Instructions for Electronic Submission of Mandatory Adverse Event Reports to FDA CVM

1 Introduction

This document provides instructions for industry stakeholders (Sponsors) to submit FDA-compliant, electronic animal Adverse Event Reports (AER) to the FDA Center for Veterinary Medicine. These electronic submissions use the Health Level Seven (HL7) Individual Case Safety Report (ICSR) Release 2 Standard and have a specific form and format (ISO/HL7 27953-1). Sponsors must follow these instructions to successfully submit electronic HL7 ICSR compliant AERs to CVM. AERs may be bundled into HL7 ICSR batches for submission.

Sponsors must register with the FDA ESG NextGen before they can begin submitting electronic AERs to CVM. Please see the instructions at:
https://www.fda.gov/industry/electronic-submissions-gateway

2 FDA Contact Information

This section contains contact information in the event sponsors need assistance.

2.1 FDA Electronic Submissions Gateway (ESG NextGen) Support

For FDA ESG technical questions and account setup, please email:

ESGNGSupport@fda.hhs.gov

2.2 CVM Office of Surveillance and Compliance (OSC) Adverse Event (AE) Support

For assistance or questions regarding AER issues related to Form FDA 1932, GFI#188, GFI#214, GFI#143, or your Marketing Authorization Holder (MAH) ID please email:

CVMAESupport@fda.hhs.gov

3 Document References

FDA and CVM provide documents to assist sponsors in correctly structuring the HL7 ICSR-compliant electronic AER submission. These documents can be found under the Supporting Documents sections of the Veterinary Adverse Event Reporting for Manufacturers webpage:

https://www.fda.gov/animal-veterinary/report-problem/veterinary-adverse-event-reporting-manufacturers

Contact CVMAESupport@fda.hhs.gov for the two Electronic Transmission Implementation Specifications technical documents that accompany GFI#214 Electronic Standards for Transfer of Data:

- Step By Step Document
- Validation Procedures Document

These documents describe the details of HL7, ICSR-compliant veterinary adverse event reports, including mandatory and optional components of the electronic ICSR message. One of these documents also describes how FDA/CVM validates electronically submitted ICSR messages.

4 FDA Electronic Submissions Gateway (ESG NextGen) Operations

The FDA ESG NextGen is the system that sponsors use to electronically transmit AERs to FDA CVM. The FDA ESG is a secure, high speed transfer method that is available seven days a week, 24 hours a day.

The FDA ESG NextGen has defined a set of procedures and processes that sponsors must accomplish prior to sending electronic submissions to FDA and CVM. Full information for completing the registration and operation of ESG NextGen software is available at the following links:

https://www.fda.gov/industry/electronic-submissions-gateway

The FDA ESG NextGen User Guide can be found at the following link:

https://www.fda.gov/industry/getting-started-esg-nextgen/user-guides

Completion of all FDA ESG requirements must be accomplished prior to transmitting files to FDA CVM.

5 Sponsor Unique Identifiers

The submitted AER requires a number of mandatory unique identifying elements that must be supplied by the Manufacturer Authorized Holder (MAH) and/or the submitter of the AER. These identifiers are from the following three organizations/sources:

- Dun & Bradstreet
- Food and Drug Administration – Office of Regulatory Affairs
- Food and Drug Administration – Office of Surveillance and Compliance

5.1 Dun & Bradstreet Data Universal Numbering System (DUNS)

Dun & Bradstreet assigns and maintains a database of the Data Universal Numbering System (DUNS) numbers, which serve as unique identifiers (codes) of business entities. On application, each business entity (e.g., registrant, establishment, importer, US agent) is assigned a distinct site-specific 9-digit DUNS number. The site-specific DUNS number is used by FDA in identifying and verifying certain business information for a given entity, e.g., proprietary names used by the entity, addresses, additional ownership information, such as the name of each partner or the name of each corporate officer and director, and the state of incorporation. If the DUNS number for a location has not been assigned, a business may obtain one for no cost directly from Dun & Bradstreet (http://www.dnb.com).

5.2 FDA Establishment Identifiers (FEI)

The FEI is a multi-digit number that the FDA uses to identify a given establishment. This number is the unique identifier for the establishment and must never be changed or reused to identify another establishment. The number is assigned to an establishment at a specific location. If a sponsor has more than one location, each location will have a unique FEI.

5.3 MAH Identifier (MAH ID)

The MAH ID is the eight-character code assigned for the specific identification of each sponsor and validation against the application numbers of any submitted AERs. Please contact CVMAESupport@fda.hhs.gov to register your MAH ID and its association with your products.

6 Procedures to Transmit Electronic AERs to CVM

All FDA ESG NextGen registration procedures MUST be completed prior to sending submissions to FDA/CVM.

6.1 Using the ESG NextGen's Unified Submission Portal (USP) Option.

ESG NextGen's Unified Submission Portal (USP) is a web-based interface which serves as the primary platform for preparing, submitting, and managing electronic regulatory submissions to the FDA. The USP replaces legacy ESG WebTrader.

To review the USP workflows and processes, please download and read the ESG NextGen USP User Guide below link.

ESG NextGen USP User Guide

6.2 Using the ESG Next Gen's AS2 Gateway to Gateway Option

ESG NextGen will continue to support legacy ESG AS2 account users. To understand updates needed to submit to ESG NextGen via AS2, please download and read the ESG NextGen AS2 User Guide in the link below.

https://www.fda.gov/industry/getting-started-esg-nextgen/user-guides

7 Electronic AER Submission Format

Electronic submissions of AERs have a specific form and format. Refer to the Electronic Transmission Implementation Specifications Step By Step technical document for details about the submission format. The Step By Step technical document specifies that the content of the submission file must start with the header from the ICSR schema specified as the "MCCI_IN200100UV01".

The schema location has been published on FDA's External Web site located at:

http://www.accessdata.fda.gov/icsr/schema/cvm/schemas/vich/multicacheschemas/MCCI_IN200100UV01.xsd

8 Responses from FDA and CVM Regarding Transmitted ICSR Submissions

8.1 FDA ESG Responses

The FDA ESG returns two messages for each submission transmitted. The first message indicates that the FDA ESG has received your submission error free. This includes the decryption of the message along with the digital certificate validation. The second message from the ESG notifies the sender that the FDA ESG has successfully transferred the submission to the FDA/CVM processing system responsible for validating and inserting the submission into the ICSR processing system.

8.2 CVM Electronic Submission System (ESS) Responses

The CVM ESS will validate and process the incoming AERs and will either accept individual ICSR for processing or reject individual messages because of data errors. CVM ESS will attempt to fully validate every ICSR message and inform you of the problems identified. The message that a submitter receives has detailed information that indicates the status of the submitted batch along with statistics of accepted and rejected ICSRs.

8.3 CVM's Adverse Event System Responses

Here are several examples of messages that you might receive from CVM's ESS Adverse Event processing system (IERS):

Figure 8 - IERS Passed Acceptance Message

This sample message is a submission of two ICSR AERs for which no errors were found on IERS validation.

```
Validation Processing Report:

FDA/CVM Adverse Event Processing System
Validation Report for ICSR Batch Submission

Your submission has been received and accepted for review.

Date/Time this validation report was generated: 03-02-2015 13:04:07
IERS Version: V2013-06-21-1.0
ESG Core Id: ci1273495943345.91658@llntap01_te
Received On: 03-02-2015, 12:56:54
Received From: GAPINDUS
Document ID: A200008
Submission ID: L60

Batch ID#:  54321
Batch Sender: Jane  Doe
================================================================================================
Validator Version: DTS_Validator_05312013
Batch Wrapper Validation Results:
No errors in batch wrapper.

================================================================================================
Message Sequence:  1 <UAER ID number: USA-GAPINDUS-42Q3> <Message Number: GAPINDUS-86903192580-42Q3>
================================================================================================
Message Sequence 2 <UAER ID number: USA-GAPINDUS-55T5> <Message Number: GAPINDUS-86903192581-55T5>
================================================================================================

No errors in ICSR message.

ICSRs Submitted: 3
ICSRs in Error: 0

<<<<<< NOTICE:  All reports have passed data quality control validations. >>>>>>
Your submission has been received and valid messages have been accepted for review
```

Figure 9 - IERS Partially Passed Acceptance Message

This sample message is for a submission consisting of three ICSR AERs. One AER (Message 2) had errors that were detected by IERS such that the AER was rejected. Two AERs (Messages 1 and 3) passed validation and were accepted.

```
Validation Processing Report:

FDA/CVM Adverse Event Processing System
Validation Report for ICSR Batch Submission

Your submission has been received and accepted for review.

Date/Time this validation report was generated: 03-02-2015 13:04:07
IERS Version: V2013-06-21-1.0
ESG Core Id: ci1273495943345.91658@llntap01_te
Received On: 03-02-2015, 12:56:54
Received From: GAPINDUS
Document ID: A200008
Submission ID: L60


Batch ID#:  12345
Batch Sender: Jane  Doe
================================================================================================
Validator Version: DTS_Validator_05312013
Batch Wrapper Validation Results:
No errors in batch wrapper.

================================================================================================
Message Sequence:  1 <UAER ID number: USA-GAPINDUS-42Q3> <Message Number: GAPINDUS-86903192580-42Q3>
No errors in ICSR message.

================================================================================================
Message Sequence:  2 <UAER ID number: USA-GAPINDUS-55T5> <Message Number: GAPINDUS-86903192581-55T5>
Error: VICH_GL42_B.7.1_BR1:The AER must contain a valid value for “Attached Document Filename”.

================================================================================================
Message Sequence:  3 <UAER ID number: USA-USFDACVM-33TY> <Message Number: GAPINDUS-86903192582-33TY>
No errors in ICSR message.

================================================================================================


ICSRs Submitted: 3
ICSRs in Error: 1

<<<<<< NOTICE:
-“Error” identifies messages that must be corrected and resubmitted.
-“Warning” identifies messages that should be reviewed by the sender for necessary follow-up submissions.
-Messages containing both “Error” and “Warning” validation results must be corrected and resubmitted.
>>>>>>>

Your submission has been received and valid messages have been accepted for review.
```

Figure 10 - IERS Rejection Message

This sample message is for a submission that consisted of one AER and had errors that were detected by IERS such that the AER was rejected.

Validation Processing Report:

FDA/CVM Adverse Event Processing System
Validation Report for ICSR Batch Submission

Your submission has been rejected. Please correct the following errors and submit the report again.

Date/Time this validation report was generated: 02-10-2015 05:42:08
IERS Version: V2010-06-21-1.0
ESG Core Id: ci1273743435665.47124@llntap02_te
Received On: 02-10-2015, 05:41:53
Received From: GAPINDUS
Document ID: N/A

Batch ID#: 537
Submission Contact Person: John Doe
==========
Validator Version: DTS_Validator_05312013
Batch Wrapper Validation Results:
No errors in batch wrapper.

==========
Message Sequence: 1 <UAER ID number: USA-FDASENDR-2009-US00023> <Message Number: FDASENDR-1102214-2009-US00023>
==========
Error: USFDACVM_GL42_A.4.4.3_BR5: When the "Profile Identifier" is "Adverse Event" and the "Type of Submission" is "EXPEDITED", "PERIODIC", or "OTHER", the value of "Type of Information in Report" must be from the vocabulary list d.Type of Information as identified in the Rule Description above.

ICSRs Submitted: 1
ICSRs in Error: 1

<<<<<< NOTICE: The complete batch of submitted reports has been rejected. >>>>>>>

Figure 11 - IERS Rejection Message Schema Violation

This sample message shows a validation failure for the reason that a compliant XML schema was not formed. This type of error prevents further validation of the message. For that reason, other errors might subsequently be identified after initial correction and resubmission.

Validation Processing Report:

FDA/CVM Adverse Event Processing System
Validation Report for ICSR Batch Submission

Your submission has been rejected. Please correct the following errors and submit the report again.

Date/Time this validation report was generated: 02-10-2015 05:42:08
IERS Version: V2010-06-21-1.0
ESG Core Id: ci1273743435665.47124@llntap02_te
Received On: 02-10-2015, 05:41:53
Received From: GAPINDUS
Document ID: N/A

Your submission has been rejected. The batch XML is not an ISO27953-1 ICSR schema compliant XML.