

**Supporting Statement for Reporting Requirements
in 21 CFR 25 - Environmental Impact Considerations**

A. Justification

1. Circumstances of Information Collection

The National Environmental Policy Act (NEPA), 42 U.S.C. 4321-4347, states national environmental objectives and imposes upon each Federal agency the duty to consider the environmental effects of its actions. Section 102(2)(C) of NEPA requires the preparation of an environmental impact statement (EIS) for every major Federal action that will significantly affect the quality of the human environment.

The FDA NEPA regulations are at 21 CFR part 25. FDA is requesting OMB approval for the reporting requirements contained in the FDA regulation "Environmental Impact Considerations." All applications or petitions requesting agency action require the submission of an Environmental Assessment (EA) or a claim of categorical exclusion. Sections 25.15(a) and (d) specify the procedures for submitting to FDA a claim for a categorical exclusion (certain classes of FDA-regulated actions have little or no potential to cause significant environmental effects and are excluded from the requirements to prepare an EA or EIS). Sections 25.40(a) and (c) specify the content requirements for EA's for nonexcluded actions.

2. Purpose and Use of Information

This collection of information is used by FDA to assess the environmental impact of agency actions and to ensure that the public is informed of environmental analyses. Firms wishing to manufacture and market substances regulated under statutes for which FDA is responsible must, in most instances, submit applications requesting approval. Environmental information must be included in such applications (when not eligible for categorical exclusion) for the purpose of determining whether the

proposed action may have a significant impact on the environment. Where significant adverse effects cannot be avoided, the agency uses the submitted information as the basis for preparing and circulating to the public an EIS, made available through Federal Register notice also filed for comment at the Environmental Protection Agency (EPA). The final EIS including the comments received is reviewed by the agency to weigh environmental costs and benefits in determining whether to pursue the proposed action or some alternative that would reduce expected environmental impact. When the agency finds that no significant environmental effects are expected, the agency prepares a Finding of No Significant Impact (FONSI).

3. Use of Improved Information Technology

For human drugs, the submissions under 21 CFR part 25 are part of an application for marketing. FDA has taken the following steps to facilitate the electronic submission of new drug applications:

Electronic Regulatory Submissions for Archive - The Food and Drug Administration Modernization Act (FDAMA), along with the Prescription Drug Marketing Act reauthorization (PDUFA II), mandate that the agency shall develop and update its information management infrastructure to allow, by fiscal year 2002, the paperless receipt and processing of INDs (investigational new drug applications) and NDAs (new drug applications), as defined in PDUFA, and related submissions. Moving an information-intensive activity, such as drug regulatory review, from a paper-based to an electronic environment will provide a number of benefits.

In September 1997, FDA published the Guidance for Industry on "Archiving Submissions in Electronic Format -- NDAs." This guidance provided for the receipt and archive of electronic Case Report Forms (CRF) and Case Report Tabulations (CRT) without an accompanying paper copy. In FY 1998, the agency established an Electronic Document Room (EDR) to manage the receipt and handling of all electronic submissions. In January 1999, FDA published the Guidance for Industry on "Providing Regulatory Submissions in Electronic Format - NDAs." This guidance document covers the full NDA and is not limited to CRTs and CRFs. Approximately 40% of original NDAs now include guidance-compliant electronic submissions (i.e., submissions for archive). Out of 86 original NDAs received since January 1999, 36 included electronic components and 9 were full electronic NDAs. The agency also received 43 electronic NDA supplements. Out of 6,978 NDA

amendments, supplements, and amendments to supplements, 100 were electronic.

Secure E-Mail - During a drug's development cycle, communications between FDA's CDER review divisions and the company developing the drug is sensitive and proprietary. Prior to using secure E-mail, CDER methods of "secure" communication included U.S. mail, courier, telephone, and facsimile. These methods, some of which are not entirely secure, can be inefficient or time consuming, and can significantly contribute to the overall length of time involved in the drug review process. The widespread use of E-mail across the Internet offers a more efficient and scaleable means of information exchange. However, security risks of communicating over the Internet are well known. The information technology industry is answering security concerns by developing new standards of cryptographic techniques, E-mail formats, authentication algorithms, and other related aspects of secure communications. In 1998, CDER conducted a formal requirements study for secure E-mail which led to the selection of Worldtalk Corporation's WorldSecure Server as the base pilot platform. CDER began testing WorldSecure Server in late 1998. A pilot system was put into place in January 1999. After the pilot's run, the production system's requirements were developed from the pilot's requirements and new information gathered from the pilot results. The design for a production system was based on these requirements. CDER recently installed a production system and additional firms are being given secure E-mail accounts.

ICH M2 - The International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH) was formed to minimize waste in the discovery, development, regulation, manufacture, marketing, and use of human therapeutic products worldwide. The regulatory authorities of Europe, Japan, and the United States joined with their respective pharmaceutical trade associations in an agreement to take action on harmonization by participating in the ICH. The ICH Multi-disciplinary Group 2 (M2) Expert Working Group (EWG) was established to determine electronic standards and provide solutions to facilitate international electronic communication in the three ICH regions. The first effort of the M2 EWG was to establish a series of recommendations that would form the basis for standardized electronic communication in each of the three regions. These recommendations included physical media formats, secure communications, and structured data formats. Building on these standards, the EWG then began work on a detailed specification for the secure, electronic transmission of individual case safety reports (adverse event reports). The specification is intended to support transmission between

industry partners, industry and regulatory authorities and between regulatory authorities in all three regions. The production of a specification for an electronic common technical document (CTD) was the next major effort assigned to the M2 EWG. The ICH steering committee agreed in March 1999 that this effort should be undertaken by the M2 EWG in cooperation with the subject matter expert working groups for each section of the CTD. The CTD working groups are charged with harmonizing the format and content of the application documents for new product applications. The resulting ICH guidances, when implemented, will change the content and format of NDA submissions to the FDA. The M2 specification will define the nature of an electronic submission for CTD submissions and could have a major impact on the way electronic submissions are received, archived, and reviewed.

In addition to the above, FDA encourages applicants to use, as applicable, computerized indexing services (databases), such as ENVIRONMENTAL, Tox-Line, and RTECS to search the scientific literature for environmental data on new or existing products. FDA has also instituted, internally, a computerized indexing system to locate data previously submitted to the agency. FDA environmental scientists meet with industry representatives and provide specific guidance documents on the types of data required for a particular action. This helps the agency and industry sponsors concentrate on those issues that may involve potentially significant environmental consequences.

4. Efforts to Identify Duplication

FDA avoids duplication by encouraging applicants to reference in their environmental documents data and information presented in other documents that are available to FDA and the public (see §25.40(d)).

FDA intends to focus environmental reviews on the use and disposal from use of FDA regulated articles. For example, FDA deleted the requirements for the submission of emission information for production sites because FDA found that FDA-regulated articles produced in compliance with all applicable requirements under Federal, State, and local law will not significantly affect the environment. Therefore, the environmental impact of the manufacture of a proposed substance will not be reviewed by FDA through an EA or an EIS unless there exist extraordinary circumstances relating to the manufacture that may have a significant environmental effect. Because FDA actively works to ensure the consistency of its protocols with those prescribed by EPA, the American Society for Testing and

Materials (ASTM), and Organization for Economic Co-operation and Development (OECD), FDA avoids unnecessary duplication of environmental testing. Thus, environmental testing that has already been performed will not have to be repeated by a different protocol when applicants move from one regulatory agency to another and from one country to another for approvals of the same chemical substance.

Where possible, existing data are used by FDA in evaluating the environmental impact of an industry-sponsored application or petition. To the extent publicly available, data in FDA files may be cross-referenced, data available in the scientific literature may be submitted, and data gathered for other government agencies, such as EPA, may be used in support of the environmental review of an application to FDA.

FDA recognizes that there are instances where the same substance may be the subject of separate environmental analyses by another agency, for example by EPA. FDA has determined that separate environmental review is not necessary for FDA approval of a food additive petition or FDA granting a request for an exemption from regulations as a food additive if the substance is already registered by EPA under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) for the same use requested in the petition. Although both agencies have worked to eliminate duplication of effort, applications submitted to FDA sometimes involve a different use of a chemical substance than the use(s) reviewed by EPA and the patterns of environmental introduction often vary. Therefore, in some circumstances, a document prepared by FDA or another agency may not suffice as the NEPA document.

5. Involvement of Small Entities

For both large and small entities, FDA has identified the types of information necessary to review the environmental impact of a new product and, where possible, provides case-by case guidance on the specific types of information required for a particular action. FDA does not have the resources to perform a firm's environmental studies and the information gathering necessary for the evaluation of a new product. However, small manufacturers may request help in applying for approval from the FDA Office of Small Manufacturer's Assistance. Because FDA has identified categories of actions that are categorically excluded from the requirement to prepare an EA and EIS, fewer EA's and EIS's are likely to be required from small businesses.

6. Consequences If Information Collected Less Frequently

Industry-sponsored applications and petitions are submitted to obtain permission to market a new product or to expand the usage of a currently regulated product. If the frequency of collection for environmental impact data were reduced, the agency could not assess the environmental impact of approving applications. Failure to take environmental factors into account in the agency decisionmaking would leave the agency susceptible to court challenge and may result in unnecessary delays in the approval for marketing of products.

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

Data collection for applications is consistent with these guidelines.

8. Consultation Outside the Agency

FDA proposed revisions to 21 CFR part 25 in the Federal Register of April, 3, 1996. FDA received comments on the proposed rule from 13 manufacturers, professional associations, environmental groups, academics, environmental consultants, and the EPA. In general the comments supported FDA's proposed revisions to more efficiently implement NEPA. One manufacturer of human and veterinary pharmaceuticals projected that the final rule would reduce by 75% the number of its products that will require EA's, and a pharmaceutical industry trade association estimated that the rule would reduce by 90% the amount of environmental information submitted to the agency. Several commenters sought clarification of the categorical exclusion criteria in §25.31(b), that is, agency action on human drug applications if the action increases the active moiety but the concentration of the substances at the point of entry into the aquatic environment will be below 1 part per billion. FDA placed additional information in the administrative record regarding this categorical exclusion and categorical exclusions that apply to foods, food additives, and color additives. Through notification in the FEDERAL REGISTER on October 22, 1996, the agency sought comments on the categorical exclusions for which the information was provided. Four additional comments were submitted as a result of the reopening of the comment period.

FDA addressed the substantive comments in the final rule and, in some instances, FDA amended the proposed regulations in response to comments.

On March 13, 2000, (65 FR 13405), FDA requested comments on the extension of this collection of information. There were no comments received.

9. Remuneration of Respondents

FDA has not provided and has no intention to provide any payment or gift to respondents under the revisions of part 25.

10. Assurance of Confidentiality

NEPA requires that EA's and EIS's be made available for public review. However, 21 CFR 25.50(b) recognizes that FDA actions involving investigations, review, and approval of applications and premarket notifications for human drugs, animal drugs, biologic products, and devices are protected from disclosure under the Trade Secret Act (TSA), the Federal Food, Drug, and Cosmetic Act (FFDCA), and 21 CFR part 20. Additionally, under 21 CFR 25.51 (a), data constituting trade secrets or confidential information under the TSA or the FFDCA must not be included in the portion of environmental documents that is made public. Thus, environmental information will be made available to the public to the extent permitted.

11. Questions of a Sensitive Nature

There are no questions of a sensitive nature in the environmental impact requirements.

12. Estimates of Annualized Hour Burden

Estimated annual reporting burden for human drugs -
Under 21 CFR 312.23(a)(7)(e), 21 CFR 314.50(d)(1)(iii), and 21 CFR 314.94(a)(9)(i), each Investigational New Drug Application (IND), New Drug Application (NDA), and Abbreviated New Drug Application (ANDA) must contain a claim for categorical exclusion under §§ 25.30 or 25.31 or an environmental assessment under § 25.40. In 1998, FDA received 2,427 IND's from 1,874 sponsors, 129 NDA's from 80 applicants, 2,500 supplements to NDA's from 238 applicants, 345 ANDA's from 101 applicants, and 3,713 supplements to ANDA's from 165 applicants. FDA estimates that it receives approximately 9094 claims for categorical exclusions as required

under §§ 25.15(a) and (d), and 20 environmental assessments as required under §§ 25.40(a) and (c). Based on information provided by the pharmaceutical industry, FDA estimates that it takes sponsors or applicants approximately 8 hours to prepare a claim for a categorical exclusion and approximately 3400 hours to prepare an environmental assessment.

Estimated Annual Reporting Burden for Human Drugs					
CFR Section	Number of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Burden Hours
25.15 (a) & (d)	2039	4.46	9,094	8	72,752
25.40 (a) & (c)	20	1	20	3400	68,000
Total					140,752

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

Estimated annual reporting burden for human foods -
 Under 21 CFR 71.1 and 21 CFR 170.39, food additive petitions, color additive petitions, and requests for exemption from regulation as a food additive must contain a claim of categorical exclusion under §§ 25.30 or 25.32 or an environmental assessment under § 25.40. In 1998, FDA received 57 food additive petitions, 9 color additive petitions, and 26 threshold of regulation exemption requests. FDA estimates that it received approximately 80 claims of categorical exclusions as required under §§ 25.15(a) and (d), and 12 environmental assessments as required under §§ 25.40(a) and (c). FDA estimates that it takes petitioners or requestors approximately 8 hours to prepare a claim of categorical exclusion and approximately 210 hours to prepare an environmental assessment.

Estimated Annual Reporting Burden for Human Foods					
CFR Section	Number of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Burden Hours
25.15 (a) & (d)	44	1.8	8.0	8	640
25.40 (a) & (c)	11	1.1	12	210	2520
Total					3160

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

The Food and Drug Administration Modernization Act (FDAMA) of 1997 (Pub. L. 105-115) amended section 409 of the Federal Food, Drug, and Cosmetic Act (the Act) to establish a premarket notification process as the primary method for authorizing a new use of a food additive that is a food contact substance. Section 409(h)(6) of the act defines a food contact substance as any substance intended for use as a component of materials used in

manufacturing , packing, transporting, or holding food if such use is not intended to have any technical effect in food. Under the notification process, FDA must be notified at least 120 days prior to the marketing of a food contact substance. If FDA does not object within 120 days to the use of a food contact substance that is the subject of a notification, the substance may be legally marketed for the notified use. FDA expects that the majority of new uses of food contact substances that will be the subject of premarket notifications would previously have been regulated under the food additive petition process or exempted from the requirement of a regulation under the threshold of regulation process.

Estimated annual reporting burden for medical devices -

Under 21 CFR 814, Pre-Market Approvals (original PMAs and supplementals) must contain a claim for categorical exclusion under §§ 25.30 or 25.31 or an environmental assessment under § 25.40. In 1998, FDA received 568 claims (original PMAs and supplementals) for categorical exclusions as required under §§25.15(a) and (d), and 0 (zero) environmental assessments as required under §§25.40(a) and (c). Based on information provided by less than 10 sponsors, FDA estimates that it takes approximately less than one hour to prepare a claim for a categorical exclusion and an unknown number of hours to prepare an environmental assessment.

Estimated Annual Reporting Burden for Medical Devices					
CFR Section	Number of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Burden Hours
25.15 (a) & (d)	94	6	568	1	568
25.40 (a) & (c)	0	0	0	0	0
Total					568

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

Estimated annual reporting burden for biological products -

Under 21 CFR 312(a)(7)(iv)(c) and 601.2(a), an IND and Biologics License Application must contain a claim for categorical exclusion under §§ 25.30 or 25.31 or an environmental assessment under § 25.40. In 1998, FDA received 492 INDs from 278 sponsors, 78 license applications from 20 applicants, and 903 supplements to license applications from 190 applicants. FDA estimates that approximately 10% of these supplements would be submitted with a claim for categorical exclusion or an environmental assessment.

FDA estimates that it receives approximately 660 claims for categorical exclusion as required under §§ 25.15(a) and (d), and

2 environmental assessments as required under §§ 25.40(a) and (c). Based on information provided by industry, FDA estimates that it takes sponsors and applicants approximately 8 hours to prepare a claim for categorical exclusion and approximately 3400 hours to prepare an environmental assessment.

Estimated Annual Reporting Burden for Biological Products					
CFR Section	Number of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Burden Hours
25.15 (a) & (d)	317	2	660	8	5280
25.40 (a) & (c)	2	1	2	3400	6800
Total					12,080

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

Estimated annual reporting burden for animal drugs -
 Under 21 CFR §§ 514.1(b)(14), New Animal Drug Applications (NADAs), Abbreviated New Animal Drug Applications (ANADA's), 514.8(a)(1) supplemental NADAs and ANADAs, 511.1(b)(10) Investigational New Animal Drug Applications (INADAs), 570.35 (c)(1)(viii) Generally Recognized as Safe (GRAS), Affirmation Petitions and 571.1(c) Food Additive Petitions must contain a claim for categorical exclusion under §§ 25.30 or 25.31 or an environmental assessment under § 25.40. Since the last OMB Approval of the subject collections of information the Center of Veterinary Medicine (CVM) has received approximately 545 claims for categorical exclusions as required under §§ 25.15(a) and (d), and 32 environmental assessments as required under §§ 25.40(a) and (c). Based on information provided by industry, FDA estimates that it takes sponsors/applicants approximately 8 hours to prepare a claim for a categorical exclusion and approximately 2160 hours to prepare an environmental assessment.

Estimated Annual Reporting Burden for Animal Drugs					
CFR Section	Number of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Burden Hours
25.15 (a) & (d)	194	2.8	545	8	4,360
25.40 (a) & (c)	29	1.1	32	2160	69,120
Total					73,480

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

Based on information provided by industry, FDA estimates that the combined burden for the Environmental Impact Considerations - Part 25 (21 CFR Part 25) are as follows:

Entire Total Estimated Annual Reporting Burden For All Centers					
CFR Section	Number of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Burden Hours
25.15(a)& ((d)	2688	17.06	10,875	33	83,600
25.40 (a)&(c)	62	4.02	66	9170	146,440
Total	2750	21.08	10,941	9203	230,040

13. Estimates of Annualized Cost Burden to Respondents

FDA's Economics Staff estimates the average industry wage rate of \$50.00 per hour for preparing and submitting the information collection requirements associated with marketing applications. Based on a total industry burden of 230,040 hours, the annualized cost burden to respondents would be \$11,502,000.

14. Estimates of Annualized Cost Burden to the Government

FDA estimates a total of 5 FTEs are devoted to the review of submissions associated with 21 CFR part 25. Based on an estimate of \$100,000 per FTE, the annualized cost burden to FDA would be \$500,000.

15. Changes In Burden

As explained under number 12 above, the revised burden estimates are the result of the average number of claims for categorical exclusions and EAs submitted over the past few years.

16. Time Schedule, Publication, and Analysis Plans

FDA does not intend to publish tabulated results of the information collection requirements that are imposed by 21 CFR part 25.

17. Displaying of OMB Expiration Date

There are no forms associated with this collection.

18. Exception to the Certification Statement

There are no exceptions to the "Certification for Paperwork Reduction Act Submissions" in item 19 of OMB Form 83-I.

approved 8/8/00.