May 8, 2014

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

And

oire_submission@omb.eop.gov

RE: Docket No. FDA-2010-D-0194: Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Draft Guidance for Industry and FDA Staff; Total Product Life Cycle: Infusion Pump—Premarket Notification Submissions

And

RE: OMB Control Number: 0910–NEW - “Draft Guidance for Industry and FDA Staff; Total Product Life Cycle: Infusion Pump—Premarket Notification [510(k)] Submissions”

Dear Sir/Madam:

The Advanced Medical Technology Association (AdvaMed) is pleased to comment on the Food and Drug Administration’s (FDA’s) Paperwork Reduction Act of 1995 Collection of Information associated with the Draft Guidance for Industry and Food and Drug Administration Staff; Total Product Life Cycle: Infusion Pump—Premarket Notification [510(k)] Submissions and to submit these comments to the Office of Management and Budget under OMB Control Number 0910-New-“Draft Guidance for Industry and FDA Staff; Total Product Life Cycle: Infusion Pump—Premarket Notification [510(k)] Submissions.”

AdvaMed represents manufacturers of medical devices, diagnostic products, and health information systems that are transforming health care through earlier disease detection, less invasive procedures, and more effective treatments. Our members produce nearly 90 percent of the health care technology purchased annually in the United States and more than 50 percent of such technology purchased annually around the world. These members range from the smallest to the largest medical technology innovators and companies. Nearly 70 percent of our members have less than $30 million in sales annually.

There are several points raised in the April 9, 2014 Federal Register (FR) Notice that we would like to comment on. These points are:
1. Clarification of the “man-month” unit of measure.
   2. Clarification of why we believe “double-counting” is not occurring in burden estimation.
   3. Clarification of why we believe our initial estimates were low.

Additionally, we would also like to discuss the process steps associated with development of a safety assurance case to demonstrate the complexity and burden associated with this task.

Finally, we would like to expand upon the comments we made in response to the March 18, 2013 Federal Register notice on the Paperwork Reduction Act of 1995 regarding the draft guidance on the Total Product Life Cycle: Infusion Pump—Premarket Notification [510(k)] Submissions.

1. **Clarification of the “man-month” as a unit of measure**
   The information provided by AdvaMed was the result of an anonymous survey sent to infusion pump manufacturers that had created a safety assurance case for submission to the FDA. For convenience purposes, the information collected by the AdvaMed survey was reported in “man-months,” a popular unit of measure used in project management. A man-month is 172 hours, and it represents a single person working 40 hours per week over the period of 1 month (4.3 weeks). Therefore, the AdvaMed estimate of 12.83 man-months is equivalent to 2,207 man-hours. It should be noted that this may not directly correlate to duration (i.e., calendar months) because human resources are not 100 percent allocated to individual tasks.

2. **Clarification of why we believe “double-counting” is not occurring in burden estimation**
   The FR Notice also states that another commenter’s time estimate of 560 hours was an overestimate due to double-counting of information that already exists, per OMB control number 0910–0073. We disagree with FDA’s premise that this is double-counting. While it is true that many elements of an assurance case already exist in Design History File artifacts, not all of the elements exist, and some amount of time is needed to document these additional elements. Additionally, for the elements that do exist, it still takes time to find, takes time to enter into an assurance case structure, and takes time to maintain this information in two places (in the original and in the assurance case) over the lifecycle of the product. This is not a non-trivial amount of time. Finally, as people are rotated on and off projects within companies, there is a continual training burden as people being rotated onto a Safety Assurance Case task are not likely to have learned Assurance Case techniques in their previous roles.

3. **Clarification of why we believe the initial AdvaMed estimates were low**
   Upon further discussion within the AdvaMed Infusion Pump Working Group, we determined there were multiple tasks associated with the development and maintenance of a Safety Assurance Case that had not been accounted for in the initial AdvaMed estimate of burden. The tasks that were not included in AdvaMed’s initial estimate are:
   
   a. The overhead involved in initially establishing an assurance case process and support tools. It takes time for the manufacturer to select an assurance case tool and acquire it. As the tool will be used for Quality Records, the tool must be validated and version controlled throughout its entire life.
b. Procedures (SOPs) need to be written to integrate the safety assurance case tool into existing risk management processes and integrated into the entire product management lifecycle.

c. Planning, review, and update tasks were often not included in AdvaMed’s original estimation process.

These tasks were not accounted for in the FDA’s 56-hour nor 112-hour time estimate, nor were they included in AdvaMed’s original 2,207 man-hours estimate.

To remedy this, AdvaMed has performed a follow-up survey with its members asking for a more detailed breakdown of the tasks involved in the development of an assurance case. The following table shows the average results from the survey.

<table>
<thead>
<tr>
<th>Assurance Case Process Steps</th>
<th>Average Man-Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Allocate resources for assurance cases work. NOTE: These resources are required to do the additional work required below.</td>
<td>76</td>
</tr>
<tr>
<td>2. Develop, publish, and train resources on assurance case development processes.</td>
<td>209.6</td>
</tr>
<tr>
<td>3. Select, configure, deploy, and train resources on assurance case development tools and mechanics for publication. NOTE: Publication may be in multiple forms: electronic (for diagrammatic navigation/review) and paper (for submissions).</td>
<td>192.8</td>
</tr>
<tr>
<td>4. Plan assurance case development effort.</td>
<td>86</td>
</tr>
<tr>
<td>5. Cross-functionally develop the claim/argument/evidence structure of the assurance cases and connect/trace to existing DHF artifacts. NOTE: This requires separating and rearranging elements of existing hazard analyses into the claim/argument/evidence structure. This takes considerable effort and is not a direct 1:1 mapping.</td>
<td>1092</td>
</tr>
<tr>
<td>6. Cross-functionally develop the assurance case trace matrix to ensure evidence and other required artifacts are integrated appropriately.</td>
<td>464.4</td>
</tr>
<tr>
<td>7. Cross-functionally review the assurance cases and trace matrix artifacts. NOTE: This review needs to be held to ensure the evidence supports the entire argument made. This can also lead to additional effort in that more evidence may be required to support the claim and argument structure than would normally be required for requirements traceability.</td>
<td>618</td>
</tr>
<tr>
<td>8. Cross-functionally develop the assurance case summary report.</td>
<td>130.4</td>
</tr>
<tr>
<td>9. Cross-functionally review the assurance case summary report.</td>
<td>79.6</td>
</tr>
<tr>
<td><strong>Total Estimate of Man-Hours</strong></td>
<td><strong>2948.8</strong></td>
</tr>
</tbody>
</table>

Based on the explanation and new survey information provided above, AdvaMed urges FDA to change its estimate of burden from 112 hours to 2950 man-hours.
Expanded Comments in Response to Question One From March 18, 2013 PWRA Request

In AdvaMed’s response to the March 18, 2013 PWRA Question (1) “whether the proposed collection of information is necessary for the proper performance of FDA’s functions, including whether the information will have practical utility,” we noted that FDA’s requirement for an assurance case for infusion pumps goes beyond the statutory requirement to demonstrate substantial equivalence to a predicate device. For this reason, imposition of assurance case reports for infusion pumps (or any other device) must be imposed via a change to the regulations (i.e., a special control). It is our understanding that FDA intended to issue a special control for infusion pumps requiring safety assurance cases. If FDA is still considering issuing a special control for infusion pumps requiring a safety assurance case, AdvaMed strongly recommends that FDA first re-issue a revised draft guidance that takes into account FDA’s learning from the immediate implementation of the initial draft guidance, and that allows for additional public comment on the revised draft guidance.

We would also like to point out that FDA and industry have faced many challenges implementing the draft guidance. At this time, AdvaMed does not believe assurance case reports are a proven risk management tool for infusion pumps. There is a possibility that assurance cases – with further development that takes into consideration the device regulatory and statutory scheme and with more specific guidance – could become a useful risk management tool for infusion pump manufacturers but with the current lack of clarity, a special control requiring assurance case reports is premature.

FDA should carefully consider its current objectives for requiring assurance case reports. To a large degree, the assurance case requirement appears to have been transformed into an initiative to make 510(k) infusion pump submissions easier to review for Office of Device Evaluation reviewers rather than about improving infusion pumps. It is not at all clear that it is appropriate for FDA to require burdensome and wholesale changes to manufacturer’s risk management practices and 510(k) submissions, as detailed above, in order to facilitate easier reading of submissions by reviewers.

If FDA has not already done so, we encourage FDA to conduct a retrospective analysis on infusion pump recalls – including the impact on infusion pump innovation as reflected in 510(k) submissions – both before and after imposition of the assurance case report requirement.

Please find attached our previous comments to OMB Paperwork Reduction Act Federal Register Notices.

In closing, thank you for the opportunity to provide comments on this Paper Work Reduction Act Collection of Information. Please don’t hesitate to contact me if you have any questions. I can be reached at tfederici@advamed.org or 202-434-7208.

Sincerely,

/s/

Tara Federici
Vice President, Technology and Regulatory Affairs

Attachment
May 14, 2013

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE:  Docket No. FDA-2010-D-0194: Agency Information Collection Activities; Proposed Collection; Comment Request; Draft Guidance for Industry and FDA Staff; Total Product Life Cycle: Infusion Pump—Premarket Notification [510(k)] Submissions; Notice

Dear Sir/Madam:

The Advanced Medical Technology Association is pleased to comment on FDA’s Paperwork Reduction Act of 1995 Collection of Information associated with the Draft Guidance for Industry and FDA Staff; Total Product Life Cycle: Infusion Pump—Premarket Notification [510(k)] Submissions.

AdvaMed represents manufacturers of medical devices, diagnostic products, and health information systems that are transforming health care through earlier disease detection, less invasive procedures, and more effective treatments. Our members produce nearly 90 percent of the health care technology purchased annually in the United States and more than 50 percent of such technology purchased annually around the world. These members range from the smallest to the largest medical technology innovators and companies. Nearly 70 percent of our members have less than $30 million in sales annually.

AdvaMed continues to support FDA’s infusion pump improvement initiative “to support the benefits of infusion pumps while minimizing the risks.” 1 AdvaMed agrees that “infusion pumps have contributed to improvements in patient care, allowing for a greater level of control, accuracy, and precision in drug delivery, and thereby reducing medication errors.” 2 As a demonstration of AdvaMed’s support for efforts to improve infusion pumps while minimizing risks, AdvaMed’s Infusion Pump Working Group developed the Infusion Pump Assurance Case (IPAC) Report Template which is discussed in more detail below.

2 Ibid. p. 2.
AdvaMed Concerns with Infusion Pump Assurance Case Requirement

AdvaMed has had several concerns with FDA’s assurance case requirement for infusion pumps. They include the following:

- “Classic” assurance case\(^3\) requirements, which include financial and other business information, and information typically found in a manufacturer’s Quality System, are incompatible with the medical device regulatory scheme;
- FDA’s lack of guidance on how to conduct and present an assurance case for infusion pumps; and
- Classic assurance cases may not be least burdensome.

AdvaMed’s Infusion Pump Assurance Case (IPAC)

In response to some of these concerns, AdvaMed’s Infusion Pump Working Group developed the Infusion Pump Assurance Case Template which has been shared with FDA. Based on the Infusion Pump Working Group’s interactions with outside assurance case experts that were offering consulting advice to FDA and consulting services to manufacturers, it became clear that some assurance case experts were unfamiliar with the multiple regulatory requirements and standards governing medical devices. As a result, these experts recommended submission to FDA of information that would be found in a “classic” assurance case which included financial information and assurances that are typically found in a device manufacturer’s Quality System and, as such, are inappropriate for inclusion in a 510(k) submission that includes a safety assurance case. AdvaMed’s IPAC is tailored to and takes into account the medical device regulatory scheme. It is a methodology of assuring claims of product safety through the use of risk management techniques such as those in ISO 14971 Medical devices – application of risk management to medical devices.

In AdvaMed’s June 23, 2010 comments to this same docket, Docket No. FDA-2010-D-0194, we recommended “that FDA develop guidance for manufacturers on how to conduct and present assurance case reports for infusion pumps.” In the absence of more specific FDA assurance case guidance, the IPAC was also developed to provide guidance to infusion pump manufacturers on the appropriate elements of an assurance case and how to develop an assurance case since assurance case reports have not previously been required by FDA.

Lastly, the IPAC is intended to provide a least burdensome assurance case structure that contains all of the elements required (either directly or by reference) to argue that the device is equivalently safe for its intended use when compared to predicate devices. It provides sufficient top level coverage (breadth) and detail (depth) to assess the safety of the device. It is comprised of descriptive narrative and a Risk-Based Table (RBT) that includes references or links to specific evidence. It comports with the recommendations for a 510(k) submission as contained in Section 6. “Assurance Case Report” of CDRH’s draft guidance document entitled Total Product Life Cycle: Infusion Pump – Premarket Notification [510(k)] Submissions.

The IPAC provides a template to manufacturers of the types of arguments and data needed to demonstrate that the device is safe for its intended use.

\(^3\) A Classic Assurance Case refers to a scoping of assurance cases that is typically used in non-medical applications such as the UK Ministry of Defense, which is not consistent with the US medical device regulatory structure.
It answers the following questions for each group of harms or risk categories:

- What are the primary hazards/harms in this group?
- What is the top level approach that has been taken to control the highest-ranked risks?
- Are there any unique or special issues or approaches that should be explained?

Importantly, the IPAC template is *maintainable and sustainable* for the following reasons:

- Aligns with risk management to ensure that changes made as part of risk management are captured in the assurance case.
- Allows for modifications to the infusion pump made through the risk management process to be readily captured in a risk-based table (RBT) (using Excel) by adding a row(s) or modifying an existing row(s) and by modifying the relevant summaries. As such use of the IPAC template obviates the need for specialized assurance case software that can be difficult to revise as changes, requiring new 510(k) submissions, are made to the infusion pump.

**Response to Question One**

In response to FDA’s Question (1) “whether the proposed collection of information is necessary for the proper performance of FDA’s functions, including whether the information will have practical utility,” we would note that FDA’s requirement for an assurance case for infusion pumps goes beyond the statutory requirement to demonstrate substantial equivalence to a predicate device. For this reason, imposition of assurance case reports for infusion pumps (or any other device) must be imposed via a change to the regulations (i.e., a special control).

**Response to Question Two**

In response to FDA’s Question (2) regarding “the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used,” AdvaMed 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. We would note that 12.83 man months is significantly higher than the 112 hours FDA estimates. 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 (i.e., man months as opposed to hours).

**Responses to Questions Three and Four**

Thus, in response to FDA’s Questions (3) “ways to enhance the quality, utility, and clarity of the information to be collected,” and (4) “ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology,” AdvaMed recommends that FDA develop infusion pump assurance case guidance (either directly or in concert with outside stakeholder groups) that:

- Clarifies that assurance case report submissions are not required to include information that are part of a manufacturer’s Quality System and are thus inconsistent with the medical device regulatory scheme, and
• Clarifies the breadth and depth of information required to be included in the assurance case similar to that outlined in the IPAC.

In conclusion, thank you for this opportunity to provide comment on the FDA’s proposed collection of information under the Paperwork Reduction Act for the Draft Guidance for Industry and FDA Staff; Total Product Life Cycle: Infusion Pump – Premarket Notification [510(k)] Submissions.

Sincerely,

/l/s/

Tara Federici
Vice President
Technology and Regulatory Affairs