

**SUPPORTING STATEMENT  
FOR  
Investigational Device Exemptions  
Reports and Records - 21 CFR 812  
OMB No. 0910-0078**

**A. JUSTIFICATION**

Section 520(g) of the Federal Food, Drug, and Cosmetic Act (the act) (21. U.S.C. 360j(g)) establishes the statutory authority to collect information regarding investigational devices, and establishes rules under which new medical devices may be tested using human subjects in a clinical setting. The Food and Drug Modernization Act of 1997 (FDAMA) added Section 520(g)(6) to the act and permitted changes to be made to either the investigational device or to the clinical protocol without FDA approval of an Investigational Device Exemption (IDE) supplement.

Such testing is conducted to provide clinical data to support a future marketing application, i.e., a premarket approval or premarket notification. Specifically, this section states that the Secretary shall prescribe regulatory procedures and conditions under which new, untested devices intended for human use may be granted an exemption from certain sections of the Act. Those sections are:

- 502 - Misbranded drugs and devices
- 510 - Registration, listing and premarket notification
- 514 - Performance standards
- 515 - Premarket approval
- 516 - Banned devices
- 519 - Records and reports on devices
- 520(e) Restricted devices
- 520(f) Good manufacturing practice requirements
- 706 - Listing and certification of color additives.

An Investigational Device Exemption (IDE) allows a device, which would otherwise be subject to provisions of the act, such as premarket notification or premarket approval, to be used in investigations involving human subjects in which the safety and effectiveness of the device is being studied. The purpose of 21 CFR Part 812 is to encourage, to the extent consistent with the protection of public health and safety and with ethical standards, the discovery and development of useful devices intended for human use. The IDE regulation is designed to encourage the development of useful medical devices, and allow investigators the maximum freedom possible, without jeopardizing the health and safety of the public or violating ethical standards.

The regulation provides for different levels of regulatory control, depending on the level of potential risk the investigational device presents to human subjects. Investigations of significant risk devices, ones that present a potential for serious harm to the rights, safety or welfare of human subjects, are subject to the full requirements of the IDE regulation. Nonsignificant risk device investigations are ones that do not present a potential risk for serious harm, and are subject to the reduced burden of abbreviated requirements.

The regulation also includes provisions for treatment IDEs. The purpose of these provisions is to facilitate the availability, as early in the device development process as possible, of promising new devices to patients with life-threatening or serious conditions for which no comparable or satisfactory alternative therapy is available.

This collection of ~~information burden~~ is the result of the consolidation of OMB Information Collections 0910-0078, 0910-0348, and 0910-0391.

**1. Circumstances Making the Collection of Information Necessary**

The Food and Drug Administration (FDA) is requesting approval from the Office of Management and Budget (OMB) for the following information collection requirements, including treatment use and modification provisions, contained in 21 CFR, Part 812 (see Attachment A).

**21 CFR 812.10 - Reporting**

Allows the sponsor of an IDE to request a waiver to all of the requirements of 21 CFR 812. FDA uses this information to determine if a waiver of requirements will impact the public's health and safety.

**21 CFR 812.20 - Reporting**

Requirements for data to be included in an IDE application. This information is required to file an original IDE application, which is only needed for significant risk devices.

**21 CFR 812.25 - Reporting**

Requirements for data contents for an investigational plan as part of an IDE application. This information is required to file an IDE application, which is only needed for significant risk devices.

**21 CFR 812.27 - Reporting**

Requirements for submission of data relating to previous investigations or testing as part of an IDE application. This information is required to file an IDE application, which is only needed for significant risk devices.

**21 CFR 812.35 - Reporting**

Requirements for submitting supplements to an IDE. This includes any changes by a sponsor which affects the scientific soundness of the study or the rights, safety, or welfare of the subjects.

**812.36(c) - Reporting**

Requirements for data to be included in an IDE application for treatment use.

**812.36(f) - Reporting**

Reporting requirements for sponsors of a treatment IDE. These reports allow FDA to monitor the size and scope of the treatment IDE, assess the sponsor's due diligence in obtaining marketing clearance of the device, and ensure integrity of the controlled clinical trials.

**21 CFR 812.140 - Recordkeeping**

Lists the recordkeeping requirements for investigators and sponsors. FDA requires this information for tracking and oversight purposes.

**21 CFR 812.150 - Reporting**

Reporting requirements for investigators and sponsors. This information is submitted to FDA as supplemental applications and is needed to assure protection of human subjects and to allow review of the study's progress.

## **2. Purpose and Use of the Information**

The IDE regulation is designed to encourage the development of useful medical devices, and allow investigators the maximum freedom possible, without jeopardizing the health and safety of the public or violating ethical standards. To avoid imposing unnecessary requirements on clinical investigations, the IDE regulation recognizes three categories of medical device investigations: significant risk devices, nonsignificant risk devices, and exempted investigations. A significant risk device is defined as a medical device which presents a potential for serious risk to the health, safety, or welfare of a subject and:

- (1) is intended as an implant;
- (2) is purported or represented to be for a use in supporting or sustaining a human life;
- (3) is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health.

An investigation of a medical device which does not meet the above criteria and which is not exempt from the regulation is a nonsignificant risk device investigation.

An investigation of a significant risk device must meet the full requirements of the IDE regulation. Both FDA and institutional review board (IRB) approval are required. An investigation of a nonsignificant risk device must meet the abbreviated requirements of the IDE regulation; this does not require FDA approval. IRB approval constitutes an approved IDE. The requirements for an IDE application for significant risk device investigations may be divided into the following categories: original application, amendments, supplemental applications, records, and reports.

A significant risk device investigation requires the submission of an IDE application to FDA. The original application is evaluated by the Center for Devices and Radiological Health to determine whether the proposed investigation will reasonably protect the public health and safety, and whether it will develop reliable scientific data. An environmental analysis report is required by Part 25 in accordance with section 102(2)(c) of the National Environmental Policy Act of 1969. FDA has determined that, generally, medical devices do not have an environmental impact. Therefore, FDA anticipates that only rarely will an IDE application require the submission of an environmental analysis report. Supplemental applications are required when a sponsor wishes to make a change in the investigation which affects the scientific soundness of the study or the rights, safety or welfare of the subjects. Records must be maintained by both sponsors and investigators and reports must be submitted at specified times.

For a nonsignificant risk device investigation, the investigator's and sponsor's recordkeeping and reporting burden is reduced. Pertinent records on the study must be maintained by both parties, and reports are made to sponsors and IRBs. Reports are made to FDA only in certain circumstances, e.g., recall of the device, the occurrence of unanticipated adverse effects and as a consequence of certain IRB actions.

Under section 812.10, a sponsor may request that FDA waive any requirement within this regulation not required by statute. The waiver request, with supporting documentation, may be separately submitted or included as part of the original IDE application. The requirements of the regulation are applied

unless FDA waives the requirement.

The consequences of not gathering this information would be that FDA could not fulfill the intent of the law, which is to protect the public health and welfare.

### **3. Use of Information Technology and Burden Reduction**

In the **Federal Register** of March 20, 1997, FDA issued a final regulation (21 CFR Part 11) (Attachment C) that would, under certain circumstances, permit the agency to accept electronic signatures and handwritten signatures executed to electronic records as generally equivalent to paper records and handwritten signatures executed on paper. These regulations would apply to records, when submitted in electronic form, that are required in Title 21 of the Code of Federal Regulations (CFR) such as IDE modifications. The use of electronic forms of record keeping and reporting submissions to FDA remains voluntary. The intended effect of this regulation is to permit use of electronic technologies in a manner that is consistent with FDA's overall mission and that preserves the integrity of the agency's enforcement activities.

### **4. Efforts to Identify Duplication and Use of Similar Information**

Investigational medical devices are not regulated by any other Federal agency. Therefore, there is no duplication of effort and similar information is unavailable. There are, therefore, no information systems which can be used or modified to meet the purpose described in item two, above.

### **5. Impact on Small Businesses or Other Small Entities**

These regulations apply to all firms, institutions or individuals involved in conducting clinical investigations of medical devices, regardless of the size of the organization. The information collection will not have a significant economic impact on a substantial number of small entities. Because most of the information will come from existing IDE's, it will be readily available and will pose little additional burden. This collection simplifies the way in which modifications are made and reported to FDA.

FDA also offers the resources of the Center for Devices and Radiological Health's (CDRH) Division of Small Manufacturers Assistance (DSMA) and the Office of Device Evaluation (ODE) staffs. CDRH established DSMA as required by the 1976 Amendments to the Act. DSMA's staff provides technical and other nonfinancial assistance to small firms expressly to aid them in complying with the requirements of the Act. The activities of DSMA include participating in and presenting conferences, workshops, seminars on the application and interpretation of relevant regulations, consulting with individual firms/sponsors, and development and dissemination of educational materials. Staff is available to respond to questions and a toll free telephone number was established to facilitate this communication link. The ODE program office, which includes the IDE staff, is also available to respond to, or meet with persons requesting information or assistance regarding investigational devices.

### **6. Consequences of Collecting the Information Less Frequently**

This information collection allows FDA to collect data to ensure that the investigational device's use will not present an unreasonable risk for the subject enrolled in the study and will not violate the subject's rights. Applications for treatment use are required only when the sponsor determines that treatment use should begin. FDA believes that semi-annual treatment use reports are necessary to assure the protection of the public health, because devices eligible for treatment use by their very nature present a risk of serious health consequences. Applications for IDE modifications are required within

5 working days of making the change in accordance with the law as amended by FDAMA. This reporting is necessary to assure that changes that may affect the public health are identified and dealt with quickly.

If the information was obtained less frequently, it would not be possible to assure protection of the public health from significant risk devices.

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

The collection is entirely consistent with 5 CFR 1320.

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

Notice was published in the Federal Register on April 13, 2000 (65 FR 19912) soliciting comments on this information collection prior to its submission to OMB. No significant comments were received.

In the past three years, FDA has received and considered several other comments from industry regarding the IDE process. Several companies submitted comments which FDA reviewed, and respondents and FDA compromised on the conclusion that the collection of information under the IDE statute is necessary and does not present an unreasonable burden to the public.

**9. Explanation of Any Payment or Gift to Respondents**

FDA will not provide any payments or gifts to respondents of this information collection.

**10. Assurance of Confidentiality Provided to Respondent**

Information in IDE's will only be released in accordance with FDA regulations implementing the Freedom of Information Act, 21 FR Part 20. Information will be protected from inappropriate disclosure.

The information obtained during an investigation may be used to support an application for marketing the device (i.e. premarket approval application or premarket notification). A summary of the safety and effectiveness data from the investigation and other information, except for trade secret, production and distribution information, will be available for public disclosure if the premarket approval application is approved, abandoned, or denied, and if the premarket notification is found substantially equivalent.

**11. Justification for Sensitive Questions**

The information required does not include questions about sexual behavior, attitude, religious beliefs, or any other matters that are commonly considered private or sensitive in nature.

**12. Estimates of Hour Burden Including Annualized Hourly Costs**

The most likely respondents to this information collection will primarily be medical device manufacturers, investigators, hospitals, health maintenance organizations, and businesses.

The number of annual respondents to this collection of information is now estimated to be 600, based on information now available due to new query capabilities of the IDE database. Based on the average number of IDE's submitted from fiscal years 1995 through 1999, approximately 600 respondents

submitted an average of 300 IDE applications (original applications) and 4,200 amendments and supplements.

The total estimated annual burden for this information collection is 61,021 hours, at a total cost of \$1,769,609.

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

Table 1 - Estimated Annual Reporting Burden					
21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
812.10	1	1	1	1	1
812.20, 812.25, and 812.27	600	0.5	300	80	24,000
812.35 and 812.150 (significant)	600	7	4,200	6	25,200
812.150 (non significant)	600	0.017	10	6	60
812.36(c)	6	1	6	120	720
812.36(f)	6	2	12	20	240
TOTALS					50,221

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

Table 2.--Estimated Annual Recordkeeping Burden

21 CFR Section	No. of Recordkeepers	Annual Frequency of Recordkeeping	Total Annual Records	Hours per Recordkeeper	Total Hours
812.140					
Original	600	0.5	300	10	3,000
Supplemental	600	7	4,200	1	4,200
Non-Significant.	600	1	600	6	3,600
Totals:					10,800

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

The estimated total cost to respondents was based on past conversations with manufacturers, industry, trade association representatives, and businesses over the last three years.

**Reporting**

Section 812.10 estimates are based on the fact that FDA has received very few, if any, waiver requests in the past, and estimates that very few will be submitted in the future. Therefore, FDA estimates a

minimal burden to account for waiver requests.

Sections 812.20, 812.25, and 812.27 estimates are based on the average of IDE's submitted from fiscal years 1995 through 1999. FDA estimates the annual reporting burden for one IDE original application to be approximately 80 hours, and the annual reporting burden for one IDE supplement to be approximately 6 hours.

Sections 812.35 and 812.150 estimates are based on the average of IDE supplements submitted from fiscal years 1995 through 1999 for significant risk device studies. FDA estimates the annual reporting burden for one IDE supplement to be approximately 6 hours.

The reporting burden for nonsignificant risk device studies (§ 812.150) is negligible. Nonsignificant risk device studies are not reported to FDA unless a problem is reported such as an unanticipated adverse device reaction, failure to obtain informed consent, withdrawal of IRB approval, or a recall of a device. In the past, an average of 10 incidences or less annually have been reported to FDA.

Section 812.36(c) and (f) estimates are based on FDA's experience with the treatment use of drugs and knowledge of the types of devices that may meet the treatment use criteria. FDA estimates that an average of six treatment use applications will be submitted each year. FDA estimates that it will take approximately 120 hours to prepare a treatment IDE and the total annual burden for preparing applications will be 720 hours. FDA also estimates that it will take approximately 20 hours to prepare a semiannual report, resulting in a total annual burden of 240 hours for annual reports.

### **Recordkeeping**

Section 812.40 estimates are based on conversations with manufacturers, industry trade association groups, and businesses over the last 3 years. For significant risk device investigations, FDA has estimated that the recordkeeping burden for preparing an original IDE submission averages 10 hours for each original IDE submission. Similarly, through the same conversations mentioned above, FDA has estimated recordkeeping for each supplement requires 1 hour. The recordkeeping burden for nonsignificant risk device investigations is difficult to estimate because nonsignificant risk device investigations are not required to be submitted to FDA. The IDE staff estimates that the number of recordkeepers for nonsignificant risk device investigations is equal to the number for active significant risk device investigations. The recordkeeping burden, however, is reduced for nonsignificant risk device studies. It is estimated that 600 recordkeepers will spend 6 hours each in maintaining these records.

### **Reporting Costs**

FDA estimates the annual reporting burden for one IDE original application to be approximately 80 hours, and the annual reporting burden for one IDE amendment and supplement to be approximately 6 hours. FDA estimates that between three and 28 days are required to compile and complete an original IDE application, depending on the complexity of the submission. Based on the Regulatory Affairs Professional Society (RAPS) "1995 Salary Survey Final Report", FDA estimates that the average cost for respondents to prepare and submit records and reports is \$29 per hour. By choosing an average time of ten days to complete an original IDE application, the total estimated cost for preparing and submitting an IDE is \$2,320. Since FDA received an average of 300 original applications per year from FY95 to FY99, the cost to respondents for submission of original applications is **\$696,000**.

In addition to the submission of an original IDE application, sponsors are also required to submit significant and non-significant supplements which are estimated to take 6 hours to complete. Using the

same cost of \$29 per hour, the estimated cost for supplement preparation is \$174. FDA averaged receipt of 4,210 significant and non-significant supplements from FY95 to FY 99, the costs to respondents for submission of supplements is estimated to be **\$732,540**.

FDA has noted that very few, if any, waiver requests have been submitted in the past, and estimates that very few will be submitted in the future. FDA has estimated that an average of 1 hours per year will be needed to account for waiver requests, and estimates total respondent reporting burden cost to be **\$29**.

Based on its experience with the treatment use of drugs and FDA's knowledge of the types of devices that may meet the treatment use criteria, FDA estimates that an average of six applications will be submitted each year. Based upon FDA's knowledge of the preparation of IDE's, FDA estimates that it will take approximately 120 hours to prepare a treatment use IDE and the total annual burden for preparing applications will be 720 hours (6 applications x 120 hours per application). FDA also estimates that it will take approximately 20 hours to prepare a semiannual report, resulting in a total annual burden of 240 hours for annual reports (6 applications x 2 annual reports x 20 hours). Therefore, FDA estimates the total cost for the treatment use section to be **\$27,840** (960 hours x \$29 per hour).

### **Recordkeeping Costs**

For significant risk devices, FDA has estimated that the recordkeeping burden for preparing an original IDE submission averages 10 hours for each original IDE submission. FDA has also estimated recordkeeping for each supplement requires 1 hour. The total cost of recordkeeping, using the same hourly figure above is \$208,800.

The recordkeeping burden for non-significant risk device investigations is difficult to estimate because nonsignificant risk device investigations are not required to be submitted to FDA. The IDE staff estimates that the number of recordkeepers for nonsignificant risk device investigations is equal to the number for active significant risk device investigations. The recordkeeping burden, however, is reduced for nonsignificant risk device studies. It is estimated that 600 recordkeepers will spend 6 hours each in maintaining these records, for a total of 3,600 hours. The total cost to recordkeepers is estimated to be \$104,400.

The recordkeeping hourly burden for this section is estimated to be 10,800 hours (3,000 original IDE hours + 4,200 IDE supplement hours + 3,600 nonsignificant risk device investigation hours). Using the RAPS figure of \$29 per hour, annual IDE recordkeeping is **\$313,200** (10,800 hours x \$29 per hour).

**13. Estimate of Other Total Annual Cost Burden to Respondents or Recordkeepers**

There will be no cost to respondents above the reporting hour burden set out in section 12 above.

**14. Annualized Cost to the Federal Government**

FDA's CDRH Automated Time Reporting System (CATRS) estimated that 97 professional and support staff years are required to process and review IDE applications (including amendments) and supplements. This amounts to a yearly total of \$8,700,900 based on a fully loaded cost of \$89,700 per staff year.

**15. Explanation for Program Changes or Adjustments**

The total annual burden requested is 61,021 hours. This represents an increase of 14,751 hours over the previous OMB submission. This increase is the result of changes to the IDE program in the past three years and the increase of a greater number of average IDE's reviewed by FDA during the past three years.

This collection of burden is also the result of the consolidation of OMB Information Collections 0910-0078, 0910-0348, and 0910-0391, and the net burden increase can also be partially attributed to this consolidation. Upon approval of this information collection, OMB collections 0910-0348 and 0910-0391 will be retired.

**16. Plans for Tabulation and Publication and Project Time Schedule**

FDA does not intend to publish the results of this information collection.

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

FDA is not seeking an exemption for display of the effective date.

**18. Exception to Certification for Paperwork Reduction Act Submissions**

There are no exceptions to the certification statement identified in item 19 of OMB Form 83-I.