.* mutagenicity studies from FDA and other collaborator archives;
- Comprehensive lists of molecular structural alerts correlated with mutagenicity in *Salmonella t.*, including previously uncharacterized alerts derived from heretofore inaccessible undeveloped lead pharmaceutical test data; and
- A *Salmonella* discovery system that should provide high coverage and high predictive performance for organic chemicals in each company's combinatorial and lead chemical data sets.

## 3. Use of Improved Information Technology

Due to security concerns, information will only be transmitted by registered mail or similar services on CD ROM or

other hard media.

4. Efforts to Identify Duplication

The reporting required as a result of this information collection is not currently required by FDA and would not duplicate any other information collection.

5. Involvement of Small Entities

Both large and small entities will participate in the study.

6. Consequences If Information Collected Less Frequently

The collection of this information will increase the ability of toxicology study data to predict the mutagenic response, mutagenic potency, and mechanism of mutagenesis of test chemicals in *Salmonella typhimurium*.

7. Consistencies with Guidelines in 5 CFR 1320.5(d)(2)

There is no inconsistency.

8. Consultations Outside the Agency

The purpose of the study is to construct and execute a mutually beneficial process by which FDA and pharmaceutical companies can share information based on their proprietary toxicology study data and thereby expand their own knowledge databases.

In the Federal Register of January 28, 2002, (67 FR 3902), the agency requested comments on the proposed collections of information. No comments were received

9. Remuneration of Respondents

There is no payment to respondents.

10. Assurance of Confidentiality

FDA intends to act as the broker for the pilot study and will be responsible for the confidentiality and integrity of each collaborator's proprietary data. After the enhanced *Salmonella* discovery system has been constructed and tested, FDA intends to custom prepare individual discovery systems for each collaborator.

11. Questions of a Sensitive Nature

This reporting does not involve any sensitive questions.

12. Estimates of Annualized Hour Burden

FDA estimates the burden of this collection of information as follows:

Estimated Annual Reporting Burden<sup>1</sup>

Number of Respondents	Annual Frequency Per Response	Total Annual Responses	Hours per Response	Total Hours
12	1	12	8	96

<sup>1</sup>There are no capital costs or operating and maintenance costs associated with this collection of information

13. Estimates of Annualized Cost Burden to Respondents

FDA estimates that the average hourly wage of industry representatives participating in this study, including overhead and related expenses, is approximately \$75 per hour. Therefore, the total cost to industry to comply with this reporting is \$7200 (8 hours x \$75 x 12).

14. Estimates of Annualized Cost Burden to the Government

FDA anticipates that approximately 0.2 FTEs are devoted to the establishment and maintenance of the study. Assuming each FTE is approximately \$100,000, the total cost to FDA is \$20,000.

15. Changes in Burden

This is a new collection.

16. Time Schedule, Publication, and Analysis Plans

FDA does not intend to publish tabulated results of the information collection requirements that would be imposed by these requirements.

17. Displaying of OMB Approval Date

There are no forms associated with this collection.

18. Exception to the Certification Statement - Item 19

There are no exceptions to the certification statement "Certification for Paperwork Reduction Act Submission."