VICH International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products

#214

GUIDANCE FOR INDUSTRY

Pharmacovigilance of Veterinary Medicinal Products Electronic Standards for Transfer of Data

VICH GL35

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only

Submit comments on this draft guidance by the date provided in the *Federal Register* notice announcing the availability of the draft guidance. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.regulations.gov. You should identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For further information regarding this document, contact Margarita Brown, Center for Veterinary Medicine, (HFV-240), Food and Drug Administration, 7519 Standish Place, Rockville, MD 20855, 240-276-9048, e-mail: margarita.brown@fda.hhs.gov.

Additional copies of this draft guidance document may be requested from the Communications Staff (HFV-12), Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Place, Rockville, MD 20855, and may be viewed on the Internet at either http://www.fda.gov/AnimalVeterinary/default.htm or http://www.regulations.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Veterinary Medicine
September 15, 2011

VICH GL35 (PHARMACOVIGILANCE: EST)
June 2010
For consultation at Step 4

PHARMACOVIGILANCE OF VETERINARY MEDICINAL PRODUCTS: ELECTRONIC STANDARDS FOR TRANSFER OF DATA

Recommended for Consultation
at Step 4 of the VICH Process
in June 2010
by the VICH Steering Committee

TABLE OF CONTENTS

PHARMACOVIGILANCE OF VETERINARY MEDICINAL PRODUCTS
Electronic Standards for Transfer of Data
VICH GL35

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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.

Introduction

The objective of this draft guidance is to provide recommended standards to construct a single electronic message to transmit Data Elements for Submission of Adverse Event Reports (AERs) to all member regions. FDA is in the process of reviewing its regulations, guidance, and forms relating to pharmacovigilance of veterinary medicinal products to ensure consistency with current policy. This guidance will not be finalized until such time as any changes to other relevant documents are also finalized.

The need to transfer and disseminate information quickly, accurately and easily between Regulatory Authorities (RA) and Marketing Authorization Holders (MAH) on a worldwide scope is especially pertinent to the notification and assimilation of information for pharmacovigilance. Whereas the recommended definition of the pharmacovigilance information has been set forth within the draft guidances entitled, "Pharmacovigilance of Veterinary Medicinal Products: Management of Adverse Event Reports (AER's)" (VICH GL24), "Pharmacovigilance of Veterinary Medicinal Products: Controlled Lists of Terms" (VICH GL30) and "Pharmacovigilance of Veterinary Medicinal Products: Data Elements for Submission of Adverse Event Reports" (VICH GL42), this draft guidance defines recommended electronic standards for transfer of data.

In order to allow for electronic exchange of this information between stakeholders, further specification of the field descriptors and their relationships, including agreement on format of the electronic message is essential.

FDA's guidance documents, including this draft 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.

Scope of Recommended Electronic Standards for Information Exchange

The scope of recommended electronic standards for exchange of veterinary pharmacovigilance data between VICH RAs and MAHs includes but is not limited to:

- **Recommendation to ensure secure transmission**
- **Definition of the electronic message structure**
- **Relationships (cardinality) between the data elements**
- **Recommend additional vocabularies for electronic transmission of data defined in draft VICH GL24, draft VICH GL30, and draft VICH GL42**
- **Business and schema validation rules and field descriptors specification for the data defined in draft VICH GL24, draft VICH GL30, draft VICH GL42, and this draft guidance**

Recommendations to Ensure Secure Transmission

Regional exchange of pharmacovigilance information preferably occurs through a Gateway that follows the International Conference on Harmonisation of Technical Requirements for Approval of Pharmaceuticals for Human Use (ICH) - Multi-Disciplinary Group 2 (M2) (ICH M2 Gateway) recommendation to the ICH Steering Committee on "Electronic Standards for the Transfer of Regulatory Information (ESTRI) General Recommendation: ESTRI Gateway" in order to allow for an automated and secure way, including all aspects of confidentiality, authentication, integrity and non-repudiation of all transactions in pharmacovigilance. MAHs should adhere to the relevant RA's gateway specifications.

Definition of the Electronic Message Structure

For the basis of describing the messaging structure, the VICH Pharmacovigilance Working Group recommends the adoption of a single standard, i.e., the International Standard ISO 27953-1. The message format should be XML.

A US Food and Drug Administration (FDA) Center for Veterinary Medicine (CVM) technical document entitled "Electronic Submission of Animal Adverse Events: HL7 Individual Case Safety Report (ICSR) Electronic Transmission Implementation Specifications [Step By Step]" (herein known as the US FDA CVM Step By Step Document) is available on the US FDA CVM website at http://www.fda.gov/downloads/AnimalVeterinary/SafetyHealth/ReportaProblem/UCM213149.pdf. This US FDA CVM Step By Step Document will serve as the core document from which VICH will develop its own specific VICH Step By Step Document in line with ISO 27953-1 for implementation. The unique adverse event processing system of each MAH and RA should be compliant with the VICH Step By Step Document (to be developed).

The purpose of this VICH Step By Step Document will be to provide recommendations to assist users, reporters, and technical staff in completing a well formed electronic message for animal veterinary medicinal products adverse event reports (AER). The draft VICH GL42 document has recommended a standard set of definitions to describe the data elements that should be submitted for compliant adverse event reports. This VICH Step By Step Document will provide a translation and mapping of draft VICH GL42 compliant adverse event elements into an electronic message. The draft VICH GL42 data elements comprise the "payload" of the message.

These adverse event submissions are intended to be sent electronically to the RAs through their respective Electronic Submissions Gateway (ESG) and upon receipt, they will be processed by the relevant RA's unique systems. In addition to the "payload" information, the electronic message also contains "wrapper" information (also known as envelope information). Unique and specific information should be included in the wrappers of the electronic message, as specified by the RAs. The purpose of this wrapper information is so that the electronic message can be processed appropriately according to each RA's administrative needs. These unique and specific data should be specified in each RA's technical documents.

Relationships (Cardinality) Between the Data Elements

The recommended relationships (cardinality) between the data elements are set forth in draft VICH GL42 and Annex A to draft VICH GL35, and will be further elaborated on in the VICH Step By Step Document and VICH Validation Procedure Document (see description below). The draft data model diagrams are found in Annex A to this draft guidance. Implementers should review and study all 4 of these documents, when finished, to understand the relationships between the data elements.

For repeatable fields, the RA should provide the maximum number of arrays that RA electronic systems will accept.

Business and Schema Validation Rules, Field Descriptors Specification for the Pharmacovigilance Data and Wrapper Information and Relationships (Cardinality)

The US FDA CVM technical document entitled "Electronic Submission of Animal Adverse Events HL7 Individual Case Safety Report (ICSR) Electronic Transmission Implementation Specifications [Validation Procedures]" (herein known as the US FDA CVM Validation Procedures Document) is available on the US FDA CVM website (http://www.fda.gov/downloads/AnimalVeterinary/SafetyHealth/ReportaProblem/UCM213150.pdf).
The US FDA CVM Validation Procedures Document will serve as the core document from which VICH will develop its own specific VICH Validation Procedures Document that will be

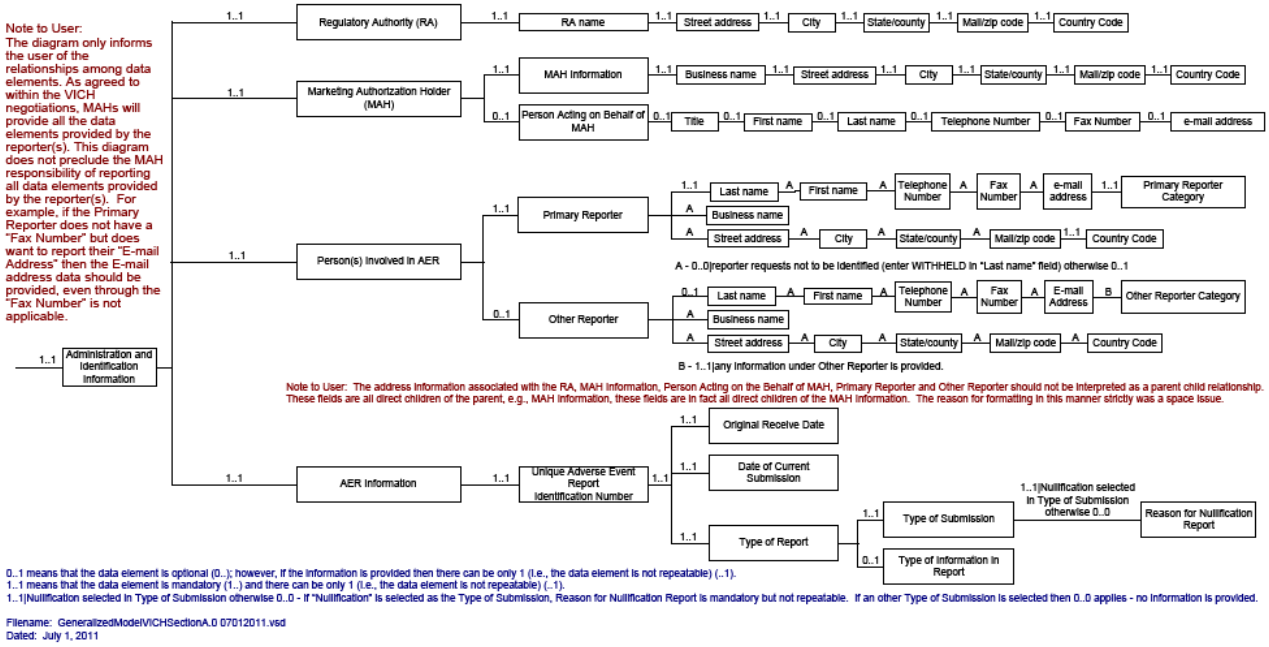
used in worldwide VICH implementation. The unique adverse event processing system of each MAH and RA should be compliant with the VICH Validation Procedures Document (to be developed).

Field Descriptions

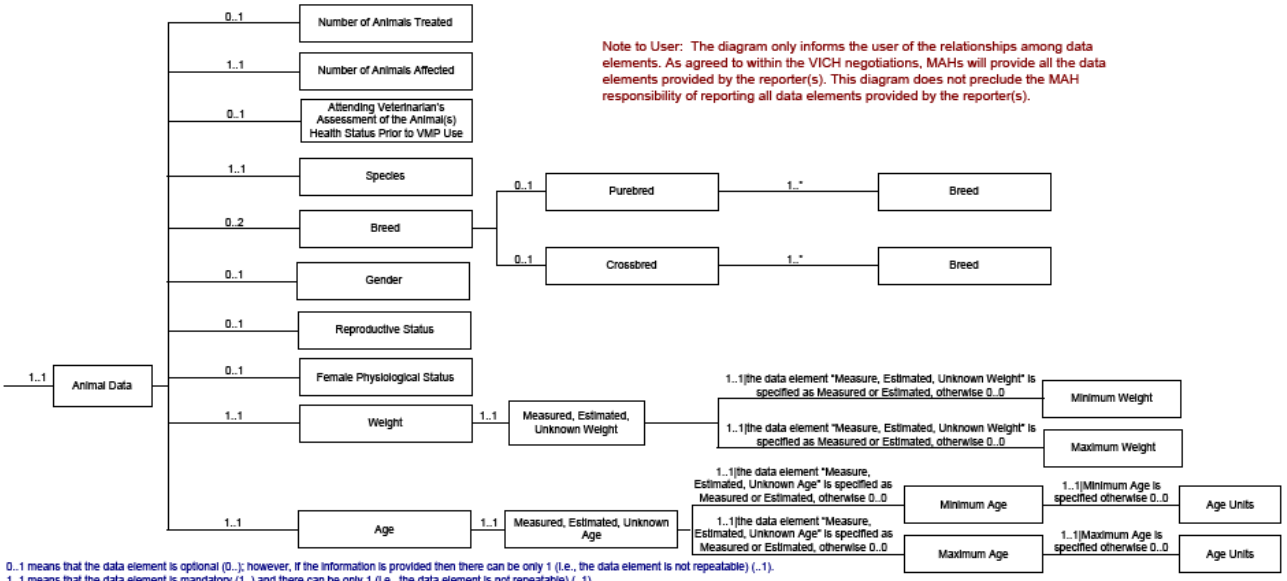
Presented in Annex B are the recommended field lengths and data types for all the data elements that will serve as the basis for discussion in the VICH implementation of electronic transmission of adverse events.

Annex A

Draft Data Model for Administrative and Identification Information



Draft Data Model for Animal Data

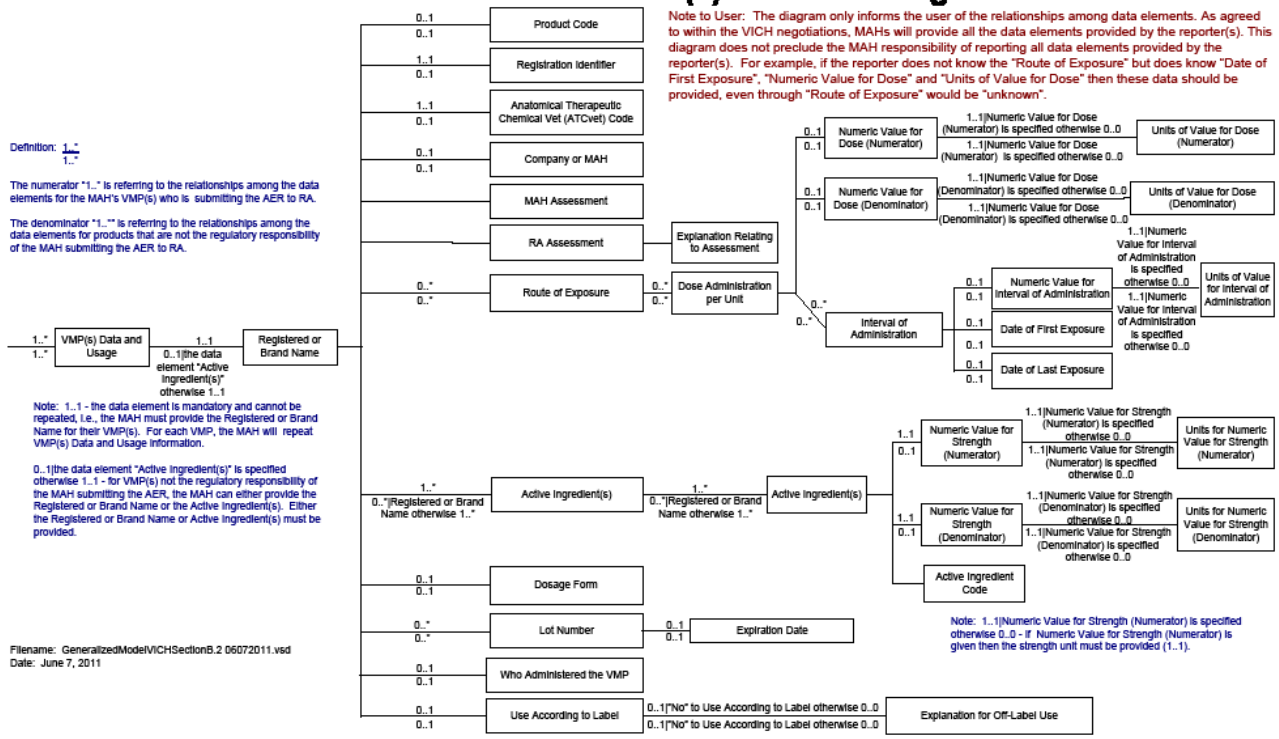


0..1 means that the data element is optional (0..); however, if the information is provided then there can be only 1 (i.e., the data element is not repeatable) (..1).
1..1 means that the data element is mandatory (1..) and there can be only 1 (i.e., the data element is not repeatable) (..1).
1..1|the data element "Measured, Estimated, Unknown Weight" is specified as Measured or Estimated, otherwise 0..0 - The data element minimum weight is mandatory but not repeatable if the data element "Measured, Estimated, Unknown Weight" is specified as Measured or Estimated or 0..0 if unknown is specified - no information is provided.
1..1|the data element "Minimum Age" is specified otherwise 0..0 - The data element age units is mandatory but not repeatable if minimum age is specified or 0..0 if unknown is specified in the data element "Measured, Estimated, Unknown Age" - no information is provided.

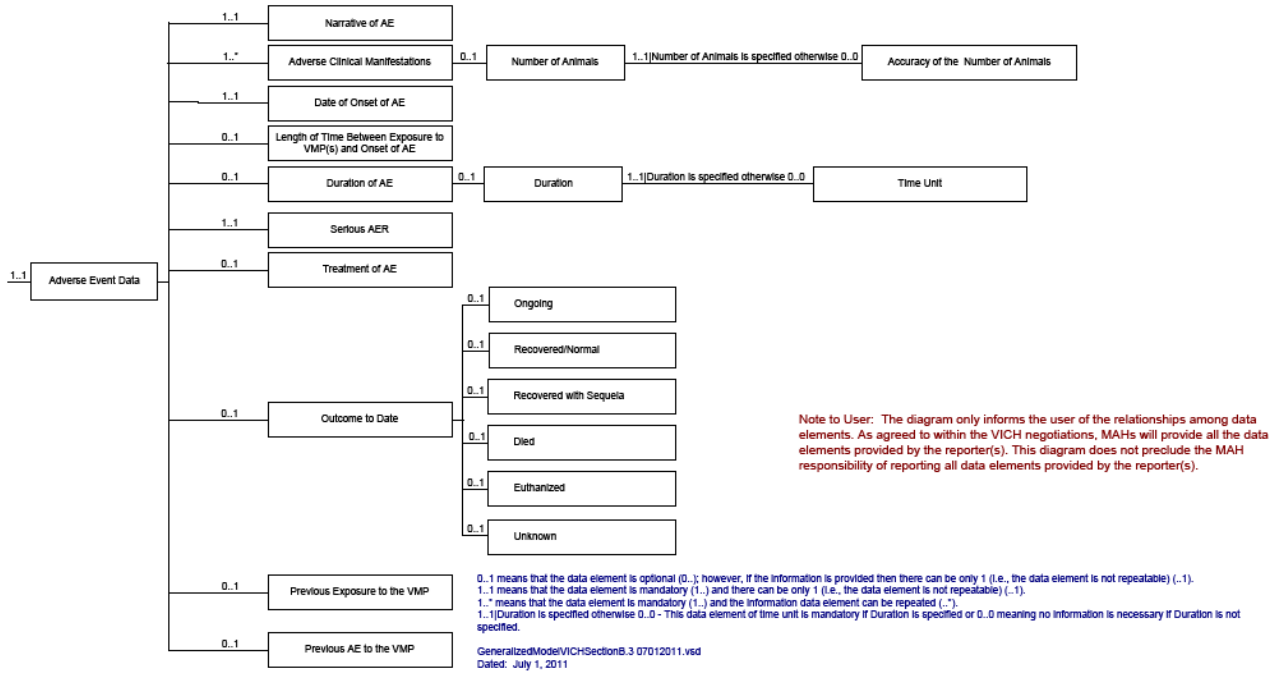
NOTE: For the data element "Breed" – 0..2 means that both purebreds and crossbreds can be expressed in the model. Purebred and Crossbreed data elements are indicators of purebred or crossbred. The data element "Breed" indicates the actual name of the breeds involved. Per the Pharmacovigilance Working Group, each region should propose cardinality limits for the data element "Breed" for harmonization by the Implementation Working Group. In cases where there is only a single crossbred animal, only 3 breeds will be allowed. In cases where there are multiple purebred or crossbred animals, the Pharmacovigilance Working Group will leave it up the Implementation Working Group to determine the number of breeds that can be given (1..*).

Filename: GeneralizedModelVICHSectionB.1 06072011.vsd
Date: June 7, 2011

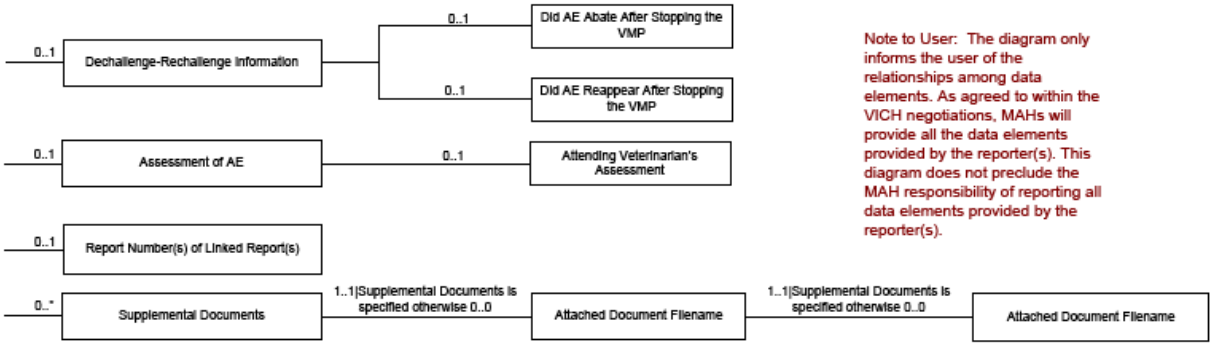
Draft Data Model for VMP(s) Data and Usage



Draft Data Model for Adverse Event Data



Draft Data Model for Dechallenge-Rechallenge Information, Assessment of AE, Report Number(s) of Linked Report(s), and Supplemental Documents



0..1 means that the data element is optional (0..); however, if the information is provided then there can be only 1 (i.e., the data element is not repeatable) (..1).
0..* means that the data element is optional (0..) and the information data element can be repeated (..*).
1..1 means that the data element is mandatory (1..) and there can be only 1 (i.e., the data element is not repeatable) (..1).

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Dated: June 7, 2011

Annex B. Field Length and Data Type by Data Elements

Section Title	Field Length (maximum length – characters)	Data Type
Regulatory Authority (RA)		
RA name	60	Open ended text
Street address	100	Open ended text
City	35	Open ended text
State/county	USA State – 15 County - 80	Single Choice Code List Open ended text
Mail/zip code	15	Open ended text
Country (3 character country codes ISO 3166)	15	single choice code list
MAH Information		
Business name	60	Open ended text
Street address	100	Open ended text
City	35	Open ended text
State/county	USA State – 15 County - 80	Single Choice Code List Open ended text
Mail/zip code	15	Open ended text
Country (3 character country codes ISO 3166)	15	single choice code list
Person Acting on Behalf of MAH		
Title	50	Open ended text
First name	35	Open ended text
Last name	50	Open ended text
Telephone	18	Formatted numeric for USA; open ended text for non-USA
Fax	18	Formatted numeric for USA; open ended text for non-USA
e-mail	100	Open ended text
Primary Reporter Information		
First name	35	Open ended text
Last name	50	Open ended text
Telephone	18	Formatted numeric for USA; open ended text for non-USA
Fax	18	Formatted numeric for USA; open ended text for non-USA
e-mail	100	Open ended text

Section Title	Field Length (maximum length – characters)	Data Type
Business name	60	Open ended text
Street address	100	Open ended text
City	35	Open ended text
State/county	USA State – 15 County - 80	Single Choice Code List Open ended text
Mail/zip code	15	Open ended text
Country (3 character country codes ISO 3166)	15	Single choice code list
Primary Reporter Category	15 (code) 80 (code description/term)	Single choice code list
Other Reporter Information		
First name	35	Open ended text
Last name	50	Open ended text
Telephone	18	Formatted numeric for USA; open ended text for non-USA
Fax	18	Formatted numeric for USA; open ended text for non-USA
e-mail	100	Open ended text
Business name	60	Open ended text
Street address	100	Open ended text
City	35	Open ended text
State/county	USA State – 15 County - 80	Single Choice Code List Open ended text
Mail/zip code	15	Open ended text
Country (3 character country codes ISO 3166)	15	Single choice code list
Other Reporter Category	15 (code) 80 (code description/term)	Single choice code list
Unique Adverse Event Identification Number	60	Open ended text
Original Receive Date	19	Date
Date of Current Submission	19	Date
Type of Submission & Code	15 (code) 80 (code description/term)	Single choice code list
Reason for Nullification Report	200	Open ended text
Type of Information in Report & Code	15 (code) 80 (code	Single choice code list

Section Title	Field Length (maximum length – characters)	Data Type
	description/term)	
Number of Animals Treated	12	Integer
Number of Animals Affected	12	Integer
Attending Veterinarian's Assessment of Health Status Prior to VMP & Code	15 (code) 80 (code description/term)	Single choice code list
Species (Type of Species) & Code	15 (code) 80 (code description/term)	Single choice code list
Breed & Code	15 (code) 80 (code description/term)	Multiple choice code list
Gender & Code	15 (code) 80 (code description/term)	Single choice code list
Reproductive Status & Code	15 (code) 80 (code description/term)	Single choice code list
Female Physiological Status & Code	15 (code) 80 (code description/term)	Single choice code list
Weight Measured, Estimated or Unknown & Code	15 (code) 80 (code description/term)	Single choice code list
Minimum Weight	12	Numeric (nnnnnnnnn.nn)
Minimum Weight Unit	kg	
Maximum Weight	12	Numeric (nnnnnnnnn.nn)
Maximum Weight Unit	kg	
Age Measured, Estimated or Unknown & Code	15 (code) 80 (code description/term)	Single choice code list
Minimum Age	12	Numeric (nnnnnnnnn.nn)
Minimum Age Units (code)	15	Single choice code list
Maximum Age	12	Numeric (nnnnnnnnn.nn)
Maximum Age Units (code)	15	Single choice code list
Registered Name or Brand Name	200	Open ended text
Product Code (Product NDC Number or Unique ID)	20	Open ended text
Registration Identifier	35	Open ended text

Section Title	Field Length (maximum length – characters)	Data Type
Anatomical Therapeutic Chemical Vet (ATCvet) Code	10	Open ended text
Company or MAH	60	Open ended text
MAH Assessment	250	Open ended text
RA Assessment	Not Applicable	Not Applicable
Explanation Relating to Assessment	Not Applicable	Not Applicable
Route of Exposure (Route of Administration)	15 (code) 80 (code description/term)	Single choice code list
Dose Per Administration		
Numeric Value for Dose	12	Numeric (nnnnnnn.nnnn)
Units of Value for Dose	15 (code) 80 (code description/term)	single choice code list
Interval of Administration		
Numeric Value for Interval of Administration	12	Integer
Units of Value for the Interval of Administration	15 (code) 80 (code description/term)	Single choice code list
Date of First Exposure	19	Date
Date of Last Exposure	19	Date
Active Ingredient(s)		
Active Ingredient(s)	200	Open ended text
Numeric Value for Strength (Numerator)	12	Numeric (nnnnnnn.nnnn)
Units for Numeric Value for Strength (Numerator)	15 (code) 80 (code description/term)	Single choice code list
Numeric Value for Strength (Denominator)	12	Numeric (nnnnnnn.nnnn)
Units for Numeric Value for Strength (Denominator)	15 (code) 80 (code description/term)	Single choice code list
Active Ingredient Code	15	Single choice code list
Dosage Form & Code	15 (code) 80 (code description/term)	Single choice code list
Lot Number(s)	35	Open ended text
Expiration Date	19	Date
Who Administered the VMP & Code	15 (code) 80 (code description/term)	Single choice code list

Section Title	Field Length (maximum length – characters)	Data Type
Use According to Label	5	Boolean
Explanation for Off-Label Use & Code	12	Integer
Narrative of AE	20,000	Open ended text
Adverse Clinical Manifestations (AER Term Name(s) & Code(s))	15 (code) 250 (code description/term)	Multiple choice code list
Number of Animal	12	Integer
Accuracy of the Number of Animals	15 (code) 80 (code description/term)	Single choice code list
Date of Onset of AE (AE Start Date)	19	Date
Length of Time between Exposure to VMP & Onset of AE	15 (code) 80 (code description/term)	Single choice code list
Duration of AE		
Duration (Time)	12	Numeric (nnnnnnn.nnnn)
Duration Time Units	15 (code) 80 (code description/term)	Single choice code list
Serious AER Reported	5	Boolean
Treatment of AE	5	Boolean
Outcome to Date	12	Integer
Previous Exposure to the VMP	5	Boolean
Previous AE to VMP	5	Boolean
Did AE Abate After Stopping the VMP?	5	Boolean
Did AE Reappear After Re-introduction of the VMP?	5	Boolean
Attending Veterinarian's Assessment of AE	15 (code) 80 (code description/term)	Single choice code list
Attached Document Filename	256	Open ended text
Attached Document Type	15 (code) 80 (code description/term)	Single choice code list