Safety Assurance Case

[OMB Approval No. 0910-NEW]

SUPPORTING STATEMENT

Terms of Clearance: None.

A. Justification

1. Circumstances Making the Collection of Information Necessary

The FDA has evaluated a broad spectrum of infusion pumps across manufacturers and has identified problems with device software, human factors, reliability and manufacturing. Based on an evaluation of reported adverse events and recalls, FDA believes that many injuries and adverse events may be avoided by improving the design verification and validation processes for these devices. The most frequently reported infusion pump device problems are: software error messages, human factors (which include, but are not limited to, use error), broken components, battery failure, alarm failure, over infusion and under infusion. In some reports, the manufacturer was unable to determine or identify the problem and reported the problem as "unknown." Subsequent root cause analyses undertaken during recall revealed that many of these design problems could be corrected.

In January 2011, the Food and Drug Administration (FDA) announced its intention to evaluate the use of assurance cases as part of our Plan of Action to strengthen the 510(k) program following the publication of the draft guidance on infusion pumps (4/26/2010, 75 FR 21632. The initial test assurance case focused on infusion pumps because the Infusion Pump Improvement Initiative was also exploring the use of assurance cases as a means of improving premarket review. The infusion pump assurance case beta testing included infusion pump devices classified under 21 CFR 880.5725.

The assurance case consists of a structured argument, supported by a body of valid scientific evidence that provides an organized and comprehensible case that the infusion pump is comparably safe for its intended use within its environment of use. The argument should be commensurate with the potential risk posed by the infusion pump, the complexity of the infusion pump, and the familiarity with the identified risks and mitigation measures.

Assurance cases are dependent on individual product specifications, hazards, design, and documentation. For this reason, assurance cases are considered to be device-specific, meaning any newly developed device would have its own unique assurance case. If the manufacturer submits a 510(k) for modifications to a legally marketed infusion pump for which no assurance case exists, FDA recommends that manufacturers develop and submit a case for their infusion pump.

Following the completion of the assurance case beta testing, FDA has written an Infusion Pump Total Life Cycle final guidance with recommendations for how manufacturers of infusion pumps should submit an assurance case with their premarket notification (510(k)) submissions. The guidance recommends that an assurance case demonstrate mitigation of infusion pump related hazardous situations through analysis of operational, environmental, electrical, hardware, software, mechanical, biological, chemical, and use hazards, as appropriate.

FDA is requesting approval for the information collection requirements contained within an assurance case. The assurance case requires the device sponsor to explicitly describe how and why their device meets FDA regulatory requirements, as they relate to safety.

Premarket Notification Submission- 21 CFR Part 807

Section 510(k) of the FD&C Act and 21 CFR 807.87(f) requires a showing that the device is similar to predicate devices and that showing needs to include data. An assurance case is a systematic showing of similarities / differences to a predicate device, as those similarities / differences relate to safety. Without systematically demonstrating how the design of device is similar or different, and how those similarities or differences impact safety, it is likely that the reviewer will not consider important information that could affect the review decision.

Additionally, 21 CFR 807.87(g) requires a manufacturer to demonstrate that consequences and effects of modifications have been adequately considered for the safety and effectiveness of the device. Typically, these analyses focus on the local impact to the device subsystems. An assurance case would demonstrate local effects, as well as systemic effects, of the modifications. This is because the assurance case is not created just for purposes of the modification, but was previously created for the complete device system. Modifications to the assurance case are therefore more likely to demonstrate the inter-relationships of the modifications to the complete system. The assurance case also requires a systematic review, thereby reducing the likelihood that information will be ignored or overlooked.

2. Purpose and Use of the Information Collection

In making a determination of substantial equivalence for an infusion pump, FDA recommends that manufacturers submit information through a framework known as an assurance case.

Assurance cases are best developed in parallel to the devices they are intended to support. Constructing an assurance case in concert with the device will not only allow for better design of safety requirements, claims, arguments, and evidence, it will reduce the costs of retrospective mitigations that may be necessary if it is determined that a finished design is not adequately safe. Furthermore, the assurance cases are intended to improve the quality of infusion pumps and thereby reduce the incident of safety and protection of public health.

Respondents to this collection of information are private sector for-profit businesses.

3. Use of Improved Information Technology and Burden Reduction

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 implemented eCopy requirements on January 1, 2013, with the issuance of the final eCopy guidance (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM313794.pdf). The guidance describes how device companies must replace at least one paper copy of a device application with an eCopy and identify the required format and technical requirements of the eCopy. The eCopy program, as well as the technical standards for an eCopy, are described in the guidance. The eCopy requirements do not require or request any information that is not already submitted to the Agency and/or covered under the existing Premarket Notification (510(k)) ICR (OMB control number 0910-0120) and, therefore, did not change the cost or hour burden.

Because an assurance case would be submitted as part of the 510(k) documentation, FDA estimates that 100% of the respondents will use electronic means to fulfill the information collection.

4. Efforts to Identify Duplication and Use of Similar Information

FDA is the only agency responsible for the collection of this information, and there are no requirements for the submission of similar information. Therefore, no duplication of data exists. No data exists from any source, other than the premarket notification submitter, that can be used to provide FDA with information regarding an assurance case for medical devices.

5. Impact on Small Businesses or Other Small Entities

FDA estimates that approximately 25% of respondents to the information collection are small businesses. FDA aids small business in dealing with the requirements of the regulations by providing guidance and information through the Division of Small Manufacturers, International, and Consumer Assistance (DSMICA), and through the scientific and administrative staff, workshops in which FDA Staff participate, and through the CDRH website at http://www.fda.gov/MedicalDevices/default.htm. These efforts help to assure that the burden on all manufacturers, including small manufacturers, is minimized.

6. Consequences of Collecting the Information Less Frequently

An assurance case is submitted when a sponsor submits a new premarket submission (510(k)) or a 510(k) supplement for a legally marketed device for which no assurance case exists. Therefore, we estimate that the information will be collected occasionally.

The information collected in the assurance case is necessary for FDA to ensure that only those submissions for devices subject to the 510(k) requirements of the FD&C Act,

which are as safe and effective as legally marketed predicate devices, are cleared for marketing in the U.S. The consequence of not obtaining this information would be that FDA would not be able to assure that device hazards are being mitigated equivalently to infusion pump predicate devices.

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 3/18/2013 (78 FR 16676). FDA received two comments for this Notice.

One commenter had created their own assurance case and used their results to assist in answering the 60 day Notice. The commenter developed an Infusion Pump Assurance Case (IPAC) report template and conducted an informal survey of infusion pump manufacturers asking them to estimate the time and resources required to prepare their assurance case submissions in man months. Based on company responses, the average in man months for development of an assurance case was 12.83 man months. The highest response was 36 man months. Even with use of a least burdensome template similar to the IPAC, we would anticipate that the number of hours to prepare an assurance case submission would be significant. The commenter does not provide the methodology used in their estimate of man months, including details regarding the number of hours in a man month. Therefore, we decline to adjust our burden hour estimate at this time.

Another commenter estimates the time that it takes infusion pump manufacturers to complete an assurance case report is approximately 560 hours for a manufacturer with experience completing assurance case reports, which is substantially longer than FDA's estimate of approximately 112 hours. Increased knowledge and experience in creating assurance case reports has reduced the number of hours required, and the commenter estimates that this equates to approximately 10 hours needed for each of the 56 hazards identified in the draft guidance, or 560 hours allotted for an experienced team.

Though the commenter's assurance case was comprehensive, it included activities that should already be conducted under their existing design controls (e.g., gathering data from all aspects of product development and performing a cross-functional review).

Table 1.--Estimated Annual Reporting Burden

Guidance Title: Infusion Pumps--Premarket Notification 510(k) Submissions	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Guidance Section 6--Assurance Case Report	31	1	31	112	3,472

These activities are already covered under the Quality Systems ICR (OMB control number 0910-0073) and, to avoid double-counting the burden, should not be counted as burden in this information collection request.

FDA has been engaged over the past two years in the creation of an assurance case argument structures for use in the final infusion pump guidance and the Association for the Advancement of Medical Instrumentation (AAMI) Technical Information Reports. These are certainly time-intensive efforts. However, in our own experience, much of the effort is focused on correct and complete identification of hazards and effective mitigation strategies. Again, these activities, while used to support the bulk of the assurance case, are already required and should therefore not be counted as burden in this information collection request.

9. Explanation of Any Payment or Gift to Respondents

No payment or gifts in any manner or form shall be provided to respondents to this information collection.

10. Assurance of Confidentiality Provided to Respondents

For this collection, an assurance case will have the same confidentiality requirements as a 510(k) because it is submitted as part of a 510(k) submission. Confidentiality of information submitted to FDA under a premarket notification is governed by the provisions of 21 CFR part 20 and section 807.95, and is mandated.

These provisions do not permit disclosure of information in a premarket notification submission that is trade secret or commercial confidential unless that information has been previously disclosed or as permitted under the Federal Freedom of Information Act. Under the Freedom of Information Act (FOIA) (5 U.S.C. 552), the public has broad access to government documents. Information provided under this collection is handled in a manner to comply with the FDA regulations on public information in 21 CFR Part 20. Data will be kept private to the fullest extent allowed by law.

11. Justification for Sensitive Questions

This information collection does not include questions pertaining to sexual behavior and attitudes, religious beliefs, and other matters that are commonly considered private.

12. Estimates of Annualized Burden Hours and Costs

12 a. Annualized Hour Burden Estimate

FDA's estimate of 46 respondents is based on the number of manufacturers of infusion pumps currently listed in FDA's Registration and Listing database (FURLS). The estimated average burden per response, 112 hours, is based on FDA's expectation of the amount of information that will be contained in the report, on public comment received regarding the burden, on consultation with stakeholders/industry, and on FDA's experience in the creation of an assurance case argument structures for use in the guidance. Our estimate also reflects that some information used to support the assurance case, such as activities conducted under existing design controls, is already covered in

another ICR (OMB control number 0910-0073) and is therefore not included in the burden estimate in this information collection request.

The respondents to this collection of information are infusion pump manufacturers. FDA estimates the burden of this collection of information as follows:

12b. Annualized Cost Burden Estimate

FDA believes that the average cost to industry per hour for this type of work is $65. This is based on May 2012 wage estimates issued by the Bureau of Labor Statistics (http://www.bls.gov/oes/current/oes_nat.htm) for the "Marketing Manager" and "Lawyer" occupations (occupation codes 11-2021 and 23-1011, respectively). Therefore, FDA estimates the total annual reporting cost to industry for submissions of an assurance case report is 5,152 total hours multiplied by $65 per hour equals $334,880. When divided by 46 submissions, this is an average of $7,280 per submission.

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

    There are no capital, start-up, operating or maintenance costs associated with this information collection.

14. Annualized Cost to the Federal Government

FDA's review of assurance cases will be conducted as part of the 510(k) submission. There are currently no plans to increase the number of full time equivalent (FTE) positions that review 510(k) submissions because of the addition of safety assurance cases to some 510(k) submissions. Additionally, there is no expectation that the review time would exceed the time allotted for 510(k) review by MDUFA because of the addition of assurance cases. The cost to Federal Government of a 510(k) review is already covered in the Premarket Notification (510(k)) ICR (OMB control number 0910-0120). Therefore, there is no additional cost to the Federal Government for assurance cases.

15. Explanation for Program Changes or Adjustments

This is a new information collection.

16. Plans for Tabulation and Publication and Project Time Schedule

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

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

FDA is not requesting an exemption for display of the OMB expiration date.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.