SUPPORTING STATEMENT FOR
HUMANITARIAN DEVICE EXEMPTION HOLDERS, INSTITUTIONAL REVIEW BOARDS (IRBS), CLINICAL INVESTIGATORS AND FDA STAFF
HUMANITARIAN DEVICE EXEMPTION (HDE) REGULATION: QUESTIONS AND ANSWERS

A. Justification

1. Circumstances Necessitating the Collection of Information

Under section 520(m) (21 U.S.C. 360j(m)of the act, the 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 (4) 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.

Title III of Food and Drug Administration Amendments Act, (FDAAA), http://www.fda.gov/opacom/laws/fdcact/fdcact5a2.htm#sec515 amended section 520(m) of the act as follows: Section 520(m)(6)(A)(ii) provides that the Secretary of Health and Human Services will assign an annual distribution number for devices indicated for use in pediatric patients or in a pediatric subpopulation. The annual distribution number shall be based on the following information in an HDE application: (1) the number of individuals affected by the disease or condition that such devices are intended to treat, diagnose, or cure, and of that number (2) the number of individuals likely to use the device and (3) the number of devices reasonably necessary to treat such individuals.

Section 520(m)(6)(A)(iii), http://www.fda.gov/opacom/laws/fdcact/fdcact5a2.htm#sec520 provides that an HDE holder immediately notify the agency if the number of devices distributed during any calendar year exceeds the annual distribution number. Section 520(m) (6)(C) provides that an HDE holder may petition to modify the annual distribution number if additional information on the number of individuals affected by the disease or condition arises. FDA is requesting OMB approval for the collection of information required under the statutory mandate of Section 520(m) of the act as amended by FDAAA.

Reporting Requirements:

515(a)(2)

Requires that an HDE application include a description of any pediatric subpopulations that suffer from the disease or condition that the device is intended to treat, diagnose, or cure and the number of affected pediatric patients.

520(m)(6)(A)(ii)

Provides that the Secretary will assign an annual distribution number for devices indicated for pediatric patients. The annual distribution number shall be based on the following information in an application: the number of individuals affected by the disease or condition that such device is intended to treat, diagnose, or cure and of that number, the number of individuals likely to use the device, and the number of devices reasonably necessary to treat such individuals.

520(m)(6)(A)(iii)

Requires an HDE holder immediately notify the agency if the number of devices distributed during any calendar year exceeds the annual distribution number.

520(m)(6)(C)

Provides that an HDE holder may petition to modify the annual distribution number if additional information on the number of individuals affected by the disease or condition arises.

2. Purpose and Use of the Information

HUDs are subject to the general restriction that no profit may be made on their use. For HUDs labeled for use in pediatric patients or in a pediatric subpopulation, FDA exempts a certain number of these devices each year from the prohibition on profit. This number is known as the annual distribution number. The information gathered by this collection enables FDA to set this number. Failure to collect this information would prevent FDA from assigning an annual distribution number.

3. Consideration of Information Technology

There are no technical or legal obstacles to the collection of this information. Data regarding pediatric populations or pediatric subpopulations are to be included in the original HDE application under 21 CFR 814.104. FDA accepts and encourages the submission of electronic copies from any manufacturer that wishes to submit an

electronic copy with a premarket submission. (See CDRH's website at http://www.fda.gov/cdrh/elecsub.html.)

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 an annual distribution number through the HDE application procedures. A separate application is not required.

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 5 HDE applications per year. Although 515A requires that HDE applications include a description of any pediatric subpopulations that suffer from the disease or condition that the device is intended to treat, diagnose, or cure and the number of affected pediatric patients, this additional information is only required if readily available. Furthermore, section 814.104(b)(5) minimizes 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 in order to set an ADN thereby exempting a certain number of these devices each year from the prohibition on profit. If FDA did not receive information from potential HUD applicants, FDA would have no basis for setting the ADN. The frequency of FDA's receipt of data regarding pediatric populations and subpopulations will be determined by the frequency with which applicants submit HDE applications as well as the frequency with which applicants notify the FDA that the number of devices distributed in the year has exceeded the ADN. This frequency cannot be reduced without unnecessarily delaying marketing clearance decisions under section 520(m) of the act or without delaying the establishment of the annual distribution number.

7. Consistency With the Guidelines in 5 CFR 1320.6

This collection of information is consistent with the guidelines prescribed in 5 CFR 1320.6.

8. Consultation Outside the Agency

As required by 5 CFR 1320(d) a notice was published in the Federal Register on August 5, 2008, 73 FR 151, http://www.fda.gov/OHRMS/DOCKETS/98fr/E8-17905.pdf, soliciting comments on this information collection prior to its submission to the Office of Management and Budget (OMB). The Agency received seven comments in response to the Federal Register notice. Six of the seven comments were substantive. Most of the comments were in the form of questions regarding the following topic areas: HDEs and Pediatric Patients, After FDA Approves an HDE, The Role of Institutional Review Boards (IRBs), and Using HUDs in Emergency Use Situations.

Changes were made to the guidance in response to some of the comments. Several of the comments sought clarification regarding when the Annual Distribution Number (ADN) reporting requirement applied. A paragraph was added to clarify that the ADN relates only to those devices that are on the market through the HDE process for a disease or condition that occurs in pediatric patients or in a pediatric subpopulation. The response to Question 27 was augmented to include the phrase "independent IRB" to clarify that not all IRBs are internal bodies within a hospital or clinic.

The word "narrowly" was removed from the phrase "narrowly exempt" in questions 29 and 30 so as not to characterize a device's exempt status as one that is narrowly exempt from regulatory requirements.

Question 31 was augmented to describe the different reporting requirements for manufacturers and for user facilities. Manufacturers must submit reports to FDA and the "IRB of record" whenever a HUD may have caused or contributed to a death or serious injury, or has malfunctioned and would be likely to cause or contribute to a death or serious injury if the malfunction were to recur (21 CFR 803.50 and 814.126(a)). User facilities must submit reports to FDA, the "IRB of record" and the manufacturer whenever a HUD may have caused or contributed to a death, and must submit reports to the manufacturer (or to FDA and the "IRB of record" if the manufacturer is unknown) whenever a HUD may have caused or contributed to a serious injury (21 CFR 803.30 and 814.126(a)).

Some of the comments related to the placement of information in the draft guidance. Question 40, "If a HUD is being investigated in an IDE study for a different indication, does it impact the number of allowable patients under the HDE" was redesignated as question 35 and moved from the IRB section of the guidance and placed in the section, "After FDA Approves an HDE" as it did not pertain directly to IRBs.

Changes were made to the section, "The Role of Institutional Review Boards (IRBs)," question 37, specifically to clarify the distinction between 'use' of and HUD and 'investigational use/clinical investigation' pf a HUD. Specifically FDA clarified that the term "use" in the guidance, when unmodified, refers to the use of a HUD according to its approved labeling and indication(s). If a HUD is being used in a clinical investigation (i.e., collection of safety and effectiveness data), whether for its HDE-approved indications or for a different indication, then this document refers to "investigational use" or "clinical investigation" of the HUD. Finally in addition to adding clarifying

information, a decision tree was also added to the guidance for ease of reference for IRBs.

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 pertaining to sexual behavior, attitude, religious beliefs, or any other matters that are commonly considered private or sensitive in nature.

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.

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

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN[1]

Section of the FDAAA	No. of Applicants	Annual Frequency per Response	Total Annual HDE Applications	Hours per Response	Total Hours
515A(a)(2)	5	1	5	100	500
520(m)(6)(A)(ii)	3	1	3	50	150
520(m)(6)(A)(iii)	1	1	1	100	100
520(m)(6)(C)	5	1	5	100	500
Total					1250

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

FDA based these estimates on the number of original HDE applications that they received in the period between Oct 1, 2004 and Sept 30, 2007. During that time, CDRH received 16 original HDE applications, or about 5 per year. FDA estimates that for each year they will receive 5 HDE applications and that 3 of these applications will be indicated for pediatric use. FDA estimates that one HDE holder will notify the agency that the number of devices distributed in the year has exceeded the annual distribution number and 5 HDE holders will petition to have the annual distribution number modified due to additional information on the number of individuals affected by the disease or condition.

Cost to Respondents

Based on the 2006-2008 Department of Labor National Compensation Survey for Civilian Workers, the hourly cost to provide this information is $39.00 per hour. The total cost is $3,900.

13. Estimates of Other Total Annual Cost Burden to Respondents

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

14. Annual Cost to the Government

FDA estimates that 22.5 full time equivalent (FTE) positions will be required to fully implement the collection of information and response to applicants and holders 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 $2,704,080 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 $118,600 ($113,600 for personnel costs and benefits and $5,000 of operating funds per year at a total cost of $118,600 for each full time position).

15. Changes in Burden

This is a new information collection.

16. Statistical Reporting

There are no statistical reporting requirements.

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. Collection of Information Employing Statistical Methods

The use of statistical methods is not applicable.