United States Food & Drug Administration

Adverse Experience Reporting for Drug Products

OMB Control No. 0910-0230 - Revision

SUPPORTING STATEMENT

**Part A: Justification**

# 1. Circumstances Making the Collection of Information Necessary

This information collection supports provisions found in sections 201, 502, 505, 701 and 760 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 321, 352, 355, 371, and 379aa) governing adverse experience reporting (AER) and associated recordkeeping for Food and Drug Administration (FDA)-regulated drug products. FDA has promulgated applicable regulations in 21 CFR §§ 4, 310.305, 314.80, 314.81, 314.98, and 329.100 that implement the statutory requirements, identify specific content and format elements, and establish reporting and retention schedules for the required information. These requirements protect the public health by facilitating the identification of FDA-regulated products that may pose a particular risk to consumers. Postmarketing safety data collection and adverse event reporting are critical elements of FDA’s monitoring of drugs. For more information, please visit [https://www.fda.gov/drugs/surveillance/postmarketing-adverse-event-reporting-compliance-program.](https://www.fda.gov/drugs/surveillance/postmarketing-adverse-event-reporting-compliance-program)

As set forth in 21 CFR 310.305, manufacturers, packers, and distributors of marketed prescription drug products not the subject of a new drug application or abbreviated new drug application are required to report serious, unexpected adverse drug experiences, as well as follow-up reports, to FDA. The regulations also establish required recordkeeping and corresponding retention periods for the associated records. Regulations in 21 CFR 329.100 set forth like requirements applicable to *non-*prescription human drug products and similarly prescribe reporting content and format elements, as well as establish mandatory timeframes for the submission of required information and the retention of records.

Adverse experience reporting for products associated with drug marketing applications and combination products are governed by regulations in 21 CFR 4.102, 4.103, 4.104, 4.105, 314.80, 314.81, and 314.98. The regulations identify required reporting content and format elements, as well as establish follow-up reporting requirements and mandatory reporting schedules. The regulations also establish associated recordkeeping and require that written procedures be developed for the surveillance, receipt, evaluation, and reporting of postmarketing adverse experiences to FDA. The regulations require reporting in an electronic format that FDA can process, although temporary waivers may be granted on a limited basis for good cause. The information collection associated with 21 CFR Part 4 Subpart B was previously approved under OMB Control Number 0910-0834. These provisions are also described in the guidance document “Postmarketing Safety Reporting for Combination Products” (July 2019), available at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/postmarketing-safety-reporting-combination-products>. The guidance describes the conditions under which respondents must provide information to the other constituent part applicants under 21 CFR 4.103, when information regarding an event that involves a death or serious injury, or an adverse event, associated with the use of a combination product that includes a drug product.

The information collection includes burden we attribute to reporting and recordkeeping discussed in the following agency guidance documents:

*Postmarketing Adverse Event Reporting for Nonprescription Human Drug Products Marketed without an Approved Application* (July 2009), implements section 760(e) of the FD&C Act (21 U.S.C. 379aa(e)). Section 760 requires that responsible persons maintain records of nonprescription adverse event reports, whether or not the event is serious, for a period of 6 years. The guidance explains that respondents maintain records of efforts to obtain the minimum data elements for a report of a serious adverse drug event and any follow-up reports. The information collection associated with the guidance document was previously approved under OMB Control No. 0910-0636. The guidance is available at: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/postmarketing-adverse-event-reporting-nonprescription-human-drug-products-marketed-without-approved>.

*Providing Postmarketing Periodic Safety Reports in the ICH E2C(R2) Format (Periodic Benefit-Risk Evaluation Report)* (November 2016), describes the conditions under which applicants may use the International Council for Harmonisation (ICH) E2C(R2) Periodic Benefit-Risk Evaluation Report (PBRER) format for certain types of reporting. Information collection associated with the guidance document was previously approved under OMB Control No. 0910-0771. The guidance is available at <https://www.fda.gov/media/85520/download>.

*Postmarketing Adverse Event Reporting for Medical Products and Dietary Supplements During a Pandemic* (May 2020), also pertains to postmarket reporting under section 760 of the FD&C Act. The guidance provides recommendations pertaining to reporting and recordkeeping applicable to any pandemic, not just influenza. The guidance document includes recommendations for planning, submitting notices, and documenting continuity of operations. Information collection associated with the guidance document was previously approved under OMB Control No. 0910-0701. The guidance is available at: <https://www.fda.gov/media/72498/download>.

We are revising this information collection to incorporate a final guidance for industry entitled “Providing Submissions in Electronic Format—Postmarketing Safety Reports” (April 2022). The guidance provides general information pertaining to electronic submission of postmarketing safety reports for certain human drugs, biological products, and combination products. The guidance is available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-submissions-electronic-format-postmarketing-safety-reports.

We therefore request OMB approval of the information collection associated with adverse event reporting requirements found in the applicable regulations and discussed in the associated agency guidance documents.

# 2. Purpose and Use of the Information Collection

The information collection implements statutory requirements governing the protection of public health by facilitating the identification of FDA-regulated products that may pose a particular health risk to consumers. The requirements are intended to signal potentially serious safety problems, focusing especially on newly marketed drugs and biological products. Although premarket testing discloses a general safety profile of a product’s comparatively common adverse effects, the larger and more diverse patient population exposed to the marketed product provides, for the first time, the opportunity to collect information on rare, latent, and long-term effects. Signals are obtained from a variety of sources, including reports from patients, treating physicians, foreign regulatory agencies, and clinical investigators. Information derived from the adverse drug experience reporting system contributes directly to increased public health protection because such information enables FDA to make important changes to the product's labeling (such as adding a new warning) and, when necessary, to initiate removal of a new drug from the market.

Respondents to the information collection are manufacturers, packers, distributors, and applicants of FDA-regulated drug and biologic products marketed with or without an FDA-approved application, including over-the-counter (OTC) drug products marketed without an approved application, OTC drug products marketed under the OTC Drug Monograph Review process (whether subject to a final monograph or not), and drug products marketed outside the monograph system.

# 3. Use of Improved Information Technology and Burden Reduction

The information collection is required electronically in a format FDA can process. On a limited basis, a temporary waiver may be granted from the electronic reporting requirements. We have established and maintain the FDA Adverse Event Reporting System (FAERS) at <https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-electronic-submissions>. Information may be submitted via FDA’s Electronic Submissions Gateway (ESG) or utilizing the “*Safety Reporting Portal* (SRP),” developed by FDA and NIH to streamline reporting and review of adverse events. The SRP was also developed as part of our MedWatch program strategic efforts.

# 4. Efforts to Identify Duplication and Use of Similar Information

We are unaware of duplicative information collection.

Adverse experience reporting applicable to biological products is approved under OMB Control No. 0910-0308. We also maintain OMB Control Nos. 0910-0291 for paper-based and electronic reporting of voluntary healthcare provider reports of adverse experiences with drug and biologic products, through our MedWatch Adverse Event and Product Experience Reporting System program. (OMB Control Number 0910-0645, FDA Adverse Event and Medical Product Reports, was previously consolidated with 0910-0291.)

# 5. Impact on Small Businesses or Other Small Entities

The information collection poses no undue burden on small entities. Temporary waivers from electronic reporting requirements may be granted on a limited basis and for good cause. We assist small business through resources available on our website at <https://www.fda.gov/industry/small-business-assistance>.

# 6. Consequences of Collecting the Information Less Frequently

The information collection schedule is consistent with statutory and regulatory requirements.

# 7. Special Circumstances Relating to the Guidelines of 5 C.F.R. § 1320.5

Under 21 CFR § 310.305, the reporting of serious unexpected adverse drug experiences and follow-up reports are required within less than 30 days (reports to FDA are required within 15 working days of receipt of information). Reports to a manufacturer by a packer and distributor are required within 3 days of receipt of information. This shorter time period is necessary because the adverse experience reports are likely to reveal serious public health safety problems with the product and, thus, potentially can result in the need for expedited agency action.

Under 21 CFR §§ 314.80, an NDA applicant is required to notify FDA of any unexpected adverse experiences within 15 working days of receipt of information on such a reaction by the sponsor. As noted above, this short time for reporting is necessary so that FDA is informed as soon as possible of any serious problems with a product, so that the agency can take appropriate action.

The regulation requires retention of most adverse event records for a period of 10 years. This extended period is due to potential litigation and matters of public safety due to possible drug interactions in addition to the adverse experiences and need for studies of delayed effects such as carcinogenicity.

Records of serious adverse event reports, including follow-up reports, submitted under section 760(b)(1) for nonprescription human drug products marketed without approval must be maintained for a period of 6 years. These retention periods help to ensure that records, which include raw data and any correspondence relating to an adverse drug experience, are available in evaluating long-term or other rare or latent effects like carcinogenicity that might be detected only after multiple years of marketing experience.

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

In accordance with 5 CFR 1320.8(d), we published a 60-day notice inviting public comment on the described information collection in the Federal Register of September 23, 2024 (89 FR 77515). No comments were received.

9. Explanation of Any Payment or Gift to Respondents

There are no incentives, payments or gifts associated with this information collection.

# 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. Data will be kept private to the extent provided by law.

 The Privacy Act of 1974

This ICR collects personally identifiable information (PII). The PII submitted via Form FDA 3500A (MedWatch Mandatory Reporting) is patient identifier, name, address, telephone number, and email address, date of birth, age, gender, and sex; name of facility point of contact, phone number; device manufacturer name, work address, work phone number. PII submitted via the Safety Reporting Portal and Electronic Submission Gateway is email address, user id, and password. FDA determined that although PII is collected, the collection is not subject to the Privacy Act of 1974 and the particular notice and other requirements of the Act do not apply. Specifically, the FDA does not use name or any other personal identifier to retrieve records from the information collected. Through appropriate form and webpage design, FDA limited submission fields and minimized the PII collected to protect the privacy of the individuals.

 The Freedom of Information Act

Under the Freedom of Information Act (FOIA) (5 U.S.C. 552), the public has broad access to government documents. However, FOIA provides certain exemptions from mandatory public disclosure of government records (5 U.S.C. 552(b)(1-9)). FDA will make the fullest possible disclosure of records to the public, consistent with the rights of individuals to privacy, the property rights of persons in trade and confidential commercial or financial information.

1. Justification for Questions of Sensitive Nature

The collection of information does not involve sensitive questions.

1. Estimates of Annualized Burden Hours and Costs

*12a. Annualized Hour Burden Estimate*

Table 1.-- Estimated Annual Reporting Burden1, 2

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| 21 CFR Section or Guidance; Activity  | No. of Respondents | No. of Responses per Respondent | Total Annual Responses | Average Burden per Response | Total Hours |
| 310.305(c)(5); AERs for prescription products not the subject of a marketing application | 36 | 88.8 | 3,197 | 1 | 3,197 |
| 314.80(c)(1); 15-day alerts for approved products | 682 | 1,832.84 | 1,250,000 | 1 | 1,250,000 |
| 314.80(c)(2); periodic reports for approved products | 682 | 1,228.73 | 838,000 | 60 | 50,280,000 |
| 329.100; AERs for non-prescription drug products  | 312 | 62.522 | 19,507 | 6 | 117,042 |
| *ICH E2C(R2) Guidance*; Periodic safety updates; Applicants with waiver for an approved application (section III.A.) | 471 | 8.885 | 4,185 | 1 | 4,185 |
| *ICH E2C(R2) Guidance*; Periodic safety updates; Applicants with no waiver for an approved application (section III.B.) | 1,115 | 16.254 | 18,123 | 2 | 36,246 |
| *AER During Pandemic Guidance*; notifying FDA when normal reporting is not feasible (section III.C.) | 1 | 1 | 1 | 8 | 8 |
| 4,102, 4.103, 4.104, 4.105,310.305, 314.80, 314.98, 329.100(c); Waiver requests from electronic reporting requirements | 1 | 1 | 1 | 24 | 24 |
| Total | 2,133,014 |  | 51,690,702 |
| 1  The reporting burdens for § 310.305(c)(1), (2), and (3), and voluntary reports by healthcare providers received under § 314.80(c)(1)(i) and (ii) are covered under OMB control number 0910-0291.2 Totals may not sum due to rounding. |

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| Table 2.--Estimated Annual Recordkeeping Burden1

| 21 CFR Section or Guidance Section; Activity | No. of Recordkeepers | No. of Records per Recordkeeper | Total Annual Records | Average Burden per Recordkeeping | Total Hours |
| --- | --- | --- | --- | --- | --- |
| 310.305; AER records – prescription product not the subject of a marketing application | 36 | 88.8 | 3,197 | 16 | 51,152 |
| 314.80(j); AER records – product associated w/ marketing application | 841 | 1,814.0606 | 1,525,625 | 16 | 24,410,000 |
| *Postmarket AER for Nonprescription Drug Products Guidance*; (§ 329.100) | 312 | 62.5224 | 19,507 | 8 | 156,056 |
| *AERs During Pandemic* *Guidance*; Continuity of operations planning(section III.B.) | 100 | 1 | 100 | 50 | 5,000 |
| *AERs During Pandemic* *Guidance*; documenting conditions and resultant high absenteeism (section III.C.2) | 350 | 1 | 350 | 8 | 2,800 |
| *AERs During Pandemic Guidance*; documenting AER process (section III.C.1.) | 350 | 1 | 350 | 8 | 2,800 |
| 4.105 Postmarketing safety recordkeeping for combination products and constituent parts  | 11 | 18 | 198 | 0.1 (6 minutes) | 19.8 |
| Total | 1,549,327 |  | 24,627,827.8 |

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1Totals may not sum due to rounding.

Table 3.--Estimated Annual Third-Party Disclosure Burden

| 21 CFR Section; Activity | No. of Respondents | No. of Disclosures per Respondent | Total Annual Disclosures | Average Burden per Disclosure | Total Hours |
| --- | --- | --- | --- | --- | --- |
| 4.103 Postmarketing Safety reporting for Combination products – Sharing information with other constituent part applicants | 11 | 18 | 198 | 0.35 (21 minutes) | 69.3 |

The total burden for this information collection is 76,318,599 hours.

All applicants who have received marketing approval for drug products (including combination products that are administered as drug products) are required to report serious unexpected adverse drug experiences (15-day “Alert reports”) (section 314.80(c)(1)(i), as well as follow-up reports (section 314.80(c)(1)(ii)) to FDA. These include all foreign or domestic AERs as well as AERs based on information from appliable scientific literature and certain reports from post marketing studies.

Sections 4.102, 4.103, 4.104 and 4.105 pertain to the submission of postmarketing safety reports for combination products and include sharing AERs with applicants for all the constituent parts of the combination product. When information regarding an event that involves a death or serious injury, or an adverse event, associated with the use of a combination product that includes a drug product, is received by the product sponsor, the information must be provided to the other constituent part applicant(s) no later than 5 calendar days after receipt under § 4.103 (21 CFR 4.103). Relatedly, 21 CFR 4.104 explains how and where to submit reports for combination products, and 21 CFR 4.105 provides for associated recordkeeping. For combination products that are administered as drug products with a constituent part, adverse event reports are submitted to the drug application under 21 CFR part 314, and constituent applicants are notified of the AER under § 4.103.”

Under section 4.105, each applicant must maintain records in accord with the longest time period required for records under the regulations applicable to the approved combination product, (e.g., for a combination product approved under a new drug application, you must submit AERs as described in section 314.) Records must be maintained for 10 years.

For marketed prescription drug products without approved new drug applications (NDAs) or abbreviated new drug applications (ANDAs), manufacturers, packers, and distributors of these products are required to report to FDA serious, unexpected adverse drug experiences as well as follow-up reports (§ 310.305(c)). Section 310.305(c)(5) pertains to the submission of follow-up reports to reports forwarded to the manufacturers, packers, and distributors by FDA. Under § 310.305(g), each manufacturer, packer, and distributor shall maintain records of all adverse drug experiences required to be reported for 10 years.

Applicants who have received marketing approval for drug products are required to report serious, unexpected adverse drug experiences (15-day “Alert reports”), as well as follow-up reports (§ 314.80(c)(1)) to FDA in electronic format. This includes reports of all foreign or domestic adverse experiences as well as those based on information from applicable scientific literature and certain reports from postmarketing studies. Section 314.80(c)(1)(iii) pertains to such reports submitted by nonapplicants.

Under § 314.80(c)(2), applicants of approved marketing applications must provide periodic reports of adverse drug experiences. For the reporting interval, a periodic report includes reports of serious, expected adverse drug experiences, all nonserious adverse drug experiences, and an index of these reports; a narrative summary and analysis of adverse drug experiences; an analysis of the 15-day Alert reports submitted during the reporting interval; and a history of actions taken because of adverse drug experiences. Periodic AERs are submitted quarterly for the first three years following marketing approval and annually thereafter. Under § 314.80(j), applicants must keep for 10 years records of all adverse drug experience reports known to the applicant.

Section 329.100 postmarketing reporting of adverse drug events under Section 760 of the FD&C Act (21 U.S.C. 379aa) also provides for mandatory safety reporting for over-the-counter (OTC) human drug products not subject to applications approved under section 505 of the FD&C Act (21 U.S.C. 355) (NDAs or ANDAs). These requirements apply to all OTC drug products marketed without an approved application, including those marketed under the OTC Drug Monograph Review process (whether or not subject to a final monograph), those marketed outside the monograph system, and including those that have been discontinued from marketing but for which a report of an adverse event was received. Under 21 CFR 329.100, respondents must submit reports according to section 760 of the FD&C Act in an electronic format.

Section 760(e) of the FD&C Act also requires that responsible persons maintain records of nonprescription drug adverse event reports, whether the event is serious or not, for a period of 6 years. FDA’s guidance recommends that respondents maintain records of efforts to obtain the minimum data elements for a report of a serious adverse drug event and any follow-up reports.

*12b. Annualized Cost Burden Estimate*

We calculated annualized cost burden by multiplying the total number of annualized hours by a mean hourly wage rate of $64.64, using 2023 Bureau of Labor Statistic wage estimates applicable to Medical and Health Services Managers (NAICS 11-9111), for an annual total of $76,318,668.40 ((51,690,771.3 + 24,627,827.8 + 69.3) \* $64.64).

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

 We also estimate annual administrative costs of $25,000 for maintaining toll-free telephone numbers and other portals that enable direct communications from consumers.

## 14. Annualized Cost to the Federal Government

Assuming an allocation of 70 full-time-employees (FTEs) to ensure compliance with applicable statutory and regulatory requirements, and using a median annual salary of $133,692 for a GS-13/5 employee for the Washington D.C. Metropolitan Area, based on OPM salary data, we calculate annual costs to the Federal government to be $9,358,440.

## 15. Explanation for Program Changes or Adjustments

The estimates of the number of respondents and the total annual responses are based on reports submitted to the Agency. This information collection IC incorporates a revision to include the guidance for industry regarding submission of adverse event reports (“Providing Submissions in Electronic Format—Postmarketing Safety Reports”) (April 2022) and adjustments to include 15-day alert reports from applicants, manufacturers, distributors, and packers that were not recorded previously in this information collection. The information collection also includes the consolidation of burden from OMB control number 0910-0834 (previously added to this collection in March 2023). We also believe adjustments in the information collection reflect anticipated fluctuations in burden after pandemic conditions, adjustments by reporters and changes in electronic reporting methodologies, use of updated technology including updates, and redefinitions of reporting software, and changes of company business practices over time. All reports and follow-up reports must be submitted to FDA in electronic format. Waivers of the electronic requirements are available.

Finally, the total burden hours of the information collection have increased by 61,614,921 hours and 2,546,112 responses as compared to the previous renewal.

1. Plans for Tabulation and Publication and Project Time Schedule

The information collected is tabulated and reported on the FDA Adverse Event Reporting System dashboard to allow for the querying of the data. The intention of the tool is to expand access of FAERS data to the general public to search for information related to human adverse events. FDA anticipates that the increased transparency will help to spur the submission of more detailed and complete adverse event reports which are helpful to the agency when identifying safety signals and particular products for further scrutiny.

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

Consistent with established practice FDA will publish a Federal Register notice announcing OMB approval of the information collection associated with the guidance documents and will display in that notice both the OMB control number and its current expiration date. In addition, the OMB control number will be displayed on the associated guidance documents cover page and include a link to www.reginfo.gov to identify the current expiration date.

## 18. Exception to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.