

**United States Department of Agriculture
Center for Veterinary Biologics**

Standard Operating Procedure

Guidelines for the Evaluation of Adverse Event Reports

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Guidelines for the Evaluation of Adverse Event Reports

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Guidelines for the Evaluation of Adverse Event Reports

1. Purpose and Scope

The purpose of this Standard Operating Procedure (SOP) is to explain the process of evaluating adverse event reports received by the Center for Veterinary Biologics and actions that may follow.

2. Evaluation of Adverse Event Reports (AERs)

AERs are initially evaluated by the Biologics Epidemiologist(s) for unusual or serious events as well as frequency, breed, or geographic trends related to a product or serial. Additional information related to a specific AER may be obtained and added to the record. The information may come as information requested from the firm, emails, telephone conversations, etc. The AER may be classified as a “case report” and include an Evaluation of Product form (**Appendix**). If so, additional material may be filed separately with an Evaluation of Product (EP) record number.

If additional AERs are implicated in an adverse event or if additional tests are requested for a single AER, a veterinary biologics investigation (VBI) may be initiated. A Special Test Request Testing will contain the VBI number in the message and a copy of the request is to be provided to the BCAs. Information related the AER(s) will be compiled in the VBI. AERs and VBIs will be cross-referenced in their respective files.

3. Triggers

Evaluations and investigations into reported adverse reactions to veterinary biological products in order to identify potential problems are needed before a decision can be made on whether or not regulatory action is appropriate.

While this guideline addresses the most likely situations where investigation is necessary, it cannot cover all possibilities. Thus, on occasion evaluations and investigations may be initiated or regulatory action may be taken based on pharmacovigilance information even if none of the criteria described below are applicable.

3.1 Reported adverse events occur at incidences higher than expected

For many reasons baseline adverse event reporting rates are difficult to establish. Although it may be possible to use doses produced or doses distributed as denominators in such calculations, this should be done with caution as these numbers do not reflect the true population at risk. Another possible approach is a disproportionality analysis that utilizes observed to expected ratios. In this approach, the reporting experience of each reported biological product-event combination is compared to the background reporting experience across biological products and events.

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Determination of appropriate comparison groups and significant trend departures will require a comprehensive adverse event reporting system to gather standardized data and periodic re-evaluation of underlying assumptions as reporting practices are not expected to remain static.

3.2 Serious, unexpected adverse events reported from one or more sources

A single, serious, unexpected adverse event report assessed as possible or probable may warrant further evaluation based on the nature of the event, species, and number of animals involved. Occurrence of serious, unexpected reactions from multiple sources during a given period (e.g. 3 months) should trigger further evaluation regardless of assessment. The unexpected adverse reactions need not appear to be directly attributable to the use of the product to initiate the investigation.

3.3 Crisis events

A crisis is defined as an event which occurs when information which could have a serious impact on animal and/or public health is received. Crises may be subdivided into those where the information has not become public and those where it has. In the latter case, the handling of communications becomes crucial. Crisis events require immediate evaluation and investigation.

4. Actions

Step 1: Decide and document that one of the triggers has been met and that there is a need for further investigation of the issue. Establishing causality, if not yet executed, is one of the first objectives. Progress to Step 2.

Step 2: Initiate evaluation or investigation of the adverse event(s) to clarify potential problems. The firm should be contacted, alerted to the concerns of the CVB and requested to comment. Where appropriate, the CVB may (for example, but not limited to):

- request copies or summaries of the investigations carried out by the firm in order to clarify the issue,
- request that testing be performed by the firm or the CVB laboratory,
- refer the matter to the CVB Pharmacovigilance Monitoring Committee

Depending on the outcome of the evaluation and investigation and on the nature of the issue, the investigation can:

- a) stop here with the documented conclusion that no further action is necessary to safeguard animal or public health.

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- b) continue to Step 3, where the CVB may take an appropriate regulatory action on the basis of the documented conclusion of the investigation.

Step 3: Take appropriate regulatory action in order to resolve the issue under investigation.

The action taken by the CVB should be appropriate in relation to the severity of the issue under investigation.

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Appendix

Evaluation of Product

EP#

Evaluation Date	Firm #	Product Code	True Name	Trade Name	Serial #
Location			AIV	VBI	

Adverse Event Description:

History of Additional Consumer Reports logged into adverse events report database:

Total

AIV(s)	Product Use Date	Location (State)	Serial #	Type Event

Doses Reported from APHIS 2008s:

Serials	Date released	CVB Tests	Expiration Date	# Doses
Total serials / total doses				

Outline of Production:

Current Date	Agent	Safety	Purity	Potency	Other

Label:

Other Information:

Conclusion:

Recommendation:

Distribution:

CVB-PEL	CVB-IC	Initiated by	Epidemiologist