United States Food and Drug Administration

Postmarketing Safety Information Sharing by Constituent Part Applicants for Combination Products

OMB Control No. 0910-0834

SUPPORTING STATEMENT

Part A: Justification

1. Circumstances Making the Collection of Information Necessary

FDA promulgated its postmarketing safety reporting regulations for combination products to enhance clarity regarding what postmarketing safety requirements apply to these products (which combine a drug, device, and/or biological product), to ensure appropriate ongoing postmarketing surveillance of risks for these products, to ensure the consistency of the agency's postmarketing regulation of combination products, to streamline and clarify requirements for reporters by avoiding duplicative reporting requirements for them.

For combination products for which the constituent parts receive marketing authorization under separate applications held by different entities, the Agency established a requirement, specific to these "constituent part applicants," that they must share safety information they receive related to certain events with the other constituent part applicant(s) and maintain records of this information sharing.

Specifically, section 4.103, requires the constituent part applicants share with one another information they receive regarding an event associated with the use of the combination product that involves a death or serious injury as described in 21 CFR 803.3 or an adverse experience as described in 21 CFR 314.80(a). Constituent part applicants are required only to share whatever information they initially receive regarding the event. They are not required to analyze, investigate or organize the information or take any other actions beyond forwarding the information as received. No further follow-up with the other constituent part applicant(s) is required. In addition, constituent part applicants must retain records regarding the information shared for the longest recordkeeping period required under the PMSR regulations applicable to that applicant's constituent part.

Generally, the requirements of 21 CFR Part 4, Subpart B, for combination products are the same as requirements applicable to drugs, devices, and biological products, and are covered by OMB control numbers supporting those information requirements. The postmarket safety reporting (PMSR) information collection requirements for drugs, biological products, and devices found in §§ 314.80, 314.81, 600.80, 600.81, 606.170, 606.171, 803.50, 803.53, 803.56, 806.10, and 806.20 are approved by OMB. The pertinent PMSR information collection provisions for § 314.80(c) and (e), as well as for § 314.81(b) are approved under OMB Control Nos. 0910-0001, 0910-0230, and 0910-

0291. The information collection provisions for §§ 600.80 and 600.81 are approved under OMB Control No. 0910-0308. Those for § 606.170 are approved under OMB Control No. 0910-0116. Those for § 606.171 are approved under OMB Control No. 0910-0458. The information collection provisions for §§ 803.50, 803.53, and 803.56 are approved under OMB Control Nos. 0910-0291 and 0910-0437. The information collection provisions for §§ 806.10 and 806.20 are approved under OMB Control No. 0910-0359.

We request extension of OMB approval for the information sharing requirement, and the associated recordkeeping requirement in FDA's postmarketing safety reporting regulations for combination products found in 21 CFR Part 4 Subpart B.

2. Purpose and Use of the Information Collection

The collection ensures that applicants evaluate and provide information to the Agency as necessary and appropriate to expedite FDA's safety review and evaluation, and thereby enhance the ability of the agency and these applicants to address safety concerns in prompt and effective manner. The information sharing requirements are necessary to ensure (1) that applicants submit consistent PMSR for combination products and constituent parts, (2) that the Agency receives necessary information to promote and protect the public health, (3) appropriate ongoing assessment of risks, and (4) consistent and appropriate postmarketing regulation of combination products.

3. Use of Improved Information Technology and Burden Reduction

Constituent part applicants are free to use whatever method they wish, including automated, electronic, mechanical, other technological collection techniques, or other forms of information technology that enables them to share information with one another. The information sharing requirement is designed to minimize burden, by requiring that information be shared only on certain types of events, and that constituent part applicants need only transmit the initial information they receive on the event, without any duty to analyze or reformat the information.

4. Efforts to Identify Duplication and Use of Similar Information

The information sharing requirement does not represent a duplication of effort. Each constituent part applicant is responsible for its product and is in the best position to assess and address safety issues with it. In some cases, both constituent part applicants may have a duty to report regarding the event, but this would be because there are safety issues relevant to each of their products that need to be brought to the Agency's attention and addressed as appropriate. If the event only implicates one applicant's constituent part, only that applicant would be obliged to report, if the event is reportable.

5. Impact on Small Businesses or Other Small Entities

Because the information sharing requirement imposes little burden on constituent part applicants; constituent part applicants represent a small proportion of all applicants for combination products, and the requirement, therefore, will have no recurring impact on the majority of small firms, the agency concludes that the rule will not have a significant economic impact on a substantial number of small businesses.

6. Consequences of Collecting the Information Less Frequently

Failing to share information consistently and promptly would defeat the purpose of the requirement, i.e., to ensure that applicants are receiving safety information for their product in a timely manner so that they can take appropriate action including submitting reports to FDA if required. Failure to share such information could result in reportable information not being provided to FDA. This could compromise the agency's ability to make sound regulatory decisions about product safety, and the ability of the agency and applicants to take appropriate action to address safety concerns, and could, thereby, jeopardize the public health.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

No special circumstances are associated with the collection of information.

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

FDA published a 60-day notice for public comment in the *Federal Register* of April 30, 2020 (85 FR 23971) No comments were received.

Enforcement compliance for elements of the rule was delayed until July 2020, for most combination products, and until January 2021 for the remainder. There has been limited to no experience with implementation of the new information request to date. FDA will consider feedback received going forward.

9. Explanation of Any Payment or Gift to Respondent

No payment or gifts are associated with this collection of information.

10. Assurance of Confidentiality Provided to Respondents

In preparing this Supporting Statement, we consulted our Privacy Office to ensure appropriate identification and handling of information collected.

This ICR does collect personally identifiable information (PII) as required by the FDA. Information collection is required for constituent part applicants to collect information from individuals who report adverse events. Information collected can include name and contact information. This ICR collects initial information received by a constituent part applicant relating to any adverse events associated with use of its product. This

information is received from users, doctors, or other caregivers. No specific form needs to be used by these entities. Regulations state that constituent part applicants must share the information amongst themselves. Submission of PII is minimized to protect the privacy of the individuals. Information is collected and stored at the applicants' facilities. If a report is necessary and sent to the FDA that information collection is covered in a separate ICR.

11. Justification for Sensitive Questions

This information collection does not contain questions of a sensitive nature.

12. Estimates of Annualized Burden Hours and Costs

FDA estimates the total annual reporting and recordkeeping burden to be 267 hours as detailed in the table below:

Table 1.--Estimated Annual Recordkeeping Burden

21 CFR Section	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
4.103(b) and 4.105(a)(2), Records of information shared by constituent part applicants	33	18	594	0.1 (6 minutes)	59

Table 2.--Estimated Annual Third-Party Disclosure

21 CFR Section	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
4.103, Sharing information with other constituent part applicants	33	18	594	0.35 (21 minutes)	208

We note in this regard that FDA extended the compliance date for 21 CFR Part 4, Subpart B until July 2020 for most combination products, and until January 2021 for the remainder, in response to stakeholder feedback, to ensure that Combination Product Applicants have sufficient time to update reporting and recordkeeping systems and

procedures associated with the rule as a whole.[1] Consequently, entities subject to this regulation have not yet had to comply with this information request or associated recordkeeping requirements. No substantive, additional information regarding the burden of the request has been available to FDA to support adjusting our initial estimate.

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

FDA believes that there are no significant operating and maintenance costs associated with this collection of information because, in order to legally market their products, applicants are required to develop and maintain systems for reporting and maintaining records of postmarketing safety events. Therefore, appropriate mechanisms for postmarketing safety reporting should already be in place, and reporters will accrue no significant additional costs to fulfill the requirements set forth here.

14. Annualized Cost to the Federal Government

This collection of information will not lead to any significant costs to the Federal government. FDA will be reviewing reports received and taking action in response to them, but these activities are ongoing, and the overall volume of such reports and actions for medical products is not anticipated to change significantly.

15. Explanation for Program Changes or Adjustments

The burden for this extension request has decreased (an adjustment) because the burden for drug, devices and biological products has been omitted from this ICR and consolidated into the appropriate center ICRs referred to in section 1 of this document.

16. Plans for Tabulation and Publication and Project Time Schedule

We have no plans to tabulate or publish this collection of information.

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

We believe that display of the OMB expiration date is appropriate for this collection of information.

18. Exceptions to Certification for Paperwork Reduction Act Submission

No exceptions to the certification statement have been identified.

[1] See Compliance Policy for Combination Product Postmarketing Safety Reporting (April, 2019) (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/compliance-policy-combination-product-postmarketing-safety-reporting).