Guidance for Industry

Providing Submissions in Electronic Format — Postmarketing Safety Reports

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact (CDER) Roger Goetsch 240-402-3730, or (CBER) Office of Communication, Outreach and Development at 240-402-7800 or 800-835-4709.

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)

June 2014
Electronic Submissions

Guidance for Industry

Providing Submissions in Electronic Format — Postmarketing Safety Reports

Additional copies are available from:
Office of Communications
Division of Drug Information, WO51, Room 2201
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993
Phone: 301-796-3400; Fax: 301-847-8714
druginfo@fda.hhs.gov
http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm

or

Office of Communication, Outreach and
Development, WO71, Room 3128
Center for Biologics Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993
Phone: 800-835-4709 or 240-402-7800
ocod@fda.hhs.gov
http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm

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)

June 2014
Electronic Submissions

TABLE OF CONTENTS

The technical specification associated with this guidance, *Specifications for Preparing and Submitting Electronic ICSRs and ICSR Attachments*, 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 (http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm115894.htm).

Guidance for Industry[1]

Providing Submissions in Electronic Format – Postmarketing Safety Reports

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This is one in a series of guidance documents intended to assist applicants making certain regulatory submissions in electronic format to the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) in the Food and Drug Administration (FDA or the Agency). This draft guidance revises and replaces the draft guidance for industry entitled *Providing Regulatory Submissions in Electronic Format – Postmarketing Individual Case Safety Reports*, issued on June 12, 2008 (73 FR 33436). It provides general information pertaining to electronic submission of postmarketing safety reports (individual case safety reports (ICSRs), attachments to ICSRs (ICSR attachments)[2] and other postmarketing safety reports) for the following products:

- Drug products marketed for human use with approved new drug applications (NDAs) and abbreviated new drug applications (ANDAs)
- Prescription drug products marketed for human use without an approved NDA or ANDA
- Biological products, other than vaccines, marketed for human use with approved biologic license applications (BLAs)
- Nonprescription (over-the-counter or OTC) human drug products marketed without an approved application.[3]

---

[1] This draft 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).

[2] See section III of this document for a description of ICSRs and ICSR attachments.

[3] See the postmarketing safety reporting requirements for:

- NDAs in 21 CFR 314.80 and ANDAs in 21 CFR 314.98;
- prescription drug products marketed for human use without an approved NDA or ANDA in 21 CFR 310.305;
- biological products marketed for human use with BLAs in 21 CFR 600.80; and

This guidance does not apply to the following:

- Vaccines[4]
- Whole blood or components of whole blood[5]
- Lot distribution reports[6]
- Human cells, tissues, and cellular and tissue-based products (HCT/Ps) regulated solely under section 361 of the Public Health Service Act[7]

Postmarketing ICSRs and ICSR attachments sent to CDER and CBER for human drug and biological products addressed by this guidance are processed into the FDA Adverse Event Reporting System (FAERS) database.[8] CDER is responsible for oversight of the FAERS database and entering information into it for both CDER and CBER. Applicants sending postmarketing ICSRs and ICSR attachments in electronic format to FDA for products regulated by CBER should follow procedures provided for CDER in this guidance and elsewhere.[9]

- nonprescription (over-the-counter or OTC) human drug products marketed without an approved application in section 760 of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 379aa). Section 760 of the FD&C Act provides for mandatory safety reporting for nonprescription human drug products not subject to applications approved under section 505 of the FD&C Act (new drug applications (NDAs) or abbreviated new drug applications (ANDAs)). Accordingly, 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. These reporting requirements became effective December 22, 2007.

[4] FDA intends to issue guidance addressing the electronic submission of postmarketing ICSRs for vaccines.

[5] Blood collection and transfusion facilities report fatalities related to blood and blood components or transfusion under 21 CFR 606.170(b). Information on submitting these reports is available on the Internet at http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/TransfusionDonationFatalities/default.htm.

[6] Lot distribution reports are not considered postmarketing safety reports; however, under FDA's final rule on electronic safety reporting, such reports are required to be submitted to FDA in electronic format (21 CFR 600.81(b)(1)). FDA intends to issue guidance addressing the submission of these reports.

[7] 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.

[8] In September 2012, the FAERS database replaced the previously used Adverse Event Reporting System (AERS) database. The transition to the FAERS database has been an important step in improving FDA's postmarketing surveillance capabilities. Information regarding the FAERS database is available on FDA's Web site at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm.

Agency guidance on electronic submissions will be updated as necessary to reflect the evolving nature of the technology and the experience of those using this technology. FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

On June 10, 2014, FDA issued a final rule requiring that postmarketing safety reports required under 21 CFR 310.305, 314.80, 314.98, 600.80, and 600.81 and section 760 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 379aa) be submitted to FDA in an electronic format the Agency can process, review, and archive. The final rule also adds 21 CFR 329.100 to address electronic submission of safety reports required by section 760 of the FD&C Act. These requirements are effective as of June 10, 2015.[10]

III. GENERAL INFORMATION ABOUT ICSR SUBMISSION

An ***ICSR*** is a description of an adverse drug experience[11] related to an individual patient or subject. An ICSR is made up of data elements, such as date of adverse drug experience, name of suspect medical product, and name of manufacturer. These data elements are listed in the relevant regulations. The information described by the data elements should be included in the ICSR submission if available and applicable to the report.

ICSR attachments include supporting information for ICSRs, such as relevant hospital discharge summaries and autopsy reports or death certificates. ICSR attachments also include published articles for ICSRs based on scientific literature (§§ 314.80(d) and 600.80(d)).

---

[9] Further information regarding regulations and guidances related to postmarketing safety reporting can be found on the FDA CDER Web site, Postmarketing Safety Reporting Requirements for Drug and Biologic Products, at http://www.fda.gov/Drugs/DrugSafety/ucm299833.htm.

[10] Section 745A(a) of the FD&C Act (21 U.S.C. 379k-1), added by section 1136 of the Food and Drug Administration Safety and Innovation Act (FDASIA) (Pub. L. 112-144), 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, does not preclude FDA from implementing such requirements by notice and comment rulemaking (5 U.S.C. 553). Accordingly, at this time, even though FDA has concluded that certain submissions that are addressed in this final rule are also within the scope of section 745A(a), FDA has determined that it is appropriate to amend the regulations on the submission of postmarketing safety reports 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. This draft guidance, when finalized, will represent the Agency's current thinking on certain topics associated with that rulemaking. FDA may consider, at a future date, whether to include information pertaining to submission of postmarketing safety reports in electronic format in guidance under section 745A(a) of the FD&C Act.

[11] For purposes of this draft guidance, the term *adverse drug experience* includes an adverse experience associated with use of a biological product.

This section addresses general information related to the electronic submission of *initial and followup ICSRs and ICSR attachments* for the types of reports listed below. The procedures for electronic submission of initial and followup ICSRs and ICSR attachments for all of these types of reports are the same.

- 15-day Alert reports (§§ 310.305(c), 314.80(c)(1), and 600.80(c)(1))
- ICSRs for serious, expected and nonserious adverse drug experiences (§§ 314.80(c)(2)(ii)(B) and 600.80(c)(2)(ii)(B))
- Serious adverse event reports required by section 760 of the FD&C Act

A. Parts of an ICSR Submission

For purposes of this discussion of electronic submissions, an initial or a followup ICSR submission is considered to have two parts:

1. ICSR
2. ICSR attachments, if applicable

Followup ICSRs 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 ICSR. Accordingly, followup ICSRs should include information about an adverse drug experience that has been previously reported as an initial ICSR along with any new information. Any ICSR attachments submitted with an initial ICSR (e.g., literature articles, hospital discharge summaries) should not be resubmitted with a followup ICSR. See section III.D for information on using unique case identification numbers to ensure that initial ICSRs and followup ICSRs are linked.

B. Options for Electronic Submission of ICSRs to FDA

FDA provides two options for electronic submission of ICSRs to FAERS: (1) direct submission through the Electronic Submissions Gateway (ESG) and (2) submission through the Safety Reporting Portal (SRP). Direct database-to-database submission through the ESG is described on our FAERS Electronic Submissions Web page.[12] 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 the FDA. Once received through the ESG, the submitted reports are processed into the FAERS database.

Submission of safety reports through the SRP is described on the FDA SRP Web Page.[13] To use the SRP, the ICSR information is entered manually into a Web-based form and then submitted to FDA to be uploaded into the FAERS database.

---

[12] The FAERS Electronic Submissions Web page is available at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm115894.htm.

[13] The FDA SRP Web page is available at http://www.safetyreporting.hhs.gov.

C. Technical Specifications for Electronic Submission of ICSRs

ICSRs and ICSR attachments must be submitted to FDA in an electronic format that we can process, review, and archive. For instructions on organizing, preparing, and submitting ICSRs and ICSR attachments using the direct submission method, see the technical specifications document entitled "Specifications for Preparing and Submitting Electronic ICSRs and ICSR Attachments" available on the FAERS Electronic Submissions Web page. The technical specifications document is incorporated by reference into this draft guidance document and addresses data elements, electronic transport format, and other aspects of the ICSR and ICSR attachment that FDA currently accepts when reports are submitted using the direct submission method. Information on how to submit ICSRs and ICSR attachments through the SRP is available on the FDA SRP Web Page.

D. Unique Case Identification Numbers for Initial and Followup ICSRs

Postmarketing safety reporting often involves submitting a series of reports consisting of the initial ICSR and followup ICSRs, along with any associated attachments, over the life cycle of an individual case. To avoid duplicate ICSRs in the FAERS database, reports for all product types addressed in this guidance should have a unique case identification number.[14] Because we need to match followup ICSRs with the initial ICSR, it is important that the unique case identification number used for the initial ICSR be included in any followup ICSRs when reports are transmitted directly through the ESG. Thus, the initial ICSR and all of its followup ICSRs will be linked in FAERS, regardless of the time or method of transmission. For further information, see the section on identification numbers for initial and followup ICSRs in the technical specifications document entitled "Specifications for Preparing and Submitting Electronic ICSRs and ICSR Attachments" available on the FAERS Electronic Submissions Web page.

When the initial ICSR is submitted through the SRP, users will be able to return to the initial ICSR and submit followup reports as more information about the reported adverse experience becomes available. Users may log in to their SRP accounts, locate the ICSR record, and modify or add to the initial ICSR to create a followup submission. Users may submit as many followup reports as necessary. More detailed information on how to modify or add to an initial ICSR is provided below in section III. G.

E. Submitting Labeling and Labels

Under the final rule, for prescription drugs marketed for human use without an approved application, each ICSR required under § 310.305 must include a copy of the current content of

[14] See §§ 310.305(d), 314.80(f), 329.100(b), 600.80(f), and 600.80(g). The unique case identification number is referred to as Manufacturer Report Number on the Form FDA 3500A. The unique case identification number is used to track ICSRs and is distinct from the unique code that should be assigned to protect the identity of the patient (under §§ 310.305(f), 314.80(i), 329.100(d), and 600.80(h)).

labeling, unless it is already on file at FDA (§ 310.305(c)(1)). For nonprescription human drug products marketed without an approved application, each ICSR required under section 760 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)). Labeling and labels should be submitted as ICSR attachments, unless already on file at FDA.[15] Persons submitting reports can satisfy the requirement to include labeling or labels by referencing the Structured Product Labeling (or SPL) file submitted through the electronic drug registration and listing system.[16]

F. Notification of Initial Electronic ICSR Submission

Before submitting an ICSR in electronic format to FDA for the first time, whether through the ESG or SRP, you should notify the FAERS Electronic Submission Coordinator of your intent at faersesub@fda.hhs.gov. The FAERS Coordinator will assist you to ensure that all steps have been completed for successful submission of ICSRs. It is not necessary to contact the FAERS Coordinator before submitting ICSRs subsequently in electronic format.

G. Sending in Submissions

ICSRs and ICSR attachments should be submitted to FDA through FDA's ESG or the SRP, which are open 24 hours a day, 7 days a week. ICSR attachments should be submitted to FDA either at the same time that the associated ICSR is submitted to FDA or after the associated ICSR is submitted to FDA. Once received either through the ESG or the SRP, the ICSRs will be processed into FAERS.

For direct transmission through the ESG of ICSRs for drug and biological products covered by this guidance, an account with FDA's ESG should be created, if not previously established.[17] To establish an account with FDA's ESG and for further information on providing submissions using the ESG, refer to http://www.fda.gov/esg. To send ICSRs for drug and biological products covered by this guidance through the SRP, an account with FDA's SRP should be created. For assistance in establishing an account, contact the FAERS Electronic Submissions Coordinator at faersesub@fda.hhs.gov. Further information about creating an SRP account is also available on the FDA SRP Web Page.

---

[15] Labeling and labels are already on file at FDA if they were submitted to FDA in Structured Product Labeling (SPL) format as part of the electronic drug establishment registration and listing process.

[16] See the guidance for industry entitled *Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Drug Listing* at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm and FDA's Web site on Structured Product Labeling Resources at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA Drugs guidance Web page at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

[17] Most entities will already have established an ESG account to comply with the establishment registration and drug listing requirements.

H. Notification of Receipt of Submissions by the FDA

1. Direct Submission Through the ESG

Once a submission (one or more ICSRs or ICSR attachments) reaches the ESG and is successfully recognized and decrypted, an ESG message delivery notice (MDN) is sent to the submitter. The date of this MDN serves as the official FDA receipt date of each successfully transmitted ICSR and ICSR attachment in the submission. See FDA's ESG Web site for further information about receipt of submissions through the ESG.[18]

After receipt of the submission, the ICSR or ICSR attachments are processed into the FAERS database, and a second automated acknowledgement message (FAERS acknowledgement) is sent to the submitter via the ESG. The FAERS acknowledgement provides the sender the status of each ICSR or ICSR attachment in the transmission. We expect that you will receive your ESG MDN and FAERS acknowledgements within 24 hours after you have submitted an ICSR or ICSR attachment to the ESG. Any ICSR or ICSR attachment that FDA is not able to load into the FAERS database should be corrected by the sender and resubmitted within the required reporting time frame. The receipt date of the corrected resubmission serves as the official FDA receipt date of the report.

If your ICSR is submitted to FDA using the ESG and your ICSR attachments are submitted on physical media, the ESG MDN acknowledgement for the ICSR serves as the official FDA receipt date of the ICSR, and the date that FDA's Central Document Room receives the physical medium containing the ICSR attachments serves as the official FDA receipt date of the ICSR attachments. Even though the ICSR and ICSR attachments can be received by FDA on different days, they must be submitted to the Agency within the time periods specified in FDA regulations and the FD&C Act. Please plan your submissions accordingly.

Additional information on the receipt date of submissions is available in the guidance for industry entitled *Providing Regulatory Submissions in Electronic Format – Receipt Date*.[19]

2. Submission Through the SRP

After the ICSR and/or ICSR attachments have been submitted, they are processed into the FAERS database, and an acknowledgement message (SRP acknowledgement) is sent to the user. The SRP acknowledgement provides the user the status of the submission and indicates whether or not it was accepted into the FAERS database. We expect that the user will receive the SRP acknowledgement immediately after the ICSR or ICSR attachment has been sent through the SRP. Any ICSR or ICSR attachment that FDA is not able to load into the FAERS database

[18] FDA's ESG Web page is available at http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/ucm113223.htm.

[19] The draft guidance is available at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

should be corrected by the user and resubmitted within the required reporting time frame. The receipt date of the corrected resubmission serves as the official FDA receipt date of the report.

I. Contingencies If the ESG, FAERS, or SRP Is Temporarily Unavailable

As stated previously, we expect that you will receive your ESG MDN, FAERS acknowledgement, or SRP acknowledgement, as appropriate, within 24 hours after you have submitted an ICSR or ICSR attachment. If you do not receive the acknowledgement(s) within 24 hours, you should first check the "ESG System Status" on FDA's Web site at http://www.fda.gov/esg to determine whether we are experiencing any problems with the ESG or the SRP.

- **If the ESG is functional**, you should contact the FAERS Electronic Submission Coordinator at faersesub@fda.hhs.gov to determine why you have not received your acknowledgements.

- **If the ESG is not functional** for more than 48 hours and you decide to meet your regulatory requirements by submitting your ICSRs or ICSR attachments on physical media, you should **not** resubmit the ICSRs to FDA using the ESG or SRP when it becomes functional. In this case, the official FDA receipt date of the ICSRs will be the date the physical media arrives at the Agency.

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

- **If the SRP is not functional**, you should contact the FAERS Electronic Submission Coordinator at faersesub@fda.hhs.gov for assistance.

- If the ESG, SRP, and/or FAERS is not functional and the FDA receipt date for resubmission of your ICSRs or ICSR attachments does not meet our regulatory requirements because the ESG, SRP and/or FAERS is not functional, we intend to work with you to reset the receipt date. In this case, you should keep relevant documentation for compliance purposes (i.e., evidence of submission of your ICSRs or ICSR attachments within the required time frame).

- If you submit ICSRs or ICSR attachments to the ESG that we are unable to load into the FAERS database because you did not use data elements and electronic transport formats that FDA supports, the FAERS acknowledgement should indicate that we could not load these ICSRs into FAERS. The acknowledgement also should indicate which, if any, ICSRs or ICSR attachments that you sent to the ESG at the same time were processed into FAERS. You should resubmit to us only those ICSRs or ICSR attachments that were not processed into FAERS. Your resubmission should be given a different file name than

the original submission and should take place within the required reporting timeframe. The date of the ESG MDN acknowledgement for the resubmission will serve as the official FDA receipt date of the ICSR or ICSR attachments.

Physical Media as a Backup Method

On occasion, it may be necessary to send an ICSR and/or ICSR attachment in electronic format to FDA using appropriate physical media. FDA recommends that physical media be **used only as a backup method for electronic submission of ICSRs** when the ESG is down for more than 48 hours. 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 biologics, companies should contact the CBER Electronic Submissions Director at esubprep@fda.hhs.gov.

For submissions sent on physical media, the Agency determines the receipt date as it does with other types of submissions sent to the FDA on paper (i.e., receipt date is the date it arrives by mail at the Agency.) The Agency intends to contact you if there are problems with the format of the report or if it does not process properly into FAERS. We intend to contact you by telephone or email within 3 working days after we receive your report to describe the problem and request a resubmission of the report in the proper format. This resubmission should take place as soon as possible. The receipt date of the resubmission will serve as the official FDA receipt date of the report.

IV. POSTMARKETING SAFETY REPORTS OTHER THAN ICSRs

For purposes of this discussion of electronic submissions, a postmarketing periodic report (§§ 314.80(c)(2) and 600.80(c)(2)) is considered to have three parts:

1. Descriptive information
2. ICSR(s)
3. ICSR attachment(s), if applicable

Submission of ICSR(s) and ICSR attachment(s) is addressed in section III above. The *descriptive information* portion of the periodic adverse drug experience report (PADER) required under § 314.80(c)(2)(ii)(A) or periodic adverse experience report (PAER) required under § 600.80(c)(2)(ii)(A) should be submitted as a portable document format (PDF) file to section 5.3.6 of the Electronic Common Technical Document (eCTD).[20] *FDA is unable to accept submission of ICSRs to the eCTD* because ICSRs submitted to the eCTD cannot be processed into the FAERS database.

[20] Information regarding the eCTD is available on FDA's Web site at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm153574.htm.

V. WAIVER REQUESTS

Any person required to submit a postmarketing safety report under §§ 310.305, 314.80, 314.98, 600.80, 600.81, or section 760 of the FD&C Act may ask FDA to waive temporarily the requirement that the safety report be submitted in electronic format.[21] 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, in a single letter and should 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 (i.e., information justifying the waiver). Reasons could include, for example, acts of nature, widespread internet outages, and temporary issues with an applicant's adverse event database(s). The waiver request also should include a proposed end date for the waiver and a description of any proposed alternative reporting method, as relevant to the circumstances. Potential alternative reporting methods could include (but are not limited to) physical media and paper (i.e., Form FDA 3500A). The waiver request should be clearly titled "**WAIVER REQUEST – POSTMARKETING SAFETY REQUIREMENTS**" in bold capital letters at the top of the first page of the submission.

B. Where to Submit Waiver Requests

For drug products (with or without an approved application) and licensed biological products regulated by CDER, waiver requests should be addressed to:

Director
Office of Surveillance and Epidemiology
Central Document Room
Center for Drug Evaluation and Research
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

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

Document Control Center
Center for Biologics Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue
Building 71, Room G112
Silver Spring, MD 20993-0002

[21] Requests for waivers under §§ 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 §§ 600.80(h)(2) or 600.81(b)(2) must be submitted in accordance with § 600.90 and should be submitted as described in this guidance.

C. FDA Response to Waiver Requests

FDA reviews waiver requests on a case-by-case basis. FDA intends to respond in writing to the requestor,[22] stating whether or not the waiver is granted. If the waiver is granted, FDA intends to also include in its response letter a description of the alternative submission method(s) the Agency intends to accept. **Waivers of the requirement to submit reports in electronic format, if granted, will be temporary.**

[22] FDA intends to contact the individual who submitted the waiver request unless an alternate contact person is provided.