
Providing Submissions in Electronic Format— Postmarketing Safety Reports Guidance for Industry

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)**

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Providing Submissions in Electronic Format— Postmarketing Safety Reports Guidance for Industry

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The technical specification associated with this guidance is provided in a separate document and is updated periodically. To ensure that you have the most recent version of the technical specifications document, check the FAERS Electronic Submissions web page at <https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm115894.htm>.

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This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA office responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance is one in a series of guidance documents intended to assist industry when making certain regulatory submissions in electronic format to FDA’s Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER). This guidance provides general information on the electronic submission of postmarketing safety reports under the following provisions:

- 21 CFR 314.80 and 314.98 (regarding products with approved new drug applications (NDAs) and abbreviated new drug applications (ANDAs), respectively, including combination products or drug constituent parts with approved NDAs or ANDAs²)
- 21 CFR 600.80 (regarding products with approved biologics license applications (BLAs), including combination products or biological product constituent parts with approved BLAs)³)
- 21 CFR part 4, subpart B (requiring additional reports for combination products with approved NDAs, ANDAs, or BLAs)⁴)
- 21 CFR 310.305 (regarding prescription drug products marketed for human use without approved NDAs or ANDAs, including prescription drug products that are compounded)

¹ This guidance has been prepared by the Office of Business Informatics and the Office of Surveillance and Epidemiology in the Center for Drug Evaluation and Research (CDER) in cooperation with the Center for Biologics Evaluation and Research (CBER) and FDA’s Office of Combination Products.

² See also *Postmarketing Safety Reporting for Combination Products: Guidance for Industry and FDA Staff* (July 2019). We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>.

³ Id.

⁴ Id.

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by facilities registered as outsourcing facilities under section 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 353b))⁵

- 21 CFR 329.100 and section 760 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 379aa) (regarding nonprescription drug products marketed for human use without approved NDAs or ANDAs)

However, this guidance does not apply to the following:

- Vaccines⁶
- Whole blood or blood components⁷
- Combination products with a drug or biological product constituent part marketed under a device application⁸
- Lot distribution reports⁹
- Human cells, tissues, and cellular tissue-based products (HCT/Ps) regulated solely under section 361 of the Public Health Service Act¹⁰

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law.

⁵ See the guidance for industry *Adverse Event Reporting for Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act* (October 2015).

⁶ Electronic submissions of postmarketing safety reports for vaccines is addressed in the guidance for industry *Providing Submissions in Electronic Format—Postmarketing Safety Reports for Vaccines* (August 2015).

⁷ Blood collection and transfusion facilities report fatalities related to blood collection or transfusion under 21 CFR 606.170(b). Information on submitting these reports is available at <https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/transfusiondonation-fatalities>.

⁸ As specified in 21 CFR 4.104, combination product applicants are required to submit Fifteen-day reports (as described in 21 CFR 314.80 or 21 CFR 600.80) in accordance with 21 CFR 803.12(a) if the combination product received marketing authorization under a device application. For additional reporting requirements for combination products marketed under a device application, see 21 CFR part 4, subpart B. For guidance on reporting requirements for combination products, see *Postmarketing Safety Reporting for Combination Products: Guidance for Industry and FDA Staff* (July 2019).

⁹ Lot distribution reports are not considered postmarketing safety reports; however, under FDA's final rule, "Postmarketing Safety Reports for Human Drug and Biological Products; Electronic Submission Requirements" (79 FR 33072, June 10, 2014), such reports are required to be submitted to FDA in electronic format that the Agency can process, review, and archive (see 21 CFR 600.81(b)(1)). Information on submitting lot distribution reports is available at <https://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Post-MarketActivities/LotReleases/ucm061966.htm> and in the guidance for industry *Electronic Submission of Lot Distribution Reports* (March 2015).

¹⁰ Submission of adverse reaction reports for HCT/Ps that are regulated solely under section 361 of the Public Health Services Act is required under 21 CFR 1271.350. Although FDA's final rule on electronic safety reporting does not require that such reports be submitted electronically, FDA encourages electronic submission of these reports, and this guidance may provide useful information to those interested in submitting HCT/P adverse reaction reports electronically.

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FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidance means that something is suggested or recommended, but not required.

II. BACKGROUND

On June 10, 2014, FDA published a final rule to amend its postmarketing safety reporting regulations for human drug and biological products to require that persons subject to mandatory reporting requirements submit safety reports in an electronic format that the Agency can process, review, and archive.¹¹ The final rule also established 21 CFR 329.100 to address electronic submission of postmarketing safety reports required by section 760 of the FD&C Act. The compliance date for these requirements was September 8, 2015.^{12, 13} At the time FDA published the final rule it also made available a revised draft guidance for industry entitled *Providing Submissions in Electronic Format—Postmarketing Safety Reports*.¹⁴ This guidance finalizes the revised draft guidance and contains recommendations on submitting postmarketing safety reports electronically in accordance with the final rule.

This guidance is intended for any party with postmarketing safety reporting responsibilities under the provisions that are within the scope of this guidance as described in section I. For purposes of this guidance, we use the terms *firm* or *you* to refer to these parties.

¹¹ See FDA's final rule "Postmarketing Safety Reports for Human Drug and Biological Products; Electronic Submission Requirements" (79 FR 33072, June 10, 2014), promulgating the requirements set forth in 21 CFR 310.305(e), §§ 314.80(g), 314.98, 329.100(c), 600.2, 600.80(h), 600.81(b)(1), and 600.90.

¹² FDA delayed the June 10, 2015, compliance date to September 8, 2015, in the final rule "Postmarketing Safety Reports for Human Drug and Biological Products; Electronic Submission Requirements; Delay of Compliance Date; Safety Reporting Portal of Electronic Submission of Postmarketing Safety Reports for Human Drugs and Nonvaccine Biological Products" (80 FR 30151, May 27, 2015).

¹³ Section 745A(a) of the FD&C Act (21 U.S.C. 379k-1) provides that submissions under section 505(b), (i), or (j) of the FD&C Act or section 351(a) or (k) of the Public Health Service Act shall be submitted in such electronic format as specified by FDA in guidance. In section 745A(a), Congress granted explicit statutory authority to FDA to implement the electronic format for submissions requirement by guidance. This grant of authority, however, did not preclude FDA from implementing such requirements by notice and comment rulemaking (5 U.S.C. 553). Accordingly, even though FDA concluded that certain submissions that are addressed in the June 10, 2014, final rule are also within the scope of section 745A(a) of the FD&C Act, FDA determined that it was appropriate to amend the regulations on the submission of postmarketing safety reports through notice and comment rulemaking to remove references to paper submissions and to specify that such reports be submitted in an electronic format that FDA can process, review, and archive (see 79 FR 33072, June 10, 2014). This guidance is not issued under section 745A of the FD&C Act and does not establish legally enforceable responsibilities. To the extent it discusses binding requirements, such requirements have been promulgated in previously issued FDA regulations.

¹⁴ See 79 FR 33200 (June 10, 2014).

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III. ICSR SUBMISSIONS

A. General Information

An Individual Case Safety Report (ICSR) is a description of an adverse drug experience¹⁵ related to an individual patient or subject.¹⁶ An ICSR is made up of data elements, such as the date of an adverse drug experience, the name of a suspect medical product, and the name of the initial reporter. These data elements are listed in the relevant regulations.¹⁷ The information described by the data elements should be included in the ICSR submission if available and applicable to the report.

An **initial ICSR** describes the adverse drug experience originally reported to the firm.

An **ICSR attachment** is a document related to an adverse drug experience described in an ICSR, such as relevant hospital discharge summaries and autopsy reports or death certificates (see 21 CFR 314.80(a) and 21 CFR 600.80(a)). ICSR attachments may also include published articles for ICSRs based on scientific literature (see 21 CFR 314.80(d) and 21 CFR 600.80(d)), and the product label (see 21 CFR 310.305(c)(1) and section 760(b)(1) of the FD&C Act (see also section V.E.)).

A **follow-up ICSR** includes new information about an adverse drug experience that has been previously reported as an initial ICSR. It should provide a complete picture of the current understanding of an adverse drug experience, rather than providing only the changes and/or updates to an initial ICSR. Accordingly, follow-up ICSRs should include information about an adverse drug experience that has been previously reported along with any new information. However, to avoid duplication, any ICSR attachments submitted with an initial ICSR (e.g., literature articles, hospital discharge summaries) should not be resubmitted with a follow-up ICSR unless there are updates to the information.

The procedures for electronic submission of initial and follow-up ICSRs and ICSR attachments for all of these types of reports are the same.¹⁸

¹⁵ See 21 CFR 314.80(a). For purposes of this guidance, the term *adverse drug experience* also refers to *adverse experience* within the meaning of 21 CFR 600.80(a), which is defined as any adverse event associated with use of a biological product in humans, whether or not considered product related.

¹⁶ 21 CFR 310.305(b), §§ 314.80(a) and 600.80(a); see also 21 CFR 329.100(b).

¹⁷ 21 CFR 310.305(d), §§ 314.80(f), 329.100(b)(1), and 600.80(f).

¹⁸ An applicant whose product is a combination product that contains a device constituent part and was approved under an ANDA, NDA, or BLA must also submit other reports (e.g., Five-day reports and Malfunction reports), in addition to the postmarketing safety reports associated with the application type, in accordance with 21 CFR part 4, subpart B (see <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products> for additional information). As discussed in the guidance *Postmarketing Safety Reporting for Combination Products: Guidance for Industry and FDA Staff* (July 2019), ICSRs for combination products describe a report of an event experienced by an individual user of a combination product, including adverse events and malfunctions, and encompass the following types of reports: Fifteen-day reports (see 21 CFR 314.80 and 600.80), Five-day reports (see 21 CFR 803.3, §§ 803.53 and 803.56), Malfunction reports (see 21 CFR 803.50 and § 803.56), and reports of deaths or serious injuries (see 21 CFR part 803).

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- 15-day alert reports required under 21 CFR 314.80(c)(1), §§ 600.80(c)(1), and 310.305(c), including for prescription drug products that are compounded by facilities registered as outsourcing facilities under section 503B of the Federal Food, Drug, and Cosmetic Act (the FD&C Act)
- Reports for serious, expected, and non-serious adverse drug experiences required under 21 CFR 314.80(c)(2)(ii)(B) and 21 CFR 600.80(c)(2)(ii)(B)
- Serious adverse event reports required under section 760 of the FD&C Act
- Five-day reports for combination products with a device constituent part required under 21 CFR 4.102(b)(1), §§ 4.102(c)(1)(i), 803.53, and 803.56
- Malfunction reports for combination products with a device constituent part required under 21 CFR 4.102(b)(1), §§ 4.102(c)(1)(ii), 803.50, and 803.56

B. Options for Electronic Submission of ICSRs: Electronic Submissions Gateway or Safety Reporting Portal

ICSRs and ICSR attachments for human drugs, biological products, and combination products addressed by this guidance are submitted to the FDA Adverse Event Reporting System (FAERS) database. FDA provides two options for electronic submission of ICSRs and ICSR attachments to FAERS: (1) direct submission through the Electronic Submissions Gateway (ESG) or (2) submission through the Safety Reporting Portal (SRP), both of which are available 24 hours a day, 7 days a week.

Direct submission through the ESG is described on the FAERS Electronic Submissions web page.¹⁹ This option involves direct transmission of ICSRs from a firm's database to FDA through the ESG. The ESG is a central transmission point for sending information electronically to FDA. Once received through the ESG, the submitted reports are processed into the FAERS database. For instructions on organizing, preparing, and submitting ICSRs and ICSR attachments using the direct submission method through the ESG, see the technical specifications document available on the FAERS Electronic Submissions web page. The technical specifications document is incorporated by reference into this guidance document and addresses topics such as data elements, electronic transport format, and types of ICSR attachments FDA currently accepts.

The submission of ICSRs and ICSR attachments through the SRP is described on the FDA SRP web page.²⁰ Users enter the ICSR information manually into a web-based form and this information is then submitted to FDA to be uploaded into the FAERS database.

¹⁹ See the FAERS Electronic Submissions web page at <https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm115894.htm>.

²⁰ See FDA's SRP web page at <https://www.safetyreporting.hhs.gov>.

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C. Create an Account Before Submitting Electronically for the First Time

To submit postmarketing safety reports electronically, either through the ESG or SRP, you should create an account with FDA if you have not previously established one. To create an account, you should notify the FAERS Electronic Submission Coordinator of your intent at faersesub@fda.hhs.gov. The FAERS Electronic Submission Coordinator will assist you in creating an account and ensuring that all steps have been completed for successful submission of postmarketing safety reports.

D. Unique Case Identification Numbers for ICSRs

Postmarketing safety reporting often involves submitting a series of reports consisting of initial and follow-up ICSRs, along with any associated attachments, over the life cycle of an individual case. Each ICSR includes a unique case identification number, which must be the same in an initial report and any subsequent follow-up reports.²¹

- **Via the SRP.** The SRP automatically generates a unique case identification number for an ICSR upon the submission of the initial ICSR. When submitting follow-up ICSRs to the SRP for initial ICSRs submitted on paper, the firm should use the manufacturer control number assigned to the initial ICSR when inputting the unique case identification number in the SRP.
- **Via the ESG.** Before submitting an initial ICSR via the ESG, the firm assigns a unique case identification number for the ICSR. When submitting follow-up ICSRs to the ESG for initial ICSRs submitted on paper, the firm should use the manufacturer control number assigned to the initial ICSR when inputting the unique case identification number in the ESG.
- **On paper (e.g., Form FDA 3500A or the CIOMS I form).**²² Before submitting an initial ICSR on paper, the firm assigns the manufacturer control number as the unique case identification number.

The same unique case identification number must be used for an initial ICSR and any follow-up ICSRs,²³ even if there is a transfer of ownership of an application or unapproved drug product, to ensure that the follow-up ICSR can be matched with the initial submission.

Firms should not submit follow-up ICSRs to the SRP if an initial report was submitted through the ESG. Instead, follow-up reports should be submitted through the ESG to maintain the unique case identification number of the initial case. If an initial report was submitted through the SRP, a follow-up report may be submitted to the ESG. In this circumstance, the follow-up ICSR must

²¹ See 21 CFR 310.305(d)(5)(vii), §§ 314.80(f)(5)(viii), 329.100(b)(5)(vii), 600.80(f)(5)(viii), and 600.80(g)(7)(viii). The unique case identification number is used to track ICSRs and is distinct from the unique code for identification of the patient that should be assigned to protect the identity of the patient under 21 CFR 310.305(d)(1)(i), §§ 314.80(f)(1)(i), 329.100(b)(1)(i), and 600.80(f)(1)(i).

²² Prior to the implementation of the final rule requiring electronic submission of postmarketing safety reports, firms submitted ICSRs on Form 3500A or the CIOMS I form (see 79 FR 33072, June 10, 2014).

²³ See 21 CFR 310.305(d)(5)(vii), §§ 314.80(f)(5)(viii), 329.100(b)(5)(vii), 600.80(f)(5)(viii), and 600.80(g)(7)(viii).

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include the unique case identification generated by the SRP upon submission of the initial ICSR.²⁴

E. Submitting Labeling and Labels for Unapproved Products

For prescription drugs marketed for human use without an approved application, 15-day alert reports required under 21 CFR 310.305(c)(1) must be accompanied by the current content of labeling in electronic format as an ICSR attachment unless it is already on file at FDA.

Similarly, for nonprescription drug products without an approved application, each report of a serious adverse event associated with such drug when used in the United States required under section 760(b)(1) of the FD&C Act must be accompanied by a copy of the label on or within the retail package of the drug (21 U.S.C. 379aa(b)(1)).

For unapproved prescription and nonprescription drug products, labeling and labels should be submitted as ICSR attachments, unless they are already on file at FDA in Structured Product Labeling format as part of the electronic drug establishment registration and listing process.²⁵ If the labeling or label is already on file, you should indicate so in the narrative of the ICSR.

F. Single Submission Versus Batched Submissions of ICSRs

When submitting ICSRs through the ESG, you can submit ICSRs either as an individual report or several individual reports in a batch. Please refer to the technical specifications document available on the [FAERS Electronic Submissions](#) web page for information on submitting an individual report reports versus several individual reports in a batch through the ESG.

If you are submitting ICSRs through the SRP, please submit a single ICSR at a time. The SRP is not able to process a batched submission.

G. Submitting ICSR Attachments

Please submit ICSR attachments through the ESG only after your associated ICSR has been submitted and accepted by FAERS. When submitting ICSRs and ICSR attachments through the SRP, firms may include the ICSR attachment at the same time they submit the ICSR.

IV. NOTIFICATION OF RECEIPT OF SUBMISSIONS BY FDA

A. ESG Message Delivery Notices and FAERS Acknowledgements

Once a submission (one or more ICSRs or ICSR attachments) is successfully recognized and decrypted, an ESG message delivery notice (MDN) is sent to the submitter. The date of this

²⁴ See 21 CFR 310.305(d)(5)(vii), §§ 314.80(f)(5)(viii), 329.100(b)(5)(vii), 600.80(f)(5)(viii), and 600.80(g)(7)(viii).

²⁵ See FDA's May 2009 for industry *Providing Regulatory Submissions in Electronic Format—Drug Establishment Registration and Drug Listing*, and FDA's Structured Product Labeling Resources at www.fda.gov/industry/fda-data-standards-advisory-board/structured-product-labeling-resources.

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MDN generally serves as the official FDA receipt date of each successfully transmitted ICSR and ICSR attachment in the submission (see [FDA's ESG](#) web page for further information about receipt of submissions through the ESG).²⁶

After receipt of the submission, the ICSR and ICSR attachments are processed into the FAERS database and a second automated acknowledgement message, the FAERS acknowledgement, is sent to the submitter via the ESG. The FAERS acknowledgement provides the sender the status of each ICSR and ICSR attachment in the transmission. You should expect to receive the ESG MDN and FAERS acknowledgements within 24 hours after you have submitted an ICSR or ICSR attachment. If you do not receive the acknowledgement within 24 hours, you should first check the "ESG System Status" on FDA's web page at <https://www.fda.gov/esg> to determine whether we are experiencing any problems with the ESG and if so, please see section V. of this guidance, which describes the contingencies when the ESG is not functional.

If the ESG is functional and you are notified that FAERS could not load your submission (e.g., because the ICSR lacks the electronic transport formats that FDA supports), the FAERS acknowledgement will indicate that FDA could not load the submission into FAERS. You should resubmit to FDA any ICSRs or ICSR attachments that were not processed into FAERS. Your resubmission should be given a different file name than the original submission and must take place within any required reporting timeframe.²⁷ The date of the ESG MDN for the resubmission will serve as the official FDA receipt date of the ICSR or ICSR attachments.

If the ESG is functional but you do not receive the MDN, you should contact the FAERS Electronic Submission Coordinator at faersesub@fda.hhs.gov to determine why you have not received the MDN. If you are notified to resubmit the ICSRs and ICSR attachments, you must do so within any required reporting timeframe.²⁸ The date of the ESG MDN for the resubmission will serve as the official FDA receipt date of the ICSR or ICSR attachments.

Additional information on the receipt date of submissions when submitting through the ESG is available in the guidance for industry *Providing Regulatory Submissions in Electronic Format—Receipt Date* (February 2014).

B. SRP Acknowledgment

After the ICSR, with or without ICSR attachments, is submitted via the SRP, an acknowledgement email is sent immediately to the user. The acknowledgement email indicates successful transmission of the report. If the ICSR did not transmit, the user will not receive an acknowledgement email. In this situation, the user should contact the FAERS Electronic Submission Coordinator at faersesub@fda.hhs.gov for assistance. The date of the acknowledgement email serves as the official FDA receipt date of the submission.

²⁶ See FDA's ESG web page at <https://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/AboutESG/default.htm>.

²⁷ See 21 CFR 310.305, §§ 314.80 and 600.80, and section 760 of the FD&C Act.

²⁸ *Id.*

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V. CONTINGENCIES WHEN THE ESG, FAERS, OR SRP IS TEMPORARILY UNAVAILABLE

As described in section IV. of this guidance, you should expect to receive your acknowledgements (i.e., ESG MDN, FAERS acknowledgement, or SRP acknowledgement) within 24 hours after submitting an ICSR or ICSR attachment.

A. Contingencies When Submitting Through the ESG

If you submit through the ESG and do not receive the acknowledgement within 24 hours, you should check the “ESG System Status” on FDA’s web page at <https://www.fda.gov/esg>. If the ESG is not functional, FDA intends to notify all companies with an ESG account by email. FDA also intends to notify companies by email when ESG functionality is restored.

If the ESG is not functional for more than 48 hours and you choose to submit your ICSRs or ICSR attachments on physical media, FDA requests that your submission be in the current version of the International Council for Harmonisation (ICH) E2B format supported by FDA.²⁹ In this circumstance, you should **not** resubmit the ICSRs or ICSR attachments to FDA using the ESG or SRP when the ESG becomes functional. (See section V.D. for additional information on submitting on physical media.)

If the ESG is functional but FAERS is not functional, you should expect to receive the MDN but not the FAERS acknowledgement. FDA intends to load your ICSRs or ICSR attachments into FAERS as soon as FAERS is functional. At that time, you should expect to receive the FAERS acknowledgement. You should **not** submit your ICSRs or ICSR attachments to FDA by other means (i.e., physical media or the SRP). The ESG MDN for the ICSRs or ICSR attachments will serve as the official FDA receipt date of the ICSR.

B. Contingencies When Submitting Through the SRP

If the SRP is not functional, users will not be able to log in to submit an ICSR. You should contact the FAERS Electronic Submission Coordinator at faersesub@fda.hhs.gov for assistance.

C. Receipt Dates

If you submitted your ICSR when the ESG, FAERS, or SRP was temporarily unavailable, and the FDA receipt date for the resubmission is after the required reporting timeframe, FDA will work with you to reset the FDA receipt date. In this case, you should retain documentation showing that you submitted the ICSRs or ICSR attachments within the required reporting timeframe.

²⁹ See ICH E2B(R3) *Electronic Transmission of Individual Case Safety Reports (ICSRs) Implementation Guide—Data Elements and Message Specification*, available at FDA’s guidance web page.

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D. Physical Media as a Backup Method

FDA recommends that physical media be **used only as a backup method for electronic submission of ICSRs or ICSR attachments** when the ESG is not functional for more than 48 hours. If submitting on physical media, you should provide the information in the current version of the ICH E2B format supported by FDA. For CDER-regulated products, FDA recommends that you contact the FAERS Electronic Submission Coordinator at faersesub@fda.hhs.gov if you are considering sending ICSR files on physical media. For CBER-regulated products, you should contact the CBER Electronic Submissions Director at esubprep@fda.hhs.gov.

For submissions sent on physical media, the Agency generally determines the receipt date as it does for submissions sent to FDA on paper. The receipt date is the date it arrives by mail at the Agency. The Agency intends to contact you by telephone or email within 3 business days after receipt of the physical media submission if there are problems with the format of the report, or if it cannot be processed into FAERS, and to request resubmission of the report in the proper format. You should resubmit the reports as soon as possible. The receipt date of the resubmission will serve as the official FDA receipt date of the report.

VI. DESCRIPTIVE INFORMATION IN PERIODIC SAFETY REPORTS

For purposes of this guidance, a periodic safety report required under 21 CFR 314.80(c)(2) or 21 CFR 600.80(c)(2) is considered to have two parts:

- Descriptive information
- ICSR(s) and ICSR attachment(s)

The *descriptive information* in these periodic safety reports must be submitted in an electronic format the Agency can process, review, and archive.³⁰ The Electronic Common Technical Document (eCTD)³¹ is the format FDA accepts for submission of the descriptive portion.

ICSRs and ICSR attachments should not be submitted to the eCTD because ICSRs submitted to the eCTD will not be processed into the FAERS database. (See section III. of this guidance for information on how to submit ICSRs and ICSR attachments.)

VII. WAIVER REQUESTS

Any person required to submit a postmarketing safety report under 21 CFR 310.305, §§ 314.80, 314.98, 600.80, or section 760 of the FD&C Act may ask FDA to waive temporarily the

³⁰ See 21 CFR 314.80(g)(1) and 21 CFR 600.80(h).

³¹ Information regarding the eCTD is available on FDA's web page at <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm153574.htm>.

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requirement that the safety report be submitted in electronic format.³² We anticipate that temporary waivers will be needed only in rare circumstances.

A. Content of Waiver Requests

The request to waive the requirement to submit reports in electronic format must be made in writing,³³ and should be in a single letter and reference all products (with or without applications) that would be covered by the electronic submission waiver. The waiver request should include the reason for the request and information justifying the waiver. Reasons could include, for example, acts of nature, widespread Internet outages, and critical issues with a firm's safety database(s), such as malware attacks. The waiver request also should include a proposed end date for the waiver and the proposed alternative reporting method, such as submission on physical media.

B. Where to Submit Waiver Requests

CDER Products

For products with an approved application that are regulated by CDER, submit your waiver requests to the application in the eCTD³⁴ format, if you have the capability to do so. The requests should be addressed to the Director of CDER's Office of Surveillance and Epidemiology (OSE). If you do not have the capability to electronically transmit a waiver request to the eCTD, you may contact OSE's Regulatory Affairs Staff by email at OSE.PMKTREGS@fda.hhs.gov to discuss how to submit your waiver request. You should indicate in the subject line of your letter or email that you are requesting a waiver of the electronic reporting requirement under 21 CFR 314.80(e)(2) or 21 CFR 600.80(h)(2), as appropriate.

For drug products marketed without an approved application, you may contact OSE's Regulatory Affairs Staff by email at OSE.PMKTREGS@fda.hhs.gov. You should indicate in the subject line of your email that you are requesting a waiver of the electronic reporting requirement under 21 CFR 310.305(e)(2) or 21 CFR 329.100(c)(2), as appropriate.

CBER Products

For licensed biological products regulated by CBER, waiver requests should be addressed to:

Document Control Center
Center for Biologics Evaluation and Research
Food and Drug Administration

³² Requests for waivers under 21 CFR 310.305(e)(2), §§ 314.80(g)(2) or 329.100(c)(2) should be submitted as described in this guidance. Requests for waivers under 21 CFR 600.80(h)(2) or 21 CFR 600.81(b)(2) must be submitted in accordance with 21 CFR 600.90 and should be submitted as described in this guidance.

³³ 21 CFR 310.305(e)(2), §§ 314.80(g)(2), 329.100(c)(2), and 600.80(h)(2).

³⁴ Information about the eCTD is available at the eCTD web page <https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/electronic-common-technical-document-ectd>.

Contains Nonbinding Recommendations

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C. FDA Response to Waiver Requests

FDA reviews waiver requests on an individual basis. The Agency plans to respond in writing to the requestor, stating whether the waiver is granted. If the waiver is granted, the response will include the agreed upon alternative method for submission as well as the end date of the waiver. Waivers of the requirement to submit reports in electronic format, if granted, will be temporary.