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.

1. Circumstances Making the Collection of Information Necessary

The Food and Drug Administration (FDA) is requesting approval from the Office of Management and Budget (0MB) for the following information collection requirements, 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 be filed in 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. FDA approval is not required, but IRB approval is required. 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) 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 2, 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.

FDA also offers the resources of the Center for Devices and Radiological Health's (CDRH) Division of Small Manufacturers, International and Consumer Assistance (DSMICA) and the Office of Device Evaluation (ODE) staffs. CDRH established DSMICA as required by the 1976 Amendments to the Act. DSMICA'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 DSMICA 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 IDEs are required only when it is determined that clinical trials should begin. FDA believes that annual IDE and semi-annual treatment use reports are necessary to assure the protection of the public health, because investigational devices by their very nature present the potential for serious health consequences. Supplemental applications for IDE modifications are required in accordance with the law. 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 May 26, 2006 (71 FR 30425) soliciting comments on this information collection prior to its submission to OMB (Attachment D). No significant comments were received.

CDRH regularly participates in outreach activities intended to assist industry as well as the clinical and academic communities to improve their understanding and compliance with the regulations. In doing so, the quality of the contents of submissions improves and there is improvement in the way clinical trials are conducted and the data generated is analyzed. This outreach occurs through meetings with professional societies, presentations at scientific meetings and to academic institutions in conjunction with the Office of Human Research Protections (OHRP) at DHHS.

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 CFR 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 estimated to be 600, based on information available via query capabilities of the IDE database. Based on the average number of

IDE's submitted from fiscal years 2000 through 2004, approximately 600 respondents submitted an average of 275 IDE applications (original applications) and 4,700 amendments and supplements.

The current wage rate per hour for the reporting and recordkeeping activities of this information collection is estimated as follows. The Regulatory Affairs Professional Society (RAPS), on their current webpage (October 2004), estimated that the average salary for regulatory affairs professionals is $104,000 ($50 per hour.) FDA estimates, therefore that the total estimated burden cost to industry for reporting and recordkeeping activities relating to this information collection will be **$3,073,550**, which is the total number of hours expended (61,471) multiplied by the RAPS average wage rate of $50 per hour.

Questions on the burden.

How did you calculate the numbers. Usually we just multiply across.
Under the explanation of burden (page 7) for 812.35 and 812.150 for non significant devices…the burden chart only lists812.150.
Page 8: in the last paragraph before Recordkeeping Costs: the cost in the last approval was $34,560 and the cost for this years approval is $8,000. Why is there such a big discrepancy?

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

Table 1 - Estimated Annual Reporting Burden [1]

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	275	80	22,000
812.35 and 812.150 (reports for significant risk studies)	600	7.8	4,700	6	28,200
812.150 (reports for non-significant risk studies)	600	0.017	10	6	60
812.36(c)	1	1	1	120	120
812.36(f)	1	2	2	20	40
Total:					50,421

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

Table 2.--Estimated Annual Recordkeeping Burden [1]

21 CFR Section	No. of Recordkeepers	Annual Frequency of Recordkeeping	Total Annual Records	Hours per Recordkeeper	Total Hours
812.140 Original	600	0.5	275	10	2750

812.140 Supplemental	600	7	4700	1	4700
812.140 Non-significant	600	1	600	6	3600
Totals:					11050

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

Explanation of Reporting Burden Estimates

The estimated total cost to respondents was based on past conversations with manufacturers, industry, trade association representatives, and businesses over the last three years. For the purpose of this supporting statement, the "number of respondents" is defined as the estimated number of potential IDE sponsors. The "annual frequency per response" is a calculation based on the number of "total annual responses" divided by the "number of respondents." "Total annual responses" are based on an average of the previous three years receipts of the responses in question. "Total hours" is calculated by multiplying the "hours per response" by the "total annual responses."

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.

812.20, 812.25, and 812.27
Estimates are based on the average of IDE's submitted from fiscal years 2000 through 2004. FDA estimates the annual reporting burden for one IDE original application to be approximately 80 hours.

812.35 and 812.150 (reports for significant risk studies)
Estimates are based on the average of IDE supplements submitted from fiscal years 2000 through 2004 for significant risk device studies. FDA estimates the annual reporting burden for one IDE supplement to be approximately 6 hours.

812.35 and 812.150 (reports for non-significant risk studies)
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.

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 one treatment use application 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 120 hours. FDA also estimates that it will take approximately 20 hours to prepare a semiannual report, resulting in a total annual burden of 40 hours for annual reports.

Explanation of Recordkeeping Burden Estimates

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) March 2003 Internet Web Home Page, FDA estimates that the average cost for respondents to prepare and submit records and reports is $50 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 $4000. Since FDA received an average of 275 original applications per year from FY00 to FY04, the cost to respondents for submission of original applications is **$1,100,000.**.

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 $50 per hour, the estimated cost for supplement preparation is $300. FDA averaged receipt of 4,700 significant and non-significant supplements from FY00 to FY 04, the costs to respondents for submission of supplements is estimated to be **$1,410,000.**. Addition of the provision of 21 CFR 812.35 (a)(3) following FDAMA which allowed for notice of IDE changes without prior FDA approval for certain modifications to the device design or protocol, resulted in a noticeable increase in IDE supplements from 4200 in the previous report to an average of 4700 for FY00-04.

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 **$50**.

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 one application 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 120 hours (1 application 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 40 hours for annual reports (1 application x 2 annual reports x 20 hours). Therefore, FDA estimates the total cost for the treatment use section to be **$8000** (160 hours x $50 per hour). Previous supporting statements estimated that the number of treatment use IDEs that would be received

annually to be six. However, for the last several years preceding this supporting statement, less than one treatment IDE per year has been received. Therefore, the estimated number (and therefore the corresponding total cost) has been decreased from previous estimates.

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 $372,500.

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 $180,000.

The recordkeeping hourly burden for this section is estimated to be 11050 hours (2750 original IDE hours + 4,700 IDE supplement hours + 3,600 nonsignificant risk device investigation hours). Using the RAPS figure of $50 per hour, annual IDE recordkeeping is **$552,500** (11050 hours x $50 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 full-time equivalents (FTEs) are required to process and review IDE applications (including amendments) and supplements. This amounts to a yearly total of $11,031,131 based on a fully loaded cost of $113,723 per FTE.

15. Explanation for Program Changes or Adjustments

The total annual burden requested is 61,411 hours. The difference between this and the previous OMB submission is due to an increase in the number of IDE supplements and decrease in number of original IDEs.

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.

LIST OF ATTACHMENTS
for
INVESTIGATIONAL DEVICE EXEMPTIONS REPORTS AND RECORDS – 21 CFR 812

Attachment A – 520(g)(6) of the FDCA \

Attachment B - 621 CFR, Part 812

Attachment C – 21 CFR Part 11

Attachment D - 60 day Federal Register Notice