Information to Accompany Humanitarian Device Exemption Applications and Annual Distribution Number Reporting Requirements

0910-0661
SUPPORTING STATEMENT

Terms of Clearance: None.

A. Justification

1. Circumstances Making the Collection of Information Necessary

Under section 520(m) (21 U.S.C. 360j(m)) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act), the FDA is authorized to exempt a humanitarian use device (HUD) from the effectiveness requirements in sections 514 and 515 of the FD&C 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; (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.

HUDs approved under a Humanitarian Device Exemption (HDE) cannot be sold for an amount that exceeds the costs of research and development, fabrication, and distribution of the device (i.e., for profit), except in narrow circumstances. Section 613 of the Food and Drug Administration Safety and Innovation Act (FDASIA) (Pub. L. 112-144), signed into law on July 9, 2012, amended section 520(m) of the FD&C Act. Under section 520(m)(6)(A)(i) of the FD&C Act, as amended by FDASIA, a HUD approved under an HDE is eligible to be sold for profit if the device meets the following criteria:

1. The device is intended for the treatment or diagnosis of a disease or condition that occurs in pediatric patients or in a pediatric subpopulation, and such device is labeled for use in pediatric patients or in a pediatric subpopulation in which the disease or condition occurs; or

2. The device is intended for the treatment or diagnosis of a disease or condition that does not occur in pediatric patients or that occurs in pediatric patients in such numbers that the development of the device for such patients is impossible, highly impracticable, or unsafe.

Section 520(m)(6)(A)(ii), as amended by FDASIA, provides that the Secretary of Health and Human Services (the Secretary) will assign an annual distribution number (ADN) for devices that meet the eligibility criteria to be permitted to be sold for profit.. The ADN is defined as the number of devices "reasonably needed to treat, diagnose, or cure a

population of 4,000 individuals in the United States," and therefore shall be based on the following information in a humanitarian device exemption (HDE) application: the number of devices reasonably necessary to treat such individuals.

Section 520(m)(6)(A)(iii) (http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/FDCActChapterVDrugsandDevices/default.htm) provides that an HDE holder immediately notify the agency if the number of devices distributed during any calendar year exceeds the ADN. Section 520(m)(6)(C) provides that an HDE holder may petition to modify the ADN if additional information arises.

On August 5, 2008, FDA issued a guidance entitled "*Guidance for HDE Holders, Institutional Review Boards (IRBs), Clinical Investigators, and Food and Drug Administration Staff – Humanitarian Device Exemption (HDE) Regulation: Questions and Answers*" (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm110203.pdf). The guidance was developed and issued prior to the enactment of FDASIA, and certain sections of this guidance may no longer be current as a result of FDASIA. The Center for Devices and Radiological Health and the Center for Biologics Evaluation and Research are currently working on a draft HDE guidance, that when finalized, will represent the FDA's current thinking on this topic.

FDA is requesting OMB approval for the collection of information required under the statutory mandate of sections 515A and 520(m) of the FD&C Act as amended.

Reporting Requirements:

Pediatric Subpopulation and Patient Information--Section 515A(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.

Exemption from Profit Prohibition--Section 520(m)(6)(A)(i) and (ii)
Provides that the HUD meets the eligibility criteria under section 520(m)(6)(A)(i) to be exempt from the profit prohibition on HUDs approved under an HDE, the Secretary will determine the ADN when the Secretary grants the HDE. The ADN shall be based on the number of such devices reasonably needed to treat, diagnose, or cure a population of 4,000 individuals in the United States.

Request for Determination of Eligibility Criteria—Section 613(b) of FDASIA
A sponsor of a HUD for which an HDE was approved prior to the enactment of FDASIA on July 9, 2012, may seek a determination that their HUD meets the eligibility criteria for exemption from the profit prohibition for an HUD under section 520(m)(6)(A)(i) of the FD&C Act. If the Secretary determines that the HUD meets the eligibility criteria, the Secretary will determine the

ADN for the HUD.

ADN Notification--Section 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 ADN.

ADN Modification--Section 520(m)(6)(C)
Provides that an HDE holder may petition to modify the ADN if additional information arises.

2. Purpose and Use of the Information Collection

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

3. Use of Improved Information Technology and Burden Reduction

There are no technical or legal obstacles to the collection of this information. Data regarding patient populations are to be included in the original HDE application under § 814.104 (21 CFR 814.104).

Section 745A(b) of the FD&C Act, added by section 1136 of the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA), provides statutory authority to require eCopies after issuance of final guidance (See Public Law No: 112-144). FDA's implementing guidance (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM313794.pdf) describes how device companies should replace one paper copy of a device application with an eCopy and identify the required format and technical requirements of the eCopy. The eCopy requirement does not require or request any information that is not already submitted to the Agency and/or covered under an existing ICR. The process is as simple as saving the submission to CD rather than printing an additional copy. Because we have determined that there is no change in the hour burden between an all-paper submission and one with an eCopy and there is no change to the cost burden (the validation software is free, and optional), FDA does not believe the new eCopy requirement will change any cost or hourly burden in any of the existing ICRs affected by eCopy. OMB approved this non-material/nonsubstantive change on December 17, 2012.

FDA estimates that 100% of the respondents will use electronic means to fulfill the agency's requirement or request.

4. Efforts to Identify Duplication and Use of Similar Information

   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 ADN through the HDE application procedures. A separate application is not required.
5. Impact on Small Businesses or Other Small Entities

   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 3 HDE applications per year. Although section 515A of the FD&C Act 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, § 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 amount to be charged for the device, in lieu of an independent certified public accountant for which the organization would be compelled to pay.
6. Consequences of Collecting the Information Less Frequently

   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 patient populations 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 approval decisions under section 520(m) of the FD&C Act or without delaying the establishment of the ADN.
7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

   There are no special circumstances for this collection of information.
8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

   In accordance with 5 CFR 1320.8(d), FDA published a 60-day notice for public comment in the Federal Register of December 17, 2012 (77 FR 74667). No comments were received.
9. Explanation of Any Payment or Gift to Respondents

   FDA will not provide payment or gifts to sponsors under the HUD provisions.
10. Assurance of Confidentiality Provided to Respondents

    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. Justification for 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 Annualized Burden Hours and Costs

12 a. Annualized Hour Burden Estimate

Table 1 provides a summary of the estimated annual reporting burden for sponsors that elect to submit an HDE application.

Table 1.--Estimated Annual Reporting Burden

Activity/Section of FD&C Act (as amended) or FDASIA	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Pediatric Subpopulation and Patient Information--515A(a)(2) of the FD&C Act	6	1	6	100	600
Exemption from Profit Prohibition Information--520(m)(6)(A)(i) and (ii) of the FD&C Act	3	1	3	50	150
Request for Determination of Eligibility Criteria--613(b) of FDASIA	2	1	2	10	20
ADN Notification--520(m)(6)(A)(iii) of the FD&C Act	1	1	1	100	100
ADN Modification--520(m)(6)(C) of the FD&C Act	5	1	5	100	500
Total					1,370

FDA based these estimates on the number of original HDE applications that they received in the period between Oct 1, 2008 and Sept 30, 2011. During that time, CDRH received 19 original HDE applications, or about 6 per year. FDA estimates that for each year they will receive 6 HDE applications and that 3 of these applications will be indicated for pediatric use. The request for determination of eligibility criteria is a new under section 613(b) of FDASIA. We estimate that we will receive approximately 2 such requests per year. Historically, no companies have exceeded the ADN; and under FDASIA the ADN has expanded to a minimum of 4,000. Therefore, FDA estimates that very few or no HDE holders will notify the agency that the number of devices distributed in the year has exceeded the ADN. FDA estimates that 5 HDE holders will petition to have the ADN modified due to additional information on the number of individuals affected by the disease or condition.

12b. Annualized Cost Burden Estimate

Based on the May 2011 Bureau of Labor Statistics wage rate estimate for Administrative Services Managers (occupation code 11-3011; http://www.bls.gov/oes/current/oes_nat.htm) the mean hourly cost to provide this information is $42.00 per hour. The total cost is $57,540.

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
Administrative services managers	1,370	$42	$57,540

13. Estimates of Other Total Annual Costs to Respondents and/or Recordkeepers/Capital Costs

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

14. Annualized Cost to the Federal 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 FD&C Act and 21 CFR 814.126. The positions range from GS-5 clerical personnel to GS-15 medical officers. The cost of a CDRH FTE in FY 2012 is $209,632 (FY 2012 President's Budget Request All Purpose Table – Total Program Level). Therefore, the expected annualized cost to the Federal government is approximately $4,716,720.

15. Explanation for Program Changes or Adjustments

FDA revised the title of the information collection to more accurately reflect its content subsequent to the FDASIA amendment.

FDA has increased the reporting burden estimate slightly to reflect the expected number of respondents for pediatric subpopulation and patient information based on updated data from the last three years and our expectation of an increase due to the FDASIA legislation. The total burden hours will, therefore, increase by 120 to 1,370.

The annualized cost burden estimate has increased by $53,640 to $57,540 due to updated wage rates and to correct a miscalculation in the previously approved cost burden estimate, which only accounted for the cost burden for a single response to a 100-hour burden.

Under section 1136 of the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA), FDA now requires an eCopy of submissions. We have added text describing the eCopy requirement in section 3 of this supporting statement, "Use of Improved Information Technology and Burden Reduction." As described in section 3, the new eCopy requirement does not change any cost or hourly burden. OMB approved this non-material/nonsubstantive change on December 17, 2012.

16. Plans for Tabulation and Publication and Project Time Schedule

There are no statistical reporting requirements.

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

FDA is not seeking approval not to display the expiration date of OMB approval.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.