

**SUPPORTING STATEMENT FOR  
MEDICAL DEVICES; HUMANITARIAN USE DEVICES  
21 CFR Part 814 – Subpart H  
OMB Number 0910-0332**

**A. Justification**

**1. Circumstances Necessitating Information Collection**

The Food and Drug Administration (FDA) is requesting Office of Management and Budget (OMB) approval of the requirements set forth in this information collection entitled: Medical Devices; Humanitarian Use Devices, 21CFR Part 814 – Subpart H. This collection enforces the requirements of 21 CFR Part 814, Subpart H (Attachment A) and the Final Rule published in the November 3, 1998 Federal Register (Attachment B).

The purpose of the regulation is to implement the humanitarian use device (HUD) provision of the Safe Medical Devices Act of 1990 (the SMDA) (Pub. L. 101-629) and its amended rule (21 CFR 814 Subpart H). The HUD provision has been incorporated into section 520(m) (21 U.S.C. 360j(m)) of the Federal Food, Drug, and Cosmetic Act (the act), as amended by the Food and Drug Administration Modernization Act of 1997 (FDAMA). Under section 520(m) of the act, FDA is authorized to exempt a HUD from the effectiveness requirements in sections 514 and 515 of the act (21 U.S.C. 360d and 360e) provided that the device (1) is used to treat or diagnose a disease or condition that affects fewer than 4,000 individuals in the United States; (2) would not be available to a person with such a disease or condition unless the exemption is granted, and there is no comparable device, other than another HUD approved under this exemption, available to treat or diagnose the disease or condition; and (3) the device will not expose patients to an unreasonable or significant risk of illness or injury, and the probable benefit to health from using the device outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. Section 203 of FDAMA made several changes to section 520(m) of the act, and implements the amendments to the HUD provision mandated by FDAMA.

FDA is requesting Office of Management and Budget (OMB) approval for the collection of information required by the amendments to 21 CFR 814 promulgated under the statutory mandate of section 520(m) of the act, as amended by FDAMA.

**Section 814.102 – Reporting**

Prior to submitting an HDE application, the applicant shall submit a request for HUD designation to FDA's Office of Orphan Products Development.

**Section 814.104 – Reporting**

After receiving a HUD designation, the applicant shall submit an HDE application to FDA. Included in the application, as required by Section 814.104(b)(5), is a report prepared by a Certified Public Accountant or an attestation by a responsible person of the organization verifying that the amount charged does not exceed the cost of the device's research, development, fabrication, and distribution. The requirement for an attestation or a report is waived if the amount charged is \$250.00 or less.

As required by Section 814.110(a), an applicant seeking a new indication for use of a HUD approved under this subpart H shall obtain a new designation of HUD status in accordance with the procedures under §814.102 and shall submit an original HDE in accordance with the requirements under §814.104.

**Section 814.106 – Reporting**

An HDE applicant may amend a pending HDE or HDE supplement to revise existing information or provide additional information.

FDA may request the HDE applicant to amend an HDE or HDE supplement with any information regarding the device that is necessary for FDA to complete review of the HDE or HDE supplement. A copy of final printed labeling submitted to FDA following approval of an HDE application but before marketing, as provided for in Section 814.116(b), will be processed as an amendment to the HDE.

An HDE applicant may resubmit an HDE or HDE supplement after withdrawing it or after it is considered withdrawn or after FDA has refused to accept it for filing or has denied approval of the HDE or HDE supplement.

If FDA refuses to file the HDE, the applicant may submit an amendment to request in writing, in accordance with Section 814.112(b), an informal conference with the Director of the Office of Device Evaluation to review FDA's decision not to file the HDE.

If FDA is proposing to withdraw approval of an HDE, the holder of the approved application may submit an amendment to request in writing, in accordance with Section 814.118(d), an opportunity for an informal hearing.

**Section 814.108 – Reporting**

After FDA approval of an original HDE, an applicant shall submit supplements for review and approval by FDA before making a change affecting the safety or effectiveness of the device for which the applicant has an approved HDE, unless the change is of a type for which FDA has advised that an alternate submission is permitted.

**Section 814.116(d)(3)** - FDA believes that it will receive approximately 1 request to withdraw an HDE application per year, based on withdrawals submitted in FY 1997 and FY 1998. FDA estimates it will take no longer than 1 staff hour to complete each written withdrawal notice.

**Section 814.124(a) - Reporting**

This section is amended to allow physicians in an emergency situation to administer a HUD prior to obtaining Institutional Review Board (IRB) approval. In such a situation, the physician is required to provide written notification to the IRB within 5 days after emergency use.

**Section 814.124(b) – Reporting**

A holder of an, approved HDE shall notify FDA of any withdrawal of approval for the use of a HUD by a reviewing IRB within 5 working days after receipt of the withdrawal of approval.

**Section 814.126(b)(1) – Reporting**

The holder of an approved HDE shall submit a periodic report. The report is required to demonstrate continued compliance with the humanitarian device exemption (HDE).

**Section 814.126(b)(2) - Recordkeeping**

An HDE holder shall maintain records of the names and addresses of the facilities to which the HUD has been shipped, correspondence with reviewing IRB s as well as any other information requested by a reviewing IRB or FDA. Such records shall be maintained in accordance with the HDE approval order.

**2. How, by Whom, and for What Purpose Information Used**

The information gathered by this collection enables FDA to determine whether an HDE holder is in compliance with the HDE requirements. It will also allow FDA to determine whether to: (1) grant HUD designation of a medical device; (2) exempt a HUD from the effectiveness requirements in sections 514 and 515 of the act (21 U.S.C. 360d and 360e) provided that the device meets requirements set forth in section 520(m) of the act; and (3) grant marketing approval(s) for the HUD. Failure to collect this information would prevent FDA from making that determination.

**3. Consideration of Information Technology**

There are no technical or legal obstacles to the collection of this information. The principal data to be submitted will be submitting a request for HUD designation under 21 CFR 814.102 and the HDE application under 21 CFR 814.104. The use of computer technology and automation has the potential to reduce the time needed to compile records.

In the **Federal Register** of March 20, 1997 (62 FR 13430) (Attachment C), FDA published a final rule establishing procedures for electronic records, electronic signatures, and electronic submissions. Under certain circumstances, this will permit the agency to accept electronic records, electronic signatures, and handwritten signatures executed to electronic records as generally equivalent to paper records and handwritten signatures executed on paper. Organizations may use appropriate technology in accordance with this rule to comply with HUD requirements.

The intended effect of this rule 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. These regulations apply to records submitted in electronic form that are called for in Title 21 of the Code of Federal Regulations (CFR).

1. Regarding Electronic Submissions: CDRH is advising the public about electronic submissions both on the FDA

Webpage (at <http://www.fda.gov/oc/electronic submissions/interfaq.htm>), and through the CDRH website at (<http://www.fda.gov/cdrh/electsub.html>). Basically, CDRH is advising the public that CDRH will accept electronic submissions with previous approval in PDF format.

The site states: “The Center for Devices and Radiological Health (CDRH) is accepting medical device applications in electronic form. The Office of Device Evaluation (ODE) is currently developing formal guidelines regarding electronic submissions. Until they are finalized, CDRH is requesting industry to give prior notification of their desire to submit an application in electronic form. This lead time is needed to discuss any special considerations with the submitter prior to development of the documents.

The application should be submitted in a PDF format since the ODE staff will use Acrobat Exchange to review the submission. This will assure that what a reviewer sees on the screen is the same as what would have been seen on paper. PDF stands for Portable Document Format. Applications may be submitted on floppy diskettes or CD-ROM. If the application would require several diskettes, the preferred medium would be a CD-ROM.

Industry should also contact the Director of the ODE Division to which its device pertains.

It should be understood that an electronic application does not change the order in which submissions are reviewed. No preferential treatment will be given to manufacturers who submit an electronic application. In addition at least one paper copy of the submission is also required. Additional copies of some reports may be requested in order to help facilitate the review.”

To date, the use of electronic forms of recordkeeping and submissions to FDA remains voluntary.

**4. Efforts to Identify Duplication and Similar Information Already Available**

FDA believes that the information being collected will not duplicate information already available. A HUD sponsor will be provided with the opportunity to obtain marketing clearance through the HDE application procedures instead of through either the premarket notification procedures or the premarket approval application procedures.

**5. Small Business**

This information collection will not have a significant economic impact on a substantial number of small entities. While the number of HDE applications FDA will approve is unknown, FDA believes that it will approve approximately 10 HDE applications per year. Moreover, submission of HDE applications is entirely voluntary. Sponsors who believe that it will be unprofitable to submit an HDE application will be unlikely to do so. Moreover, the proposed rule will help small businesses by exempting them from full PMAs. Furthermore, these amendments minimize the burden on all entities by allowing a responsible individual of the HDE holder's organization to submit an attestation regarding the charges, in lieu of a CPA for which the organization would be compelled to pay.

**6. Consequences of Less Frequent Information Collection and Technical or Legal Obstacles**

This information is necessary to FDA to determine whether a device is eligible for HUD designation and thus exempted from the effectiveness requirements of Sections 514 and 515 of the act (21 U.S.C. 360d and 360e). (Attachment D). It is also necessary to determine whether an HDE holder is in compliance with the HDE requirements (sections 510(m)(3) and (5)) of the act.

If FDA did not receive information from potential HUD sponsors, FDA would have no basis for granting HUD exemptions. The frequency of FDA's receipt of HDE applications from sponsors will be determined by the frequency with which sponsors submit HDE applications. This frequency cannot be reduced without unnecessarily delaying marketing clearance decisions under section 520(m) of the act. The 18-month time frame for approval, which required submission of requests for extension of approval, has been removed by the amendment to § 814.100(d).

**7. Consistency With the Guidelines in 5 CFR 1320.6**

This information collection is consistent with 5 CFR 1320.6.

**8. Consultation Outside the Agency**

Notice has been published in the Federal Register on July 19, 1999 (64 FR 38673) soliciting comments on this information collection prior to its submission to the Office of Management and Budget (OMB) as required by 5 CFR 1320.8(d) (see Attachment E). No comments were received.

**9. Payment or Gifts to Respondents**

FDA will not provide payment or gifts to sponsors under the HUD provisions.

**10. Confidentiality of Information**

Section 814.122(a) states that any record in the HDE file, including all data and information submitted with or incorporated by reference into the HDE, any HDE supplement, any report under §814.126, any master file, or any other related submission, will be available for public disclosure in accordance with the restrictions and conditions available to PMA files under §814.9(b) through (h), the public information regulations at 21 CFR part 20, and any other applicable regulation governing confidentiality of information or public disclosure of information. The confidentiality of information is not affected by the amendments.

**11. Sensitive Questions**

The information collected does not include questions concerning sex, behavior, attitudes, religious beliefs, or any other private or sensitive matters.

**12. Estimates of Burden Hours and Explanation**

Table 1 provides a summary of the estimated annual reporting burden for sponsors that elect to submit an HDE application. Table 2 provides a summary of the estimated annual recordkeeping burden for sponsors. An explanation of the hour burden estimates and annualized hour burden cost follows the tables.

TABLE 1 – Estimated Annual Reporting Burden for HDE Sponsors

CFR Section	Number Of Respondents	Annual Frequency Per Respondent	Total Annual Responses	Hours Per Response	Total Hours
814.102	20	1	20	40	800
814.104	15	1	15	320	4800
814.106	15	4	60	50	3000
814.108	12	1	12	80	960
814.116(d)(3)	1	1	1	1	1
814.124(a)	5	1	5	1	5
814.124(b)	1	1	1	2	2
814.126(b)(1)	15	1	15	120	1800
TOTAL	20*		129		11368

\* There are estimated to be only 20 respondents to this information collection. Several of the respondents also are required to submit information under other sections of 21 CFR 814.100.

TABLE 2 Estimated Annual Recordkeeping Burden for HDE Sponsors

CFR Section	Number of Record Keepers	Annual Frequency Of Record Keeping	Total Annual Records	Hours per Record Keeper	Total Hours
814.126 (b) (2)	15	1	15	2	30
Total	.....	.....	.....	.....	30

**Explanation of Report Burden Estimate:**

Overall, the information requested from respondents represents, for the most part, an accounting of information already in the possession of the applicant.

**§814.102** – It is estimated that 20 sponsors per year will submit a request for HUD designation. It is estimated to require 40 staff hours to complete each HUD designation request.

**§814.104** – FDA estimates that 15 sponsors per year will submit an HDE application after receiving HUD designation. FDA estimates that it will require an average of 320 staff hours to complete each HDE application. **§814.104(b)(5)** is information required to be submitted as part of an HDE application. **§814.110(a)** requires that a new indication for use of a HUD approved under this part be submitted as a new HDE application complying with **§814.104**; however, information may be included by reference from the previous HDE application.

**§814.106** – It is estimated that 4 times per year FDA will request or the sponsor will submit additional information or resubmit an HDE or HDE supplement for approximately 15 of the submitted HDE applications. FDA estimates that it will require an average of 50 staff hours to complete each amendment or resubmitted application. Requests for an informal conference, under **§814.112(b)**, if FDA refuses to file the HDE application, will be processed as an HDE amendment. Responses to approvable letters, **§814.116(b)**, will be processed as HDE amendments. A request for an opportunity for an informal hearing, under prior to FDA issuing an order withdrawing approval, under **§814.118(d)**, will be processed as an HDE amendment.

**§814.108** – FDA anticipates that it will receive approximately 12 supplements for the submitted HDE applications. It is estimated that it will take approximately 80 staff hours to complete each supplemental application.

**814.116(d)(3)** - FDA believes that it will receive approximately 1 request to withdraw an HDE application per year, based on withdrawals submitted in FY 1997 and FY 1998. FDA estimates it will take no longer than 1 staff hour to complete each written withdrawal notice.

**§814.124(a)** - FDA anticipates that 5 physicians will use HUDs in emergency situations before obtaining IRB approval. FDA estimates that notification under this section will take an average of one hour per response.

**§814.124(b)** – FDA anticipates that 1 holder of an approved HDE will notify FDA of IRB withdrawal of approval. FDA estimates that it will take an average of one quarter of 2 staff hours to notify FDA of IRB withdrawal.

**§814.126(b)(1)** - FDA anticipates that because of this amendment, the 15 HDE holders will remain active and therefore, estimates that 15 periodic reports will be received. FDA also estimates that it will take an average 120 of staff hours to complete a periodic report as a result of this amendment.

**Explanation of Recordkeeping Burden Estimate:**

**§814.126(b)(2)** - FDA anticipates that 15 HDE holders per year will maintain records of certain information. It is estimated that it will take an average of 2 staff hours to maintain this information.

**b. Estimated Annualized Cost for the Burden Hours**

Multiplying the total reporting and recordkeeping hours (11,368) by an average rate of \$25 per hour, yields an estimate annual cost to respondents of \$284,200.

**13. Annualized Cost to Respondents**

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

**14. Annual Cost to the Government**

FDA estimates that the equivalent of 22.5 full time positions will be required to fully implement the collection of information and response to applicants/sponsors required as a result of the requirements of section 520(m) of the act and the implementing regulation. These positions are expected to cost the government about \$1,350,000 on average, based on the mix of staff expertise required to implement the HUD. The positions range from GS-5 clerical personnel to GS-15 medical officers; and the average cost for each position is \$60,000 (\$55,000 for personnel costs and benefits and \$5,000 of operating funds per year at a total cost of \$60,000 for each full time position).

**15. Changes in Burden**

This collection of burden is the result of the consolidation of OMB Information Collections 0910-0332 and 0910-0384. The net burden for this collection, due to its consolidation is a reduction of burden of 673 hours, which is the result of an adjustment to the new, combined information collection.

**16. Statistical Reporting**

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

**17. Exemption for Display of Expiration Date**

No exemption approval is requested.

**18. Exemption to Certification Statement**

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

**19. Certification for Paperwork Reduction Act Submissions**

## 19. Certification for Paperwork Reduction Act Submissions

On behalf of this Federal Agency, I certify that the collection of information encompassed by this request complies with 5 CFR 1320.9

**NOTE:** The text of 5 CFR 1320.9, and the related provisions of 5 CFR 1320.8(b)(3), appear at the end of the instructions. *The certification is to be made with reference to those regulatory provisions as set forth in the instructions.*

The following is a summary of the topics, regarding the proposed collection of information, that the certification covers:

- (a) It is necessary for the proper performance of agency functions;
- (b) It avoids unnecessary duplication;
- (c) It reduces burden on small entities;
- (d) It used plain, coherent, and unambiguous terminology that is understandable to respondents;
- (e) Its implementation will be consistent and compatible with current reporting and recordkeeping practices;
- (f) It indicates the retention period for recordkeeping requirements;
- (g) It informs respondents of the information called for under 5 CFR 1320.8(b)(3):
  - (I) Why the information is being collected;
  - (ii) Use of information;
  - (iii) Burden estimate;
  - (iv) Nature of response (voluntary, required for a benefit, mandatory);
  - (v) Nature and extent of confidentiality; and
  - (vi) Need to display currently valid OMB control number;
- (h) It was developed by an office that has planned and allocated resources for the efficient and effective management and use of the information to be collected (see note in Item 19 of instructions);
- (I) It uses effective and efficient statistical survey methodology; and
- (j) It makes appropriate use of information technology.<sup>1</sup>

If you are unable to certify compliance with any of the provisions, identify the item below and explain the reason in Item 18 of the Supporting Statement.

Signature of Senior Official or designee

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**B. Collection Of Information Employing Statistical Methods**

The use of statistical methods is not applicable.

List of Attachments:

- Attachment A - U.S. Code of Federal Regulations, 21 CFR Part 814
- Attachment B - Federal Register Notice 63 FR 59217, November 3, 1998, Notice of Final Rule
- Attachment C - Federal Register Notice 63 FR 13430, March 20, 1997, Notice regarding Electronic Records and Signatures
- Attachment D - Federal Food, Drug, and Cosmetic Act, Sections 514 & 515 (21 U.S.C. 360d and 360e)
- Attachment E - Federal Register Notice (64 FR 38673), July 19, 1999, 60 Day notice seeking comment on this information collection
- Attachment F - Federal Register Notice 63 FR 19185, April 17, 1998, Notice seeking comment on OMB Information Collection 0910-0384